Caractérisation quantitative et qualitative des apports alimentaires en contexte prénatal

Thèse

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Résumé

L'alimentation en contexte prénatal peut, en induisant des variations dans l'environnement *in utero*, influencer le développement et la santé de l'enfant à naître. Des apports nutritionnels inadéquats et une qualité alimentaire sous-optimale peuvent également constituer un risque pour la santé de la femme enceinte. Cette dernière doit faire face à de nombreux changements et adaptations physiques, hormonaux et psychologiques qui bouleversent sa vie et influencent ses choix alimentaires. Ces changements, et la façon dont les femmes y réagissent, peuvent compliquer l'étude des associations entre l'alimentation et les variables de la santé maternelle. D'ailleurs, la caractérisation des habitudes alimentaires des femmes enceintes est souvent effectuée de façon incomplète, c'est-à-dire que seuls les apports en nutriments ou aliments spécifiques sont mesurés, sans tenir compte des facteurs qui les influencent. La présente thèse examine donc de façon prospective les apports et la qualité alimentaires d'un échantillon de femmes enceintes québécoises, en comparaison avec les recommandations et en association avec des variables sociodémographiques, physiologiques et comportementales. Les résultats générés par cette thèse suggèrent que les habitudes alimentaires des femmes enceintes québécoises ne sont pas optimales, tant au niveau nutritionnel que sur le plan de la qualité alimentaire globale. De nombreuses variables physiologiques, sociodémographiques et comportementales semblent également influencer l'alimentation durant la grossesse. Celles-ci devraient être pris en considération dans le développement d'interventions nutritionnelles et l'élaboration de messages de promotion des saines habitudes alimentaires auprès des femmes enceintes.

Abstract

Prenatal nutrition can, by inducing variations in the *in utero* environment, influence the health and development of the unborn child. Inadequate nutritional intakes and suboptimal dietary quality can also pose a risk to the pregnant woman's health. The latter must cope with numerous physical, hormonal and psychological changes and adaptations that can turn her life upside down as well as influence her food choices. These changes, and the way women respond to them, can complexify the study of the associations between diet and maternal health outcomes. Moreover, the characterization of pregnant women's eating habits is often done incompletely, i.e. only intakes of specific nutrients or foods are measured, without taking into account the influencing factors. This thesis therefore examines dietary intakes and quality in a sample of pregnant women from Québec, in comparison with the recommendations and in association with sociodemographic, physiological and behavioral variables. The results generated by this thesis suggest that the eating habits of pregnant women from Québec are not optimal, both nutritionally and in terms of overall diet quality. Many physiological, socio-demographic and behavioral variables also seem to influence diet during pregnancy. These variables should be taken into consideration in the planning of nutritional interventions and the development of messages aimed to promote healthy eating habits among pregnant women.

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Liste des abréviations

25(OH)D: 25-hydroxyvitamin D
25(OH)D2: 25-hydroxyergocalciferol
25(OH)D3: 25-hydroxycholecalciferol
3-epi-25(OH)D3: 3-epi-25-hydroxyvitamin D3
AHEI: Alternate healthy eating index
AI: Adequate intake
AMDR: Acceptable macronutrient distribution range
AMPM: Automated multiple pass method
ANGE: Apports nutritionnels durant la grossesse
ANGE-Ctrl: Apports nutritionnels durant la grossesse – Cohorte contrôle
ANOVA: Analyses of variance
ANR: Apport nutritionnel recommandé
ANREF: Apports nutritionnels de référence
AS: Apport suffisant
BÉE: Besoin énergétique estimé
BME: Besoin moyen estimatif
BMI: Body mass index
BMR: Basal metabolic rate
CA : Coefficient d'activité
CFG: Canada's Food Guide
C-HEI: Canadian healthy eating index
CHU: Centre hospitalier universitaire
CRP: Protéine C-Réactive
DÉR: Dépense énergétique au repos
DÉT: Dépense énergétique totale
DFE: Dietary folate equivalent
DII: Dietary inflammatory index
DII-S: Dietary inflammatory index calculated with the inclusion of intakes from supplements
DIN: Drug identification number
DRI: Dietary reference intake
E% or %E: proportion of energy intake
EAR: Estimated average requirement
EE: Energy expenditure
EER: Estimated energy requirement
EI: Energy intake
EPR: Estimated protein requirement
ÉVAM: Étendue des valeurs acceptables pour les macronutriments
EXS: Excessive gestational weight gain
FFQ: Food frequency questionnaire
GWG: Gestational weight gain
HEI: Healthy eating index
HSD: Honestly significant difference
IES-2: Intuitive eating scale-2
IL-6: Interleukine-6

INA: Inadequate gestational weight gain
INAF: Institut sur la nutrition et les aliments fonctionnels
IOM: Institute of Medicine
IPAQ: International physical activity questionnaire
IU: International unit
kcal: kilocalories
LC-MS/MS: Liquid chromatography tandem mass spectroscopy
MANOVA: Repeated measures analyses of variance
MDS: Mediterranean diet score
MUFA: Monounsaturated fatty acids
NE: Niacin equivalent
NHPN: Natural health product number
NS: Not significant
NUTRISS: Nutrition, santé et société
NW: Normal weight
OW: Overweight
PAGG: Prise alimentaire, apports nutritionnels et gain de poids durant la grossesse
PAL: Physical activity level
PICOS: Population, intervention or exposure, comparison, outcome and study design
PPAQ: Pregnancy physical activity questionnaire
ppBMI: Prepregnancy body mass index
Pre: Preconception
PREDISE: Prédicteurs individuels, sociaux et environnementaux
PRISMA: Preferred reporting items for systematic reviews and meta-analyses
PUFA: Polyunsaturated fatty acids
PWGAS: Pregnancy weight gain attitude scale
R24W: Rappel de 24 heures Web
RAE: Retinol activity equivalent
RDA: Recommended dietary allowance
REC: Recommended gestational weight gain
REE: Resting energy expenditure
rEI: Reported energy intake
SD: Standard deviation
SFA: Saturated fatty acids
TEE: Total energy expenditure
TFEQ: Three-factor eating questionnaire
UL: Upper intake limit
USDA: United States Department of Agriculture
UVB: Ultraviolet β
UW: Underweight
VDSCP: Vitamin D standardization certification program

À ma grand-maman Hénédine, qui m'a toujours inspirée par sa douceur, sa résilience et son ouverture d'esprit.

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Avant-propos

Cette thèse présente l'ensemble des travaux de recherche réalisés lors de mes études doctorales, sous la supervision de ma directrice, Dre Anne-Sophie Morisset, et de ma co-directrice, Dre Simone Lemieux. La thèse est divisée en différentes sections, soit une introduction générale, une synthèse des connaissances en nutrition prénatale (chapitre 1), les objectifs de mon doctorat et les hypothèses qui y sont associées (chapitre 2), une description des cohortes sur lesquelles se basent mes travaux (chapitre 3), une revue systématique de la littérature (chapitre 4), six articles originaux publiés (chapitres 5 à 10), ainsi qu'une conclusion générale.

Il convient de souligner que les différents articles rédigés dans le cadre de mon doctorat font partie de la programmation de recherche de ma directrice, Dre Anne-Sophie Morisset. Les données de trois études ont été utilisées, soit le projet ANGE (Apports nutritionnels durant la grossesse), le projet ANGE-Contrôle (Apports nutritionnels durant la grossesse – Cohorte contrôle) et le projet PREDISE (Prédicteurs individuels, sociaux et environnementaux). Le projet ANGE a débuté lors de ma maîtrise et j'ai été dès lors impliquée dans l'élaboration des objectifs, la rédaction du protocole, le recrutement des 86 participantes, la gestion des visites, la saisie et l'analyse des données. J'ai ensuite été impliquée dans l'élaboration, le recrutement et la gestion du projet ANGE-Contrôle, qui a également débuté durant ma maîtrise et qui inclut à ce jour près de 300 femmes en préconception. Pour la gestion de ces deux projets, je tiens à souligner le travail important d'Anne-Sophie Plante et de Sarah Chouinard Castonguay, professionnelles de recherche. Des données du projet PREDISE ont également été utilisées dans le cadre de la rédaction d'un article original (chapitre 8). Ce projet fait partie de la programmation de recherche de ma co-directrice, Dre Simone Lemieux, et était coordonné par Louise Corneau, professionnelle de recherche, et Élise Carbonneau, auparavant étudiante au doctorat sous la supervision de Dre Lemieux. Finalement, il convient de mentionner que la presque totalité des articles rédigés dans le cadre de mon doctorat (chapitres 5 à 8 et 10) ont utilisé des données alimentaires recueillies via la plateforme R24W, qui inclut un rappel de 24h Web auto-administré développé à l'INAF par Dre Simone Lemieux, Dre Julie Robitaille, Dr Benoît Lamarche, Louise Corneau, Catherine Laramée et Simon Jacques. Les différentes cohortes ainsi que les données recueillies auprès des participantes seront décrites brièvement au chapitre 3.

Le **chapitre 4** de cette thèse est une revue systématique de la littérature intitulée : « **Energy expenditure during pregnancy: a systematic review »** et publiée dans le journal *Nutrition Reviews*. L'objectif de la revue était de répertorier et d'analyser les études longitudinales ayant mesuré la dépense énergétique totale et au repos durant la grossesse. Pour cette revue, j'ai effectué le tri des titres et des résumés ainsi que la revue des articles complets. J'ai ensuite effectué la collecte et l'analyse de données ainsi que l'évaluation de la qualité des études incluses dans la revue. Finalement, j'ai réalisé les différents tableaux et figures résumés puis j'ai rédigé l'article. Je remercie Audrée Lebrun, auparavant étudiante à la maîtrise sous la supervision de Dre Anne-Sophie Morisset, qui a effectué en double le tri des titres et résumés ainsi que la revue des articles complets. Je tiens aussi à remercier Dr François Haman, Dre Bénédicte Fontaine-Bisson ainsi que Sarah O'Connor, étudiante au doctorat sous la supervision du Dr Paul Poirier, qui m'ont appuyée dans la réalisation de cette revue. Je veux également souligner l'aide précieuse de Carole Brault, bibliothécaire scientifique retraitée du Centre de recherche du CHU de Québec -Université Laval. Finalement, je remercie Dre Anne-Sophie Morisset pour sa supervision lors de la réalisation et de la rédaction de la revue.

Le **chapitre 5** présente l'article original « **Trimester-specific dietary intakes in a sample of French-Canadian pregnant women in comparison with national nutritional guidelines** », publié dans le journal *Nutrients*. Cet article présente les premiers résultats découlant de mon projet de doctorat et provenant de la cohorte ANGE. L'objectif de cet article était de mesurer les changements dans les apports énergétiques et nutritionnels au cours des trimestres de grossesse, puis de comparer ces apports aux recommandations nutritionnelles nationales. La plateforme R24W a été utilisée pour recueillir les données alimentaires des participantes. Après avoir effectué la cueillette et la saisie de données étalée sur les trois trimestres de grossesse (environ 27 semaines) avec l'aide d'Anne-Sophie Plante, j'ai réalisé les analyses statistiques et rédigé la première version du manuscrit. Je tiens à remercier les co-auteurs de cet article, Dre Simone Lemieux, Dr S. John Weisnagel, Dre Bénédicte Fontaine-Bisson, Dre Claudia Gagnon et Dre Julie Robitaille, qui m'ont guidée lors de l'analyse de mes résultats et qui ont révisé le manuscrit en profondeur. Je remercie finalement Dre Anne-Sophie Morisset pour sa supervision lors du processus de rédaction de cet article.

Le **chapitre 6** présente des résultats portant sur le statut en vitamine D des femmes de la cohorte ANGE sous la forme d'un article original ayant comme titre « **Longitudinal assessment of vitamin D status across trimesters of pregnancy** », publié dans *The Journal of Nutrition*. Cet article visait à

évaluer les concentrations de vitamine D au cours des trimestres et selon le statut pondéral des femmes enceintes, puis à analyser les associations entre les concentrations de vitamine D, le statut pondéral et les apports en vitamine D. Je tiens à remercier les infirmières de recherche de l'équipe du Dr S. John Weisnagel, Valérie-Ève Julien, Elise Cant et Louise Rhéaume ainsi que Marie-Savane Goyette pour les prélèvements sanguins effectués chez les participantes du projet ANGE. Le dosage de la vitamine D dans les échantillons sanguins a été effectué au laboratoire de Santé Canada par l'équipe de Dre Hope A. Weiler, plus précisément par Agnieszka Bielecki, technicienne de laboratoire. J'ai réalisé les analyses statistiques de l'article avec l'aide de Dre Claudia Gagnon, Dre Hope A. Weiler et Dre Anne-Sophie Morisset et j'ai rédigé la première version du manuscrit. Je tiens à remercier les deux autres co-auteures de cet article, Anne-Sophie Plante, professionnelle de recherche, et ma codirectrice, Dre Simone Lemieux.

Le **chapitre 7** présente l'article «**Trimester-specific assessment of diet quality in a sample of Canadian pregnant women** », publié dans l'*International Journal of Environmental Research and Public Health*. En utilisant encore une fois les données du projet ANGE, cet article visait à évaluer prospectivement la qualité alimentaire durant la grossesse et à identifier les facteurs qui y sont associés. Je tiens à remercier Élise Carbonneau, qui m'a appuyée dans l'analyse des données relatives aux connaissances en nutrition des participantes. Pour cet article, j'ai effectué les analyses statistiques et rédigé la première version du manuscrit. Les autres co-auteures, Dre Simone Lemieux, Dre Véronique Provencher, Dre Claudia Gagnon, Dre Julie Robitaille et Dre Anne-Sophie Morisset ont toutes lu et révisé l'article.

Le **chapitre 8** présente une étude comparative intitulée « **Do pregnant women eat healthier than nonpregnant women of childbearing age**? » publiée dans l'*International Journal of Food Sciences and Nutrition*. Cet article visait à comparer l'alimentation au premier trimestre des femmes de la cohorte ANGE à celle de femmes en âge de procréer. Les femmes de la cohorte ANGE ont été appariées pour l'âge et l'IMC, en premier lieu, à des participantes de la cohorte ANGE-contrôle, une cohorte de femmes planifiant une grossesse dans la prochaine année et qui ont complété plusieurs questionnaires Web, dont trois rappels de 24h Web. Je remercie Anne-Sophie Plante, professionnelle de recherche et Marianne Gagnon, étudiante à la maîtrise, qui m'ont grandement aidée dans la collecte et l'analyse de données de la cohorte ANGE-contrôle. En deuxième lieu, les femmes de la cohorte ANGE ont été appariées à des participantes du projet PREDISE. Pour les besoins de l'article, seulement les femmes

en âge de procréer et de la région de Québec du projet PREDISE ont été incluses. Ainsi, j'ai pu réaliser les analyses statistiques et comparer la qualité alimentaire, les apports énergétiques et les apports nutritionnels entre trois groupes de femmes, soit 55 femmes de la cohorte ANGE, 55 femmes de la cohorte ANGE-contrôle et 55 femmes de la cohorte PREDISE. J'ai ensuite rédigé la première version du manuscrit sous la supervision de Dre Morisset. Je remercie également les co-auteurs de l'article, Anne-Sophie Plante, Dre Simone Lemieux, Élise Carbonneau, Dre Claudia Gagnon, Dre Julie Robitaille et Dr Benoît Lamarche, qui ont participé à la présentation des résultats et à la révision du manuscrit.

Le **chapitre 9** présente l'article « **Positive attitudes toward weight gain in late pregnancy are associated with healthy eating behaviours** ». Cet article publié dans le journal *Eating and Weight Disorders – Studies on Anorexia, Bulimia and Obesity* avait comme objectif d'évaluer les attitudes des femmes enceintes envers le gain de poids gestationnel, et d'examiner les associations entre ces attitudes et leurs comportements alimentaires. Les données relatives aux attitudes envers le gain de poids et aux comportements alimentaires ont été recueillies via des questionnaires Web complétés par les participantes du projet ANGE. Ces données ont été analysées par Emmanuelle Yan, stagiaire dans l'équipe de Dre Morisset, et Anne-Sophie Plante, professionnelle de recherche. Ces analyses m'ont permis de rédiger le manuscrit, qui a ensuite été révisé par les différentes co-auteures, Dre Catherine Bégin, Dre Julie Robitaille, Dre Andréanne Michaud, Dre Simone Lemieux et Dre Véronique Provencher. Je remercie ma directrice, Dre Anne-Sophie Morisset, pour sa supervision lors du processus de rédaction du manuscrit.

Un sixième article original est présenté au **chapitre 10** de cette thèse et s'intitule « **Longitudinal changes in circulating concentrations of inflammatory markers throughout pregnancy: are there associations with diet and weight status?** ». Cet article a été publié dans le journal *Applied Physiology, Nutrition and Metabolism*. L'objectif de l'article était de mesurer prospectivement les concentrations sériques de certains marqueurs inflammatoires durant la grossesse et d'examiner leur association avec la qualité alimentaire. Cet article a également utilisé les données de la cohorte prospective ANGE. Je remercie à nouveau les infirmières Valérie-Ève Julien, Elise Cant, Louise Rhéaume et Marie-Savane Goyette pour les prélèvements sanguins effectués chez les participantes du projet ANGE. Je tiens aussi à remercier Marie-Frédérique Gauthier, professionnelle de recherche, pour l'analyse des concentrations d'IL-6 et d'adiponectine, réalisée à l'Institut universitaire de

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Durant mes quatre années au doctorat, j'étais responsable de l'élaboration et de la gestion du projet pilote PAGG (Prise alimentaire, apports nutritionnels et gain de poids durant la grossesse). Ce projet a débuté lors de ma première année de doctorat et a recruté 33 femmes enceintes dans le but de caractériser les sensations d'appétit et l'évolution des hormones liées à la prise alimentaire au cours de la grossesse. Cette thèse ne comprend aucun article original découlant des données du projet PAGG puisque des délais de livraison occasionnés par la pandémie de COVID-19 ont retardé le dosage des hormones d'intérêt. Néanmoins, je tenais à mentionner mon implication dans ce projet (élaboration des objectifs, rédaction du protocole, recrutement des participantes, gestion des visites, cueillette de données et analyses préliminaires) puisque j'y ai consacré plus de trois ans. Je remercie Dre Anne-Sophie Morisset ainsi qu'Anne-Sophie Plante pour leur appui tout au long des étapes de réalisation du projet.

Enfin, mon doctorat m'aura permis de collaborer à différents projets imprévus, mais très formateurs. En effet, j'ai pu participer à la révision d'une section du guide « *Mieux-vivre avec notre enfant de la grossesse à deux ans* », qui s'adresse à tous les futurs parents de la province de Québec. J'ai également pu me familiariser avec le milieu de la santé publique en effectuant, grâce à une bourse des Fonds de Recherche du Québec en santé, un stage au sein de la Fondation Olo. Je remercie mes superviseures de stages, Julie Strecko et Julie Deschamps, toutes deux nutritionnistes à la Fondation Olo, de m'avoir intégrée dans leur équipe et d'avoir contribué à mon développement professionnel. Finalement, j'ai aussi rédigé, sous la supervision de Dre Anne-Sophie Morisset, un chapitre de livre portant sur la malnutrition périnatale faisant partie d'un ouvrage sur la période de la périnatalité et de son impact sur la santé des nouveau-nés et des enfants. Le livre a comme titre provisoire : « *Prévention en période périnatale, principaux facteurs de risque et interventions reconnues* » et est présentement en processus de révision.

Introduction

La période de la grossesse est déterminante pour la santé de la mère et celle de l'enfant à naître. Il a en fait été établi que des variations dans l'environnement *in utero* pouvaient avoir un impact sur la programmation métabolique du fœtus et pourraient limiter sa croissance, prédisposant ainsi l'enfant à différentes maladies chroniques [1-3]. La grossesse représente également une étape cruciale dans la vie de la mère, notamment en raison des nombreux changements métaboliques et anatomiques auxquels elle devra faire face [4]. La grossesse en soi est d'ailleurs de plus en plus considérée comme un facteur de risque pour la santé à long terme de la femme [5]. À cet effet, certains facteurs modifiables ont été identifiés pour assurer la santé optimale de la femme enceinte, dont son alimentation. Bien qu'autrefois, l'épidémiologie nutritionnelle en période prénatale s'intéressait principalement aux déséquilibres nutritionnels [2, 6, 7], la littérature actuelle se penche davantage sur la qualité globale de l'alimentation [8, 9]. En fait, la combinaison de l'évaluation des apports et du statut nutritionnels à celle de la qualité de l'alimentation permettrait de détecter des excès et des carences nutritionnels en plus d'identifier des habitudes alimentaires associées à la santé de la mère [8]. Cependant, très peu d'études ont évalué et caractérisé l'alimentation des femmes enceintes à chaque trimestre de la grossesse. Il s'agit d'une lacune importante dans la littérature, puisque l'alimentation peut avoir des implications différentes selon le trimestre durant lequel les apports alimentaires sont évalués [10, 11]. Une caractérisation prospective de l'alimentation durant la grossesse combinée à l'évaluation des variables qui y sont associées pourrait ainsi générer des données essentielles à l'élaboration d'interventions nutritionnelles personnalisées.

Le premier chapitre de cette thèse constitue une revue de la littérature en lien avec l'importance des apports nutritionnels et de la qualité alimentaire durant les différentes périodes de la grossesse. Les associations entre l'alimentation et certaines variables physiologiques, sociodémographiques et comportementales seront également abordées. Ensuite, les chapitres 2 et 3 présentent les objectifs et hypothèses, ainsi qu'une brève description des cohortes sur lesquelles se basent les travaux de la présente thèse. Finalement, la revue systématique de la littérature et les articles originaux sont présentés aux chapitres 4 à 10, puis une conclusion générale discutera des principaux résultats.

Chapitre 1 – État des connaissances en lien avec la nutrition prénatale

1. Chronologie et physiologie de la grossesse

La grossesse est souvent considérée comme un évènement unique, alors qu'il s'agit plutôt d'un ensemble d'évènements qui s'étirent sur 40 semaines et qui peuvent être catégorisés en deux périodes, soit les périodes embryonnaire et fœtale (Figure 1). Ces périodes sont toutes les deux importantes pour le développement de l'enfant à naitre, mais elles diffèrent, entre autres, quant à leur impact sur le métabolisme de la femme enceinte. En outre, certaines études suggèrent que la période précédant la fécondation pourrait aussi influencer le déroulement de la grossesse et le développement prénatal. Les sections qui suivent détailleront les différentes étapes de la période prénatale.

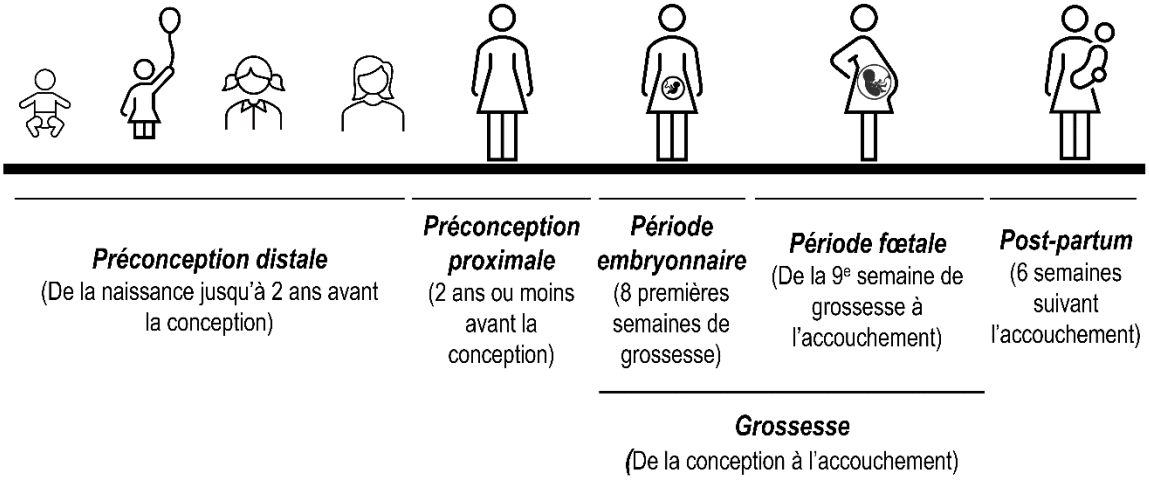

Figure 1. Chronologie et définition des périodes pré- et postnatales

1.1. Préconception

Un intérêt grandissant s'est développé dans les dernières années quant à l'impact de la période de préconception sur les variables de santé maternelle et néonatale [12-14]. La période de préconception peut être catégorisée comme proximale, soit deux ans ou moins avant la conception, ce qui inclut également l'intervalle de temps entre deux grossesses consécutives, ou distale, soit plus de deux ans avant la conception [15]. La présente thèse discutera seulement de la préconception proximale.

D'abord, le statut pondéral de la femme en préconception est une variable déterminante pour plusieurs variables de la santé néonatale et maternelle. Selon une méta-analyse de 60 études, les nouveau-nés de mères présentant un surpoids ou une obésité prégrossesse ont un risque significativement plus élevé de macrosomie (poids à la naissance >4 kg), d'admission aux unités de soins intensifs néonataux et de mortinatalité (mort à la naissance) et ce, par rapport aux nouveau-nés de mères ayant un indice de masse corporelle (IMC) normal avant la grossesse [16]. À l'inverse, les nouveau-nés de mères présentant un poids prégrossesse insuffisant sont plus à risque de naître prématurément, d'être petits pour l'âge gestationnel et de présenter un faible poids à la naissance [16]. Chez la mère, une obésité prégrossesse est associée à un risque plus élevé de diabète gestationnel, de prééclampsie, d'hypertension gestationnelle et d'accouchement par césarienne [17, 18]. De plus, selon une méta-analyse récente, les femmes avec une obésité prégrossesse présenteraient un risque 33% plus élevé de développer des symptômes dépressifs au cours de la grossesse, comparativement aux femmes de poids normal [19]. Ainsi, en raison des risques mentionnés ci-haut, certains experts recommandent aux femmes qui prévoient concevoir et qui présentent un poids insuffisant, un surpoids ou une obésité de modifier leurs habitudes de vie, afin d'atteindre un IMC de catégorie normale avant de devenir enceinte [16, 20-22].

À ce sujet, l'alimentation et le statut nutritionnel en préconception pourraient influencer les variables de santé maternelle, d'une part, en ayant un impact sur le statut pondéral prégrossesse et, d'autre part, via un statut nutritionnel inadéquat (ex. carences nutritionnelles) [12]. En fait, puisque plusieurs femmes ne savent pas qu'elles sont enceintes avant un certain nombre de semaines suivant la conception, le statut nutritionnel en début de grossesse peut refléter celui en préconception [23]. L'alimentation avant la conception a donc le potentiel d'influencer certaines étapes critiques du développement embryonnaire, comme l'implantation de l'embryon dans la paroi de l'utérus, la différenciation cellulaire et le développement placentaire, qui seront discutés plus loin [15, 24].

De plus, au-delà des apports en nutriments spécifiques, l'adhésion, en préconception, à certains modèles alimentaires (*dietary patterns*) riches en aliments d'origine végétale ainsi que la pratique d'activité physique ont été associées à un risque moindre de diabète et d'hypertension gestationnels [25-28]. D'autres comportements comme l'usage de tabac et la consommation d'alcool représentent quant à eux des facteurs de risque dont on recommande la cessation avant la grossesse [12, 29].

En somme, la période de préconception proximale semble avoir le potentiel d'influencer plusieurs variables de la santé au courant de la grossesse. Néanmoins, les 40 semaines de grossesse sont caractérisées par de nombreux changements anatomiques, hormonaux et métaboliques qui risquent à leur tour d'influencer les variables de la santé. Ces changements seront décrits plus en détail dans les prochaines sections.

1.2. Période embryonnaire

Avant d'être un embryon, l'ovule fécondé, ou le zygote, doit se segmenter en plusieurs cellules pour former la morula, puis le blastocyte. Ce dernier devra se fixer à la paroi de l'utérus (implantation) et se segmenter à nouveau en deux structures : l'embryoblaste, qui deviendra l'embryon, et le trophoblaste, qui deviendra la portion fœtale du placenta. Ces étapes se déroulent durant la première semaine de grossesse et sont cruciales au développement embryonnaire. En fait, les tissus qui sont à l'origine des structures des organes commencent à se développer dès les quatre premières semaines de grossesse [30]. Ces tissus embryonnaires vont croître de façon plus importante au cours de la période fœtale, dont il sera question plus loin, mais la structure et la fonctionnalité des organes sont davantage déterminées lors du développement embryonnaire [30]. C'est pourquoi il a été suggéré que des déséquilibres nutritionnels au cours de cette période pouvaient entraîner des malformations ou des anomalies congénitales [24, 31]. Les besoins en micronutriments durant la grossesse ainsi que l'impact potentiel d'apports nutritionnels inadéquats seront discutés à la section 2.2 du présent chapitre.

Les étapes de développement embryonnaire sont modulées, entre autres, par de nombreuses adaptations hormonales [30]. Une de ces adaptations est l'augmentation marquée et rapide de l'hormone gonadotrophine chorionique (hCG) durant le premier trimestre de grossesse, qui stimule la sécrétion de progestérone et d'œstrogènes, des hormones nécessaires à l'établissement et au maintien de la grossesse [32]. Contrairement aux concentrations sanguines d'hCG, qui diminuent rapidement après la 10^{e} semaine de grossesse, les concentrations d'œstrogènes et de progestérone augmentent jusqu'à l'accouchement [32]. Il a été suggéré que certains de ces changements hormonaux seraient associés à des inconforts gastro-intestinaux chez la femme enceinte, comme des nausées et des vomissements [32, 33]. Ces inconforts sont plus prévalent en début de grossesse [33], ce qui concorde avec l'augmentation rapide des concentrations d'hCG au cours des 10 premières semaines de grossesse. Les associations entre la présence d'inconforts gastro-intestinaux et les apports alimentaires seront discutées dans la section 3.3.3 de ce chapitre.

Ensuite, dès les premiers jours de grossesse, une inflammation de bas grade s'installe, reflétant le développement de nouveaux tissus et le bon déroulement du processus d'implantation du blastocyte, entre autres [34, 35]. Cette inflammation physiologique est caractérisée, en début de grossesse, par des concentrations plus élevées de cytokines pro-inflammatoires, comme l'interleukine-6 (IL-6) et l'interleukine-8 (IL-8) [36]. Cet état pro-inflammatoire de bas-grade n'est généralement pas indicatif de désordres métaboliques, mais en présence de certains facteurs de risque comme un IMC prégrossesse élevé ou un gain de poids supérieur aux recommandations, il peut s'amplifier et être associé au développement de différentes complications, comme le diabète gestationnel et la prééclampsie [37-39]. Il est donc pertinent de s'intéresser aux changements dans les concentrations de marqueurs inflammatoires durant la grossesse et aux facteurs qui pourraient y être associés, comme l'alimentation et le statut pondéral [40, 41]. Ces associations seront discutées à la section 3.4.1 de ce chapitre.

1.3. Période fœtale

Comme il a été mentionné plus tôt, la période fœtale est principalement caractérisée par la croissance et le développement des structures (membres, organes, squelette, etc.) qui ont débuté leur formation au cours de la période embryonnaire. En fait, de la neuvième semaine de grossesse jusqu'à l'accouchement, le poids du fœtus passera d'environ 30 g à 3,4 kg [30]. Parallèlement au poids du bébé, le gain pondéral de la mère est beaucoup plus important durant les derniers mois de la période fœtale. Ce gain de poids maternel reflète, en plus du poids du bébé, le développement et l'accumulation de plusieurs tissus maternels, comme l'augmentation du volume sanguin et du liquide amniotique, le poids du placenta et de l'utérus qui augmente progressivement, ainsi que l'accumulation de réserves adipeuses [42]. L'augmentation du volume sanguin maternel entraîne à son tour une augmentation du débit (20 à 30 %) et de la fréquence (10 à 15%) cardiaque, ce qui contribue aux besoins énergétiques élevés de la femme enceinte, qui seront discutés dans la prochaine section [30].

La croissance fœtale et le gain de poids gestationnel sont aussi influencés par plusieurs mécanismes hormonaux et métaboliques. En fait, les besoins énergétiques et nutritionnels accrus du fœtus nécessitent une altération de l'homéostasie métabolique maternelle, notamment au niveau de la fonction pancréatique [32]. La grossesse est en effet caractérisée par une plus grande sécrétion d'insuline, ce qui, au début de la grossesse, permet d'utiliser le glucose pour la formation de nouveaux tissus et l'accumulation de réserves adipeuses (lipogenèse) [43]. Au cours de la période fœtale,

parallèlement à l'augmentation progressive des concentrations de progestérone et d'autres hormones liées à la grossesse, la sensibilité à l'insuline diminue et une résistance à l'insuline s'installe chez la mère. Cette résistance diffère de celle observée chez les diabétiques de type 2, puisqu'elle est combinée à une plus grande sécrétion d'insuline par les cellules β du pancréas, permettant ainsi un transfert de glucose au fœtus en pleine croissance [43]. Lorsque les cellules β ne peuvent contrebalancer la résistance à l'insuline par une augmentation de sa sécrétion, la femme enceinte peut développer un diabète gestationnel [44]. Ce dernier est généralement diagnostiqué à la fin du deuxième trimestre de grossesse, mais certains marqueurs mesurés au début de la grossesse pourraient permettre d'identifier les femmes qui en sont à risque [45]. En fait, trois cytokines sécrétées par le tissu adipeux (adipocytokines) sont associées au développement du diabète gestationnel et à la résistance à l'insuline durant la grossesse, soit l'interleukine-6, la leptine et l'adiponectine [43]. La pathophysiologie et le traitement du diabète gestationnel ne seront pas discutés dans le cadre de la présente thèse, mais les adipocytokines liées à la résistance à l'insuline et leurs associations avec l'alimentation durant la grossesse seront abordées à la section 3.4.2 de ce chapitre.

En résumé, de nombreuses adaptations et altérations métaboliques s'installent progressivement au cours de la grossesse, afin de maintenir l'équilibre entre le métabolisme de la mère et les besoins du fœtus. En raison du contexte particulier de la grossesse, des apports nutritionnels de référence (ANREF) ont été développés pour cette période. Ces ANREF seront discutés dans les prochaines sections. À noter que seul le besoin moyen estimatif (BME), ou l'apport suffisant (AS), selon le cas, sera présenté, puisque c'est à lui que doivent être comparés les apports d'un d'une population. L'apport nutritionnel recommandé (ANR) ne sera pas utilisé, puisqu'il représente une cible individuelle [46].

2. Besoins nutritionnels durant la grossesse

2.1. Besoins en énergie

2.1.1. Recommandations

Il convient de rappeler que la croissance et le gain de poids du fœtus ont principalement lieu durant la période fœtale, c'est-à-dire après la huitième semaine de grossesse. Ainsi, les ANREF, développés aux États-Unis et utilisés au Canada, recommandent un apport calorique plus élevé à partir du deuxième trimestre de grossesse seulement. Plus précisément, 340 et 452 kcal supplémentaires par

jour sont recommandées aux femmes lors des deuxième et troisième trimestres, respectivement [47]. Les besoins en protéines évoluent de façon similaire, puisqu'ils sont augmentés seulement à partir de la deuxième moitié de la grossesse. Le BME pour les protéines passe en effet de 0,66 à 0,88 g de protéines par kg de poids corporel, de la préconception à la 21e semaine de grossesse [47]. Les recommandations pour la contribution des macronutriments à l'apport énergétique durant la grossesse sont les mêmes qu'en préconception. Ainsi, l'apport en énergie devrait provenir à 45-65% des glucides, 10-35% des protéines et 20-35% des lipides et ce, pour toute la durée de la grossesse [47].

Durant le premier trimestre de grossesse, l'apport énergétique recommandé correspond au besoin énergétique estimé (BÉE) des femmes adultes non enceintes. Comme cela est indiqué à la Figure 2, ce dernier est calculé en utilisant le poids prégrossesse, la taille, l'âge et le coefficient d'activité (CA) correspondant au niveau d'activité physique de la femme. Il s'agit de l'apport énergétique de base auquel on ajoute les 340 et 452 kcal préalablement mentionnées.

$$\text{BÉE} = 354 - (6{,}91 \times \text{âge}) + \text{CA} \times ([9{,}36 \times \text{poids (kg)}] + [726 \times \text{taille (m)}])$$

Figure 2. Équation du besoin énergétique estimé pour une femme adulte non enceinte [47]

Les calories supplémentaires recommandées aux deuxième et troisième trimestres proviennent principalement d'un modèle théorique développé par Hytten et Chamberlain en 1991 [48]. Ce modèle estimait l'énergie nécessaire pour soutenir 1) une augmentation de la dépense énergétique pour une femme de 60 à 65 kg, 2) un gain de poids gestationnel de 12,5 kg et 3) un poids du bébé à la naissance de 3,4 kg. Les auteurs de ce modèle théorique ont donc calculé le coût énergétique d'un gain de poids composé de tissu adipeux et de protéines, qu'ils ont ensuite additionné à l'augmentation de la dépense énergétique de la femme enceinte [48, 49]. Un nombre limité d'études prospectives évaluant la dépense énergétique totale de femmes enceintes ont ensuite été évaluées et considérées, par la *National Academy of Medicine* (anciennement *Institute of Medicine*), pour l'élaboration des recommandations mentionnées ci-haut [50-64]. L'utilisation de ces études dans le développement des recommandations énergétiques a récemment été questionnée, notamment parce que la majorité d'entre elles n'ont pas considéré l'adéquation du gain de poids gestationnel de leurs participantes [65]. En fait, il est probable que l'inclusion, dans ces études, de femmes ayant un gain de poids gestationnel excessif ait contribué à une surestimation de l'augmentation de la dépense énergétique en grossesse

et donc, à une surestimation des besoins des femmes enceintes [65]. Les auteurs d'une méta-analyse avaient d'ailleurs suggéré, après avoir observé une stabilité dans les apports énergétiques des femmes enceintes, que les besoins énergétiques durant la grossesse étaient possiblement surestimés [66]. À cet effet, le chapitre 4 de cette thèse présente une revue de la littérature qui visait à répertorier les études ayant mesuré prospectivement la dépense énergétique durant la grossesse.

Bref, bien que la grossesse soit associée à une augmentation des besoins énergétiques, l'amplitude de cette augmentation est remise en question. De plus, l'estimation de ces besoins se base sur un modèle théorique très précis et datant de plus de 30 ans, ainsi que sur un nombre restreint de preuves scientifiques publiées il y a plus de 15 ans. Il est donc très probable qu'une femme enceinte ait des apports énergétiques à l'extérieur des cibles recommandées. Les conséquences potentielles d'un apport énergétique à l'extérieur des recommandations durant la grossesse sont discutées ci-dessous.

2.1.2. Impact d'un apport énergétique inadéquat durant la grossesse

Durant la grossesse, un apport énergétique inférieur aux besoins a été associé inversement au développement du fœtus, qui est quant à lui déterminant de la santé à long terme de l'enfant et de l'adulte. Cette association fut observée pour une première fois par les chercheurs de la *Dutch famine birth cohort study*, réalisée auprès de plus de 2000 adultes nés durant la Deuxième Guerre mondiale, à l'époque de la famine néerlandaise [67]. Leurs résultats ont montré que l'exposition *in utero* à la famine était associée à un faible poids à la naissance, ce dernier étant lié à une plus grande susceptibilité de développer différentes maladies non transmissibles durant la vie adulte (ex. intolérance au glucose, maladies cardiovasculaires, maladies pulmonaires obstructives) [67]. Bien sûr, un contexte comme celui de la famine néerlandaise n'entraîne pas seulement des apports insuffisants en énergie, mais aussi en plusieurs macro- et micronutriments essentiels. Néanmoins, un apport insuffisant en énergie peut être associé, chez la femme, à un gain de poids gestationnel inférieur aux recommandations de la *National Academy of Medicine* (Tableau 1). En fait, l'apport énergétique total des femmes enceintes semble être directement corrélé à leur gain de poids gestationnel [10, 68]. Un gain de poids insuffisant durant la grossesse a été associé à un plus grand risque d'accoucher prématurément et d'un bébé ayant un poids faible pour son âge gestationnel [69, 70].

Tableau 1. Recommandations de gain de poids gestationnel[1]

Catégories d'IMC	Gain de poids total		Rythme de gain de poids[2] (deuxième et troisième trimestres)	
	kg	lbs	kg/semaine	lbs/semaine
Insuffisant (<18,5 kg/m^2)	12,5-18	28-40	0,51	1,0
Normal (18,5-24,9 kg/m^2)	11,5-16	25-35	0,42	1,0
Surpoids (25,0-29,9 kg/m^2)	7-11,5	15-25	0,28	0,6
Obésité (≥30 kg/m^2)	5-9	11-20	0,22	0,5

[1]Ces recommandations s'appliquent aux femmes âgées de 18 ans et plus enceintes d'un seul fœtus.
[2]Au premier trimestre, il est recommandé de gagner un total de 0,5 à 2,0 kg (1,1 à 4,4 lbs) et ce, peu importe la catégorie d'IMC prégrossesse [71].
Abréviations : IMC, indice de masse corporelle.

Des apports en énergie qui excèdent les ANREF pourraient quant à eux être associés à un gain de poids gestationnel excessif, une problématique de plus en plus prévalente en Amérique du Nord [68, 72-74]. Un gain de poids qui excède les recommandations est associé à différentes complications, notamment la prééclampsie et le diabète gestationnel chez la mère et un poids élevé pour l'âge gestationnel chez le nouveau-né [70, 75]. Il convient cependant de mentionner que, malgré l'association entre les apports énergétiques et le gain de poids, ce dernier demeure une variable complexe influencée par des facteurs d'ordre physiologique, social, psychologique et comportemental [76-78]. Ainsi, bien qu'il soit important pour assurer un gain de poids gestationnel optimal d'évaluer l'adéquation des apports énergétiques par rapport aux recommandations en vigueur, il est aussi pertinent de considérer la situation socioéconomique, le niveau de stress, les attitudes et les comportements face à l'alimentation ainsi que le niveau d'activité physique de la femme.

Parallèlement aux apports en énergie, l'adéquation des apports en micronutriments est également essentielle tout au long de la grossesse. Un résumé des ANREF de certains micronutriments est présenté au Tableau 2. Les vitamines et les minéraux ont tous un rôle crucial à jouer durant les périodes embryonnaires et fœtales. Toutefois, certains micronutriments ont reçu plus d'attention dans le milieu scientifique; c'est le cas de l'acide folique, du fer et de la vitamine D.

Tableau 2. Apports nutritionnels de référence pour les femmes âgées de plus de 18 ans [79]

Micronutriments	Apport de référence quotidiens[1]		Augmentation (↑) ou stabilité (–)
	Femme non enceinte	Femme enceinte	
Folate[2]	0,32 mg ÉFA	0,52 mg ÉFA	↑
Fer	8,1 mg	22 mg	↑
Vitamine D	400 UI	400 UI	–
Calcium	800 mg	800 mg	–
Vitamine B_{12}	2,0 µg	2,2 µg	↑
Vitamine B_6	1,1 mg	1,6 mg	↑
Vitamine C	60 mg	70 mg	↑
Vitamine A	0,5 mg ÉAR	0,55 mg ÉAR	↑
Vitamine E	12 mg	12 mg	–
Choline	425 mg	450 mg	↑
Thiamine	0,9 mg	1,2 mg	↑
Riboflavine	0,9 mg	1,2 mg	↑
Niacine	11 mg	14 mg	↑
Acide pantothénique	5 mg	6 mg	↑
Sélénium	45 µg	49 µg	↑
Magnésium[3]	255 à 265 mg	290 à 300 mg	↑
Manganèse	1,8 mg	2,0 mg	↑
Zinc	6,8 mg	9,5 mg	↑
Iode	95 µg	160 µg	↑

[1]Le besoin moyen estimatif est utilisé comme référence à l'exception de la choline, l'acide pantothénique et du manganèse, où l'apport suffisant est présenté.
[2]Le folate réfère à la forme naturelle de la vitamine B_9, alors que le terme acide folique est utilisé pour la forme synthétique, présente dans les aliments enrichis et les suppléments.
[3]L'apport le plus faible s'applique aux femmes de 19 à 30 ans et le plus élevé aux femmes de 31 ans et plus.
Abréviations : ÉAR, équivalent d'activité du rétinol; ÉFA, équivalent de folate alimentaire; UI, unités internationales.

2.2. Besoins en micronutriments

2.2.1. Folate et acide folique

2.2.1.1. Recommandations

Comme il est présenté au Tableau 2, le BME du folate passe de 0,32 mg en préconception à 0,52 mg au premier trimestre de grossesse. Des recommandations plus précises de Santé Canada encouragent la consommation d'aliments contenant naturellement du folate ou qui sont enrichis en acide folique, la forme synthétique du folate, comme les légumineuses, les légumes vert foncé, la farine blanche et les pâtes alimentaires enrichies. Néanmoins, ces mêmes lignes directrices mentionnent le fait que les sources alimentaires de folate, qu'elles soient naturelles ou synthétiques, ne sont pas suffisantes pour combler les besoins plus élevés associés à la grossesse [80]. Pour cette raison, Santé Canada recommande aux femmes enceintes et à celles qui pourraient le devenir de prendre une multivitamine contenant au moins 0,4 mg d'acide folique, afin de prévenir le risque de malformations du tube neural, qui se développe dès les premiers jours suivant la fécondation [81, 82]. Le groupe de travail américain sur les services préventifs (*US Preventive Task Force*) recommande quant à lui un supplément contenant de 0,4 à 0,8 mg d'acide folique à toutes les femmes planifiant ou pouvant devenir enceintes [83]. Au Royaume-Uni, en Australie et en Nouvelle-Zélande, des experts recommandent aux femmes ayant un IMC prégrossesse ≥30 kg/m^2 de prendre une dose plus élevée d'acide folique (5 mg) tout au long de leur grossesse, puisque celles-ci présenteraient un risque plus élevé de déficience en folate [84]. Au Canada, une dose de 5 mg d'acide folique est seulement recommandée aux femmes qui ont des antécédents personnels et/ou familiaux d'anomalies du tube neural [85].

2.2.1.2. Impact d'un apport inadéquat en folate durant la grossesse

Le folate est un micronutriment essentiel qui assure plusieurs rôles dans la prolifération et la différenciation cellulaire [86]. Il intervient aussi à titre de coenzyme dans les réactions biochimiques du cycle du carbone. Ce cycle peut, entre autres, modifier de façon durable comment certains gènes sont utilisés par les cellules [87]. Ainsi, des perturbations dans les apports nutritionnels en folate pourraient affecter la fonction de certains gènes impliqués dans la croissance fœtale, par exemple [87]. En fait, des apports maternels insuffisants en folate peuvent entraîner une déficience, qui est depuis longtemps associée au risque de malformations du tube neural [88]. La relation entre la déficience en folate et le

développement de telles malformations ne semble toutefois pas être causale chez toutes les femmes. En fait, un statut déficient en folate représenterait un facteur de risque, mais seulement en présence d'une susceptibilité ou une prédisposition génétique au développement de malformations du tube neural [89]. Néanmoins, la supplémentation en acide folique, seule ou en combinaison avec d'autres nutriments, est toujours considérée comme une mesure de prévention efficace contre le développement de malformations du tube neural [90, 91]. En fait, la prévalence de déficience en folate chez les femmes enceintes ou qui pourraient le devenir semble dorénavant rare au Canada [92-94]. Chez la femme enceinte, une déficience en folate est associée au développement d'une anémie mégaloblastique, caractérisée par une diminution du nombre et une augmentation de la taille des globules rouges [95].

L'apport maximal tolérable (AMT) pour le folate est établi à 1 mg et s'applique uniquement à sa forme synthétique, l'acide folique, retrouvée dans les aliments enrichis et les suppléments [79]. Des apports élevés en acide folique sont associés au masquage d'une déficience en vitamine B_{12}, qui elle est liée à des malformations du tube neural, même dans des populations bénéficiant d'un enrichissement obligatoire en acide folique [96]. Un apport excessif en acide folique pourrait aussi être associé à différentes modifications épigénétiques fœtales, en raison de son implication dans le cycle du carbone [87, 97]. En fait, une équipe de chercheurs a observé une plus grande résistance à l'insuline chez les enfants nés des femmes qui, durant leur grossesse, présentaient les niveaux de folate érythrocytaire les plus élevés [98]. Des études chez les rongeurs ont également démontré les effets néfastes d'un excès d'acide folique sur le métabolisme fœtal [99, 100]. Cependant, d'autres études sont nécessaires et les effets potentiels d'un apport excessif en acide folique n'ont pas encore été suffisamment étudiés chez l'humain. Il serait tout de même prudent de surveiller les apports en acide folique auprès des femmes enceintes, considérant qu'une majorité d'entre elles rapporte prendre un supplément ou une multivitamine contenant de l'acide folique [101-104]. D'ailleurs, le contenu en acide folique des différentes multivitamines prénatales vendues au Québec varie entre 0,6 et 5 mg, ce qui, combiné aux apports alimentaires en acide folique, peut mener à un apport supérieur à l'AMT [105-108]. L'évaluation de l'adéquation des apports en folate en comparaison avec les ANREF pour la période gestationnelle est présentée et discutée au chapitre 5.

2.2.2. Fer

2.2.2.1. Recommandations

Les besoins en fer sont presque triplés durant la grossesse; le BME passant de 8,1 mg en préconception à 22 mg dès le premier trimestre de grossesse [79]. Ce nutriment a plusieurs fonctions, notamment liées au processus de production des cellules sanguines [31]. Durant la grossesse, le fer est essentiel au développement du fœtus mais aussi au développement et à la vascularisation du placenta [109, 110]. Les apports en fer doivent également soutenir l'augmentation des volumes sanguins et plasmatiques de la mère, qui est progressivement plus importante au cours des deuxième et troisième trimestres [79, 111]. De plus, c'est durant cette période que le fœtus accumulera ses réserves en fer, qui seront utilisées durant ses six premiers mois de vie [112]. Pour toutes ces raisons, Santé Canada recommande aux femmes enceintes de prendre une multivitamine contenant de 16 à 20 mg de fer, parallèlement à la consommation d'aliments riches en fer et en vitamine C (pour en faciliter l'absorption) tout au long de la grossesse [81]. Une méta-analyse de 44 essais cliniques a d'ailleurs conclu qu'une supplémentation en fer réduisait significativement le risque de déficience et d'anémie ferriprive durant la grossesse, dont il est question ci-dessous [113].

2.2.2.2. Impact d'un apport inadéquat en fer durant la grossesse

Des apports insuffisants en fer durant la grossesse peuvent entraîner une déficience, qui elle est associée à un sentiment de fatigue, une diminution de la concentration, des maux de tête ainsi qu'à un risque accru d'anémie [114, 115]. L'anémie causée par une déficience en fer est relativement prévalente en contexte gestationnel, étant donné les besoins élevés mentionnés ci-dessus. Selon les données de quatre cohortes nord-américaines, la prévalence d'anémie ferriprive varie de 2 à 2,7% au premier trimestre, et de 2 à 42% aux deuxième et troisième trimestres [116]. La prévalence plus élevée aux deuxième et troisième trimestres s'explique, entre autres, par les besoins plus élevés du fœtus et de la femme enceinte au cours de cette période [79, 111, 112, 117]. Pour le nouveau-né, une déficience en fer durant la grossesse a été associée à un plus grand risque de naissance prématurée et à un poids à la naissance petit pour l'âge gestationnel [114].

Contrairement aux conséquences d'un apport insuffisant en fer, les effets d'un apport qui excède l'AMT de 45 mg [79] ont été peu étudiés en contexte prénatal. Étant donné la supplémentation en fer recommandée aux femmes enceintes et le fait que les multivitamines prénatales contiennent généralement entre 24 et 35 mg de fer, il est possible que les apports totaux en fer de certaines femmes enceintes excèdent l'AMT [105-108, 118]. Les effets connus d'une supplémentation en fer durant la grossesse sont principalement des symptômes ou des inconforts gastro-intestinaux comme des nausées, des vomissements, de la constipation ainsi que de la diarrhée [118-120]. Récemment, des associations ont été observées entre l'apport, la supplémentation et le statut en fer et le développement du diabète gestationnel [121-127]. Une méta-analyse de 14 études prospectives et de cas-contrôle a d'ailleurs observé une association significative entre les concentrations de ferritine, dont les niveaux reflètent les réserves en fer, et le risque de développer un diabète gestationnel [128]. La même association n'a toutefois pas été observée avec l'apport nutritionnel en fer [128]. Bien que la littérature actuelle ne permette pas de conclure qu'un apport et un statut élevé en fer peuvent entraîner le développement du diabète gestationnel, ces associations méritent tout de même d'être investiguées davantage. L'évaluation de l'adéquation des apports en fer par rapport aux recommandations en contexte gestationnel, est présentée et discutée au chapitre 5.

2.2.3. Vitamine D

2.2.3.1. Recommandations

À l'inverse des besoins en folate et en fer, le BME de la vitamine D n'est pas augmenté de la préconception à la grossesse, demeurant stable à 400 UI [129]. La vitamine D joue tout de même plusieurs rôles essentiels durant la période prénatale, notamment par rapport à l'absorption du calcium par la mère et le fœtus, ce qui en fait un nutriment important pour la minéralisation et la croissance osseuse fœtale [130]. Outre son implication dans le métabolisme du calcium, la vitamine D est reconnue pour agir sur différents organes et systèmes, comme le pancréas et le système immunitaire [129]. Malgré ces rôles importants, Santé Canada ne spécifie pas que la multivitamine recommandée durant la grossesse doive contenir de la vitamine D [81], contrairement au fer et à l'acide folique. De leur côté, l'*American Endocrine Society* et la Société canadienne de pédiatrie suggèrent qu'un apport total en vitamine D pouvant aller jusqu'à 2 000 UI pourrait être nécessaire pour assurer un statut suffisant chez certaines femmes [131, 132]. Au Royaume-Uni, via le *National Institute for Health and Care Excellence,* il est recommandé aux femmes enceintes et celles prévoyant une grossesse de

prendre un supplément d'au moins 400 UI de vitamine D [133]. Au Québec, le contenu en vitamine D des principales multivitamines prénatales est généralement de 600 UI [105-108]. Cette dose permet, si la femme enceinte adhère à la recommandation de prendre une multivitamine, de complémenter les apports en vitamine D provenant de l'alimentation, qui semblent être insuffisants pour une proportion considérable de femmes enceintes canadiennes [102, 134-136].

2.2.3.2. Impact d'un apport inadéquat en vitamine D durant la grossesse

De faibles apports en vitamine D peuvent mener à une diminution des concentrations sériques en 25-hydroxyvitamine D, ou 25(OH)D, le métabolite de la vitamine D qui est mesurée pour en évaluer le statut. Au Canada, la prévalence d'un statut insuffisant en vitamine D durant la grossesse varie entre 2 et 46% [137-143]. Il importe de mentionner qu'outre un apport insuffisant en vitamine D, certaines variables peuvent influencer négativement le statut en vitamine D, comme une faible exposition aux rayons ultraviolets β du soleil et un IMC prégrossesse plus élevé [144-147]. Ainsi, la variabilité observée dans la prévalence de statut insuffisant en vitamine D pourrait s'expliquer en partie par le statut pondéral et l'exposition solaire des femmes enceintes étudiées. Selon des études observationnelles, des concentrations sous-optimales de 25(OH)D sont associées à un risque plus élevé de naissance prématurée et, à plus long terme, à une masse osseuse moindre et au rachitisme chez l'enfant [148-151]. Chez la femme enceinte, des méta-analyses ont conclu qu'un statut sous-optimal ou déficient (<50 nmol/L) en vitamine D était associé à un risque accru de diabète gestationnel et de prééclampsie [151-154]. Ces associations pourraient s'expliquer par l'action de la vitamine D sur le pancréas et dans des mécanismes liés à l'homéostasie du calcium, respectivement [147]. Plus d'études sont toutefois nécessaires pour mieux comprendre l'impact d'un statut inadéquat en vitamine D sur les variables de la santé durant la grossesse.

Comme pour le folate et le fer, l'impact d'un apport excessif en vitamine D durant la grossesse est peu documenté. Un apport en vitamine D équivalent à l'AMT de 4,000 UI ne semble pas être associé à des niveaux toxiques de 25(OH)D. Dans la population adulte générale, des apports supérieurs à 10,000 UI/jour sont quant à eux associés à un risque de toxicité pouvant mener à une hypercalcémie (niveaux sériques de calcium supérieurs à 10,5 mg/dL) et à une hypercalciurie (excrétion urinaire de calcium qui excède 250 mg/jour) [129]. Ces deux conditions sont associées au développement de pierres aux reins et, chez la femme enceinte, au développement d'une hypertension gestationnelle [155, 156]. L'hypercalcémie semble toutefois peu prévalente en contexte de grossesse [157]. Ensuite, dans la

population adulte générale, une association non linéaire, en forme de « U », a été observée entre les concentrations de 25(OH)D et le risque de maladies cardiovasculaires, ce qui signifie que des concentrations à la fois très faibles et très élevées de 25(OH)D semblent être associées à un risque cardiovasculaire plus élevé [129]. Les mécanismes derrière ces associations doivent cependant être investigués davantage. Enfin, le comité d'experts en charge de réviser les ANREF de la vitamine D et du calcium suggère que des concentrations sériques de 25(OH)D qui se situent en dessous de 125 nmol/L ne seraient pas associées à des conséquences défavorables pour la santé des adultes [129]. Les apports en vitamine D et les concentrations de 25(OH)D de femmes enceintes québécoises ont été évalués dans le cadre de cette thèse et sont présentés aux chapitres 5 et 6.

2.2.4. Autres nutriments à considérer

Plusieurs nutriments n'ont pas été abordés dans cette section, mais il importe de mentionner que des nutriments comme les acides gras essentiels, la vitamine A, la vitamine B_{12} et la choline ont des rôles importants à jouer dans le développement cérébral et neurologique du fœtus [31, 96, 150, 158]. Ensuite, comme il a été discuté dans la section sur la vitamine D, l'apport en calcium est aussi déterminant pour le développement osseux et la croissance du fœtus ainsi que pour d'autres variables de santé chez la mère [130, 159]. Enfin, les protéines, dont les besoins sont augmentés en cours de grossesse, sont quant à elles nécessaires au développement de plusieurs tissus maternels et fœtaux [160].

Bref, considérant l'importance de la nutrition pour le développement du fœtus et le bon déroulement de la grossesse, il est impératif d'évaluer l'adéquation des apports nutritionnels durant la grossesse. La section qui suit s'intéresse à deux méthodes d'évaluation de l'adhésion aux recommandations nutritionnelles, soit l'estimation des apports nutritionnels et leur comparaison avec les ANREF, et la mesure du statut nutritionnel.

2.3. Évaluation de l'adéquation des apports nutritionnels

2.3.1. Comparaison des apports nutritionnels estimés aux apports de référence

Les ANREF peuvent être utilisés afin d'évaluer l'adéquation des apports énergétiques et nutritionnels d'un individu ou d'une population [161]. Cela implique l'estimation, par un outil validé, des apports alimentaires d'un groupe d'individus. Il existe de nombreux outils d'évaluation alimentaire, les plus

connus étant le questionnaire de fréquence alimentaire (QFA), le journal alimentaire ainsi que le rappel de 24h [162]. Ces outils ne seront pas décrits de manière exhaustive dans la présente thèse, mais il convient de mentionner que chaque outil possède des avantages et des faiblesses qui doivent être pris en considération lors du choix d'une méthode d'évaluation alimentaire [163]. Le contexte dans lequel l'outil sera utilisé est aussi à considérer. Par exemple, durant une période comme la grossesse où les apports alimentaires sont susceptibles de changer d'un trimestre à l'autre, il peut être plus intéressant d'opter pour un rappel de 24h ou un journal alimentaire, qui reflètent les apports nutritionnels d'une période plus courte que celle généralement évaluée par un QFA [164-166]. De plus, le rappel de 24h est habituellement moins long et ardu à compléter qu'un journal alimentaire, encore plus si une version Web et auto-administrée est utilisée [167, 168].

Ensuite, les apports nutritionnels peuvent être comparés aux ANREF afin d'estimer la prévalence ou le risque d'apports inadéquats d'une population [161]. La prévalence d'apports insuffisants est déterminée en calculant la proportion d'individus dont les apports sont inférieurs au BME ou à l'AS [161]. De façon similaire, la proportion d'individus dont l'apport est supérieur à l'AMT peut également être calculée pour estimer la prévalence d'apports excessifs [161]. Cependant, il importe de mentionner que ces méthodes reposent sur des données alimentaires auto-rapportées et sujettes à certains biais (ex. biais de mémoire et de désirabilité sociale) et sur des ANREF qui possèdent aussi leurs limites [164, 165, 169]. En effet, ces derniers ne prennent pas en considération certaines variables individuelles (ex. le statut pondéral et la présence d'une condition médicale) et biochimiques (ex. biodisponibilité d'un nutriment dans un aliment) qui peuvent influencer l'absorption et le métabolisme des nutriments [170]. Ainsi, des apports nutritionnels inférieurs au BME ou supérieurs à l'AMT ne reflètent peut-être pas nécessairement un statut nutritionnel inadéquat. Il est donc pertinent, surtout dans un contexte comme la grossesse, où les nutriments sont utilisés à la fois par la mère et le fœtus, de combiner l'évaluation des apports nutritionnels, qui sera présentée au chapitre 5, à une mesure plus objective du statut nutritionnel des femmes enceintes, dont il est question ci-dessous.

2.3.2. Évaluation du statut nutritionnel

Le statut nutritionnel peut être défini comme le reflet physiologique de la relation entre les apports alimentaires et les besoins d'un individu ou d'une population [162]. Il est généralement mesuré par le dosage de biomarqueurs nutritionnels présents dans le sang, le sérum, ou d'autres tissus organiques. Bien que les concentrations d'un biomarqueur nutritionnel peuvent représenter une mesure objective

du statut nutritionnel et un reflet des apports nutritionnels, celles-ci peuvent quand même être influencées par de nombreux facteurs individuels [162, 169]. Par exemple, et comme il a été mentionné plus tôt, les niveaux sériques de 25(OH)D, qui reflètent le statut en vitamine D, sont influencés par l'exposition solaire et l'IMC d'une personne [144-147]. Ainsi, même si des apports suffisants en vitamine D sont observés chez une certaine population, il est possible que le statut en 25(OH)D de cette même population ne soit pas optimal, si, par exemple, la majorité des individus ont un IMC élevé. La mesure de biomarqueurs nutritionnels est donc complexe et il est essentiel de prendre en considération les variables individuelles qui peuvent influencer le statut nutritionnel d'une personne. Cela est encore plus vrai dans un contexte comme celui de la grossesse, où les nombreuses variations hormonales pourraient avoir un impact sur les concentrations de certains marqueurs, comme la 25(OH)D [171]. Enfin, il convient de mentionner que la mesure d'un biomarqueur nutritionnel est spécifique à un nutriment en particulier et ne permet pas d'évaluer l'alimentation sur le plan global.

En somme, l'évaluation de l'adhésion des apports nutritionnels aux ANREF et du statut nutritionnel fournit des informations précises et pertinentes, mais ne permet pas d'évaluer l'alimentation dans son ensemble. C'est pourquoi on évalue désormais la qualité globale de l'alimentation en association avec différentes variables de la santé durant la grossesse.

3. Qualité alimentaire durant la grossesse

3.1. Définition

Les concepts de modèles et de qualité alimentaires découlent de l'hypothèse que les liens existants entre l'alimentation et la santé s'expliquent par l'effet combiné de plusieurs nutriments [172]. La qualité alimentaire fait donc référence à l'évaluation des habitudes alimentaires dans leur ensemble et est généralement mesurée en comparant les apports alimentaires à des lignes directrices ou à un modèle alimentaire ayant été associé favorablement à des variables de la santé [173]. Selon la littérature, une alimentation de meilleure qualité peut être définie par des apports élevés en fruits et légumes, grains entiers, protéines végétales et en acides gras insaturés ainsi que des apports faibles et modérés en viande rouge, charcuteries, acides gras saturés et en aliments transformés [9, 28, 173]. En plus de cette définition plutôt générale d'une meilleure qualité alimentaire, plusieurs indices ont été élaborés dans les dernières années afin d'évaluer plus précisément la qualité de l'alimentation de la population générale ou bien des femmes enceintes [174, 175]. Trois de ces indices sont présentés ci-dessous.

3.2. Indices mesurant la qualité alimentaire

3.2.1. Adaptation canadienne de l'indice de qualité alimentaire

Le *Healthy Eating Index* (HEI), initialement élaboré aux États-Unis en 1995, vise à mesurer le niveau d'adhésion aux lignes directrices nutritionnelles américaines [176]. Il s'agit d'un score de 100 points répartis selon des composantes alimentaires (produits céréaliers, légumes, fruits, lait et viande) et nutritionnelles (gras totaux et saturés, cholestérol et sodium) ainsi que selon une composante de variété alimentaire. Un score de 100 signifie que l'alimentation d'une personne respecte parfaitement les recommandations nutritionnelles américaines. Le score total, qui est ajusté pour l'apport énergétique des répondants, a été associé positivement à des apports et des concentrations plus élevés en certains nutriments, notamment le folate, la vitamine C et certains caroténoïdes, tous des marqueurs liés à la consommation de fruits et légumes [177]. Enfin, même si le HEI n'a pas été élaboré spécifiquement pour la période de la grossesse, certains auteurs l'ont précédemment utilisé pour évaluer la qualité alimentaire de femmes enceintes [178-181].

Une version canadienne du HEI (C-HEI) fut développée en 2009, suivant la publication de la version 2005 du HEI américain [182]. Cette première version canadienne du HEI se basait sur les recommandations du guide alimentaire Canadien de 2007. Ce dernier, contrairement à sa version plus récente publiée en 2019, recommandait un nombre de portions quotidiennes à consommer pour les quatre groupes alimentaires principaux (fruits et légumes, produits céréaliers, lait et substituts ainsi que viandes et substituts). D'autres recommandations spécifiques du guide suggéraient de consommer des poissons gras ainsi que des légumes de couleur orange et vert foncé, de choisir des huiles et matières grasses à base d'acides gras insaturés ainsi que de limiter la consommation d'aliments à haute densité énergétique riches en sucres, gras et sodium [183]. Ainsi, la consommation de fruits, légumes, produits céréaliers, lait et substituts, viandes et substituts et les apports en gras insaturés sont corrélés positivement au C-HEI, tandis que les apports en gras saturés, sodium et en aliments hautement transformés sont inversement corrélés au C-HEI. Contrairement à la version américaine, le C-HEI n'est pas ajusté pour l'apport énergétique total des répondants [182]. Enfin, selon des données de l'Enquête sur la santé des collectivités canadiennes de 2004, le score C-HEI moyen des adultes canadiens âgés de 19 à 50 ans se situait entre 55,4 et 59,6 sur 100 [182]. Au Québec, selon une étude réalisée entre 2015 et 2017 auprès de 1147 adultes, le score C-HEI pour le même groupe d'âge variait plutôt entre 51,7 et 53,8 sur 100 [184]. Selon cette même étude, le score C-HEI était plus élevé chez

les femmes vs. les hommes, chez les adultes avec un diplôme universitaire vs. collégial et secondaire ainsi que chez les adultes avec un IMC normal, vs. chez les adultes présentant une obésité [184]. Ces données canadiennes et québécoises n'incluaient cependant pas de femmes enceintes. Ainsi, une évaluation prospective de la qualité alimentaire de femmes enceintes québécoises a été réalisée dans le cadre de cette thèse et est présentée au chapitre 7.

3.2.2. Score d'adhésion à la diète méditerranéenne

L'intérêt scientifique pour la diète méditerranéenne s'explique par ses nombreux bénéfices sur la santé, notamment par rapport à son effet protecteur sur le risque cardiovasculaire [185, 186]. Les effets de la diète méditerranéenne sur la santé pourraient s'expliquer, entre autres, par des mécanismes liés au stress oxydatif et à l'inflammation [187]. Il existe plusieurs variations de la diète méditerranéenne, mais cette dernière est généralement caractérisée par une consommation élevée d'aliments d'origine végétale (fruits, légumes, huile d'olive, grains entiers, légumineuses et noix), modérée en poisson, œufs, volaille, et produits laitiers et faible en viande rouge et aliments transformés [188]. Il existe plusieurs scores pour mesurer l'adhésion à la diète méditerranéenne, dont certains ayant été utilisés auprès de femmes enceintes [189], ainsi qu'un autre élaboré par une équipe de l'Université Laval [190]. Ce score et les critères utilisés pour le calculer seront décrits plus en détail au chapitre 10 de cette thèse, qui présente les associations entre la qualité alimentaire et différents marqueurs inflammatoires au cours des trimestres de la grossesse.

3.2.3. Indice inflammatoire alimentaire

Comme il fut mentionné plus tôt, l'impact de la diète méditerranéenne sur la santé des populations pourrait s'expliquer par son effet protecteur sur le profil inflammatoire [187]. Vu cette hypothèse, et considérant qu'un état inflammatoire de bas grade est associé à d'autres conditions comme le diabète de type 2, le syndrome métabolique et la dépression [191, 192], des auteurs ont voulu développer un indice permettant d'estimer le potentiel inflammatoire de l'alimentation [193]. L'indice inflammatoire alimentaire (*dietary inflammatory index)* a donc été élaboré à partir d'une revue de la littérature pour identifier les nutriments et composants alimentaires qui étaient associés à une augmentation ou une diminution des concentrations d'un ou plusieurs biomarqueurs inflammatoires. Depuis la publication de sa version révisée, cet indice a été associé au risque cardiovasculaire ainsi qu'au risque de cancer colorectal [194, 195]. Puis, considérant le contexte inflammatoire de la grossesse, il est intéressant

d'évaluer les associations potentielles entre cet indice et les concentrations de différents marqueurs inflammatoires. L'indice inflammatoire alimentaire a d'ailleurs été calculé puis évalué en association avec des variables métaboliques dans le cadre de plusieurs études réalisées auprès de femmes enceintes [196-199]. Les associations entre cet indice et certains marqueurs inflammatoires ont également été examinées au sein de la cohorte ANGE et sont présentées au chapitre 10, où la méthode de calcul de l'indice inflammatoire alimentaire est aussi détaillée. Enfin, bien que de plus en plus d'auteurs s'intéressent à la qualité alimentaire en contexte gestationnel, presqu'aucune étude ne l'a mesurée de façon prospective, à chaque trimestre de la grossesse. Il importe de caractériser cette évolution, puisque, comme mentionné en introduction, l'impact de l'alimentation pourrait différer selon le trimestre durant lequel elle est évaluée.

3.3. Variation de la qualité alimentaire pendant la grossesse et facteurs pouvant l'influencer

3.3.1. Évaluation prospective de la qualité alimentaire durant la grossesse

Il a souvent été suggéré que la grossesse était une période associée à un plus grand intérêt pour les informations nutritionnelles spécifiques à la grossesse, à une plus grande sensibilisation par rapport à la nutrition ainsi qu'à une plus grande motivation à adopter de saines habitudes alimentaires [200-203]. De plus, et considérant certaines recommandations nutritionnelles spécifiques à la grossesse, comme manger davantage et adopter de saines habitudes alimentaires [81], il serait logique de croire que la consommation d'aliments « sains » est augmentée durant la grossesse. Cependant, la littérature actuelle ne permet pas de confirmer cette hypothèse. En effet, d'une part, une étude réalisée en Malaisie a observé une augmentation du score HEI, du premier au deuxième trimestre, suivie par une diminution entre le deuxième et le troisième trimestre [204]. D'autre part, une diminution progressive du score HEI chez des femmes enceintes avec un surpoids ou une obésité ainsi qu'une association inverse entre ce même score et l'avancement de la grossesse ont aussi été rapportées dans deux études distinctes [178, 180]. Des études prospectives supplémentaires sont donc nécessaires pour mieux comprendre comment évolue la qualité alimentaire en contexte prénatal. Une caractérisation des facteurs pouvant potentiellement influencer la qualité de l'alimentation des femmes enceintes serait également pertinente. Pour ces raisons, le chapitre 7 de cette thèse présente une caractérisation prospective de la qualité alimentaire d'un échantillon de femmes enceintes québécoises, évaluée par le C-HEI, ainsi qu'une évaluation des facteurs qui y sont associés.

3.3.2. Habitudes alimentaires en préconception

La qualité de l'alimentation en préconception pourrait influencer les habitudes alimentaires durant la grossesse de deux façons. D'un côté, si l'alimentation en préconception n'est pas perçue comme optimale par la femme enceinte, celle-ci pourrait décider d'y apporter des changements, pour sa santé et celle de son bébé [205, 206]. En fait, selon une revue de la littérature, les femmes augmenteraient leurs apports en fruits et légumes puis diminueraient leur consommation d'aliments de type fast-food, et ce, de la préconception à la grossesse [207]. D'un autre côté, il est possible que les habitudes alimentaires en préconception soient maintenues durant la grossesse, si celles-ci étaient déjà perçues comme adéquates par la femme enceinte, par exemple. D'ailleurs, trois études ont rapporté que l'alimentation des femmes changeait très peu, de la préconception à la grossesse [208-210]. La variabilité des résultats rapportés dans la littérature pourrait être liée au fait que certaines grossesses sont intentionnelles, et d'autres non. En fait, des études ont noté des habitudes de vie plus saines (ex. diminution ou arrêt de la consommation d'alcool, prise d'un supplément d'acide folique, etc.) chez les femmes qui planifiaient une grossesse, en comparaison avec celles qui n'avaient pas l'intention de devenir enceintes [211-214]. Une récente revue de la littérature n'a cependant pas observé d'association entre le caractère intentionnel d'une grossesse, la consommation de fruits et légumes et la pratique d'activité physique en préconception [215]. Toutefois, cette même revue rapporte que les femmes qui avaient l'intention de devenir enceintes avaient, durant leur grossesse, de meilleures habitudes alimentaires et d'activité physique [215]. Les associations entre la planification d'une grossesse et l'alimentation en préconception mériteraient donc plus d'attention. C'est d'ailleurs pourquoi nous avons comparé l'alimentation de femmes enceintes à celle de femmes en âge de procréer et planifiant une grossesse. Les résultats de cette analyse sont présentés au chapitre 8.

D'autres variables en préconception ont aussi été associées à la qualité alimentaire des femmes enceintes. En fait, un IMC prégrossesse plus élevé est lié à une qualité alimentaire moindre durant la grossesse [180, 216-218]. Il est probable, comme mentionné plus tôt, que des habitudes alimentaires non optimales en préconception contribuent à un IMC prégrossesse plus élevé [12]. Cela pourrait expliquer le lien observé entre le statut pondéral prégrossesse et la qualité alimentaire des femmes enceintes, d'autant plus si les habitudes alimentaires sont maintenues de la préconception à la grossesse. Cette association devrait tout de même être étudiée plus en profondeur, comme il en sera question au chapitre 7.

3.3.3. Facteurs physiologiques associés à la qualité alimentaire

Comme il a été mentionné à la section 1.2, les nombreuses adaptations physiologiques essentielles au bon déroulement de la grossesse peuvent occasionner des inconforts gastro-intestinaux comme des nausées et des vomissements [32, 33]. Selon une méta-analyse ayant utilisé des données provenant de 13 pays, la prévalence de ces symptômes auprès des femmes enceintes varierait entre 35 et 91% [219]. Bien que l'étiologie de ces symptômes ne soit pas tout à fait connue, il est possible qu'ils aient une influence sur la quantité et le type d'aliments consommés, notamment en ayant un effet sur les sensations d'appétit durant la grossesse [220]. Toutefois, les liens entre les nausées et vomissements et la qualité alimentaire des femmes enceintes semblent complexes. En fait, la présence de nausées et vomissements a été associée à des modèles alimentaires indiquant à la fois une meilleure ainsi qu'une moins bonne qualité alimentaire [221-225]. Des femmes enceintes canadiennes ayant participé à des groupes de discussion ont quant à elles identifié la présence de nausées et vomissements comme une barrière à l'adoption de comportements alimentaires sains [226]. Puis, d'autres symptômes ayant été associés aux changements hormonaux de la grossesse, comme l'apparition de fortes envies ou aversions alimentaires, semblent aussi être associés, favorablement ou non, aux habitudes alimentaires des femmes enceintes [227-230]. Ainsi, plus d'études sont nécessaires pour mieux caractériser les associations entre les symptômes gastro-intestinaux liés à la grossesse, les préférences alimentaires et la qualité de l'alimentation des femmes enceintes. Ces facteurs sont analysés et discutés au chapitre 7.

3.3.4. Facteurs sociodémographiques associés à la qualité alimentaire

Plusieurs variables socioéconomiques et démographiques ont été identifiées comme étant associées à la qualité alimentaire des femmes enceintes. En fait, selon une revue de la littérature incluant 17 articles de 12 cohortes distinctes, il existerait un gradient social en ce qui concerne la qualité de l'alimentation des femmes enceintes [231]. Ainsi, le fait d'être plus âgée, plus éduquée et d'avoir un revenu plus élevé serait associé à l'adoption d'habitudes alimentaires plus saines [231]. En outre, une étude de cohorte canadienne avait observé une association positive entre le support social perçu par les femmes enceintes et la qualité de leur alimentation, évaluée par la version canadienne du *Diet Quality Index for Pregnancy* [232]. Ces associations entre le statut socioéconomique et la qualité alimentaire avaient été rapportées dans la population adulte générale, et pourraient s'expliquer, en partie, par le coût plus élevé des aliments qui sont généralement associés à une meilleure qualité

alimentaire [233-235]. D'autres variables, comme la proximité des supermarchés ainsi que le niveau de connaissances en nutrition, pourraient aussi expliquer les associations entre le statut socioéconomique et la qualité de l'alimentation [236-238]. Enfin, peu d'études ont exploré les associations entre la qualité alimentaire et le niveau de connaissances en nutrition durant la grossesse. Il semblerait néanmoins que ce dernier soit lié aux habitudes alimentaires et d'activité physique, selon des groupes de discussion effectués auprès de femmes enceintes canadiennes [226]. Une autre étude canadienne a d'ailleurs rapporté qu'une meilleure compréhension des impacts de l'alimentation prénatale sur la santé de l'enfant à naître était associée à une qualité alimentaire plus élevée chez des femmes enceintes [239]. Les facteurs sociodémographiques mentionnés ci-haut ont été évalués en association avec la qualité alimentaire des femmes enceintes dans le cadre de cette thèse et seront discutés au chapitre 7.

3.3.5. Facteurs comportementaux associés à la qualité alimentaire

Dans la population adulte générale, les individus qui rapportent un comportement considéré comme bénéfique pour la santé, par exemple le fait de consommer beaucoup de fruits et légumes, semblent aussi rapporter d'autres comportements sains, comme la pratique régulière d'activité physique [240]. Plusieurs études réalisées auprès de femmes enceintes ont d'ailleurs observé que celles qui rapportaient une qualité alimentaire moindre avaient un niveau d'activité physique plus bas [231, 232, 241, 242]. Cette relation n'est peut-être pas causale, mais il semble que la qualité de l'alimentation et la pratique d'activité physique font partie d'un ensemble de comportements perçus comme étant plus sains. Toutefois, les associations entre la qualité alimentaire et l'activité physique n'ont pas été évaluées de façon prospective, à chaque trimestre de la grossesse. Ces associations mériteraient d'être investiguées davantage, notamment, en raison de la diminution documentée du niveau d'activité physique des femmes enceintes au cours des trimestres [243-246]. Le chapitre 7 présente d'ailleurs les associations, à chaque trimestre, entre la pratique d'activité physique et la qualité alimentaire des femmes enceintes.

D'autres comportements pourraient être associés à la qualité alimentaire en contexte prénatal. En fait, bien qu'ils aient été peu étudiés durant la grossesse, certains comportements et attitudes face à l'alimentation semblent être corrélés à une alimentation de meilleure qualité chez différentes populations non enceintes [247-252]. Des chercheurs australiens ont quant à eux rapporté que des habitudes alimentaires plus saines durant la grossesse étaient associées à certaines dimensions du

principe de l'alimentation intuitive et/ou « pleine conscience » (*mindful eating*) [253]. Ces principes ont chacun leur définition, mais ils se basent tous les deux sur une écoute et une prise de conscience des signaux physiologiques de faim et de satiété [254]. De plus, des résultats publiés par notre équipe de recherche ont montré des associations entre la « concordance entre les besoins du corps et les apports alimentaires », une des quatre dimensions du score d'alimentation intuitive, et le C-HEI aux deuxième et troisième trimestres de grossesse [255]. Bien qu'intéressants, ces résultats et ceux mentionnés ci-haut ne sont toutefois pas suffisants pour conclure que les attitudes et comportements face à l'alimentation sont corrélés à la qualité de l'alimentation des femmes enceintes.

Il demeure pertinent de s'intéresser aux attitudes et comportements des femmes enceintes face à leur alimentation, puisque ceux-ci pourraient être influencés par le contexte particulier de la grossesse et les changements corporels qui y sont associés. En fait, l'image corporelle des femmes enceintes, un concept de plus en plus étudié dans la population générale et enceinte, a été associée à certaines attitudes et comportements face à l'alimentation. La prochaine section discutera de ces associations.

3.3.5.1. Image corporelle et attitudes face au gain de poids gestationnel

L'image corporelle est un construit multidimensionnel englobant les perceptions, les pensées, les sentiments et les comportements d'une personne envers son corps, en particulier son apparence [256]. Durant la grossesse, l'image corporelle des femmes enceintes peut être affectée par leur prise pondérale rapide ainsi que par les nombreux changements émotionnels et psychologiques associés à la période prénatale [257, 258]. En fait, l'insatisfaction par rapport au poids ou à l'image corporelle semble être de plus en plus prévalente auprès des femmes enceintes et associée à différents symptômes dépressifs ainsi que certains comportements alimentaires défavorables, comme une plus grande restriction alimentaire [259-265]. À l'inverse, certains auteurs ont suggéré que la grossesse serait associée à une image corporelle plus positive, voire améliorée, en comparaison avec la préconception [266, 267]. Considérant ces résultats contradictoires, et puisque l'image corporelle est un concept multidimensionnel et complexe à évaluer, il peut être pertinent de s'intéresser à une dimension précise de l'image corporelle, comme les attitudes des femmes enceintes face à leur gain de poids gestationnel. D'ailleurs, l'insatisfaction corporelle durant la grossesse semble varier selon le statut pondéral en préconception ainsi que selon le gain de poids gestationnel [259, 268-271].

Il convient de mentionner que malgré sa nécessité, le gain de poids gestationnel va à l'encontre de l'idéal de minceur mis de l'avant par la culture sociale de plusieurs pays, ce qui peut contribuer à une image corporelle altérée [272-274]. En fait, selon une analyse qualitative des expériences de femmes enceintes australiennes par rapport à leur image corporelle, les changements relatifs au gain de poids (ex. augmentation du volume des seins, de l'abdomen, des hanches, rétention d'eau, etc.) ont été mis en évidence pour leur impact sur la satisfaction des femmes par rapport à leur apparence [275]. Ainsi, le fait de concevoir le gain de poids gestationnel de façon positive ou négative semble être déterminant de l'image corporelle durant la grossesse. Des attitudes négatives et une préoccupation par rapport au poids durant la grossesse ont aussi été associées à des comportements alimentaires restrictifs, c'est-à-dire une restriction consciente de l'apport alimentaire dans le but de contrôler le poids corporel [272, 276]. Cependant, plus d'études sont nécessaires pour caractériser les associations entre les attitudes face au gain de poids gestationnel et d'autres comportements alimentaires, comme l'alimentation intuitive. Le chapitre 9 présente une analyse des attitudes de femmes enceintes québécoises face à leur gain de poids gestationnel, en association avec leurs comportements alimentaires, leur statut pondéral prégrossesse ainsi que leur gain de poids.

En somme, la qualité de l'alimentation durant la grossesse est associée à de nombreux facteurs physiologiques, sociodémographiques et comportementaux qui, ensemble, ont le potentiel d'influencer la santé de la mère et celle de l'enfant à naître. Étant donné l'aspect longitudinal de la grossesse, il est probable que ces facteurs et leurs associations avec la qualité alimentaire varient au cours des trimestres. Ainsi, une caractérisation prospective de la qualité alimentaire durant la grossesse est essentielle, d'autant plus que cette dernière semble sous-optimale pour une proportion considérable de femmes enceintes [277-280]. Cette donnée est préoccupante, considérant qu'une alimentation de moindre qualité a été associée à certaines variables métaboliques impliquées dans le développement de différentes complications de grossesse [9]. Ces associations sont d'ailleurs abordées dans la prochaine section.

3.4. Liens entre la qualité alimentaire et différents marqueurs métaboliques

3.4.1. Marqueurs inflammatoires

Le potentiel anti-inflammatoire de certains modèles alimentaires riches en fruits, légumes, grains entiers et gras insaturés, comme la diète méditerranéenne, est plutôt bien documenté dans la

population adulte générale [281-284]. Cependant, les associations entre ces modèles alimentaires et les concentrations de différents marqueurs inflammatoires, comme la protéine C-réactive (CRP) et l'IL-6, sont moins claires lorsqu'elles sont analysées dans le contexte de la grossesse. En effet, alors que certains auteurs ont observé qu'une meilleure adhésion à la diète méditerranéenne ou qu'un faible indice inflammatoire alimentaire durant la grossesse étaient associés à des concentrations plus basses de CRP et IL-6, d'autres auteurs n'ont observé que très peu et même aucune corrélation entre l'alimentation et les marqueurs inflammatoires [40]. Ces résultats mitigés pourraient s'expliquer par une variation, au cours des étapes de la grossesse, des concentrations de différents marqueurs inflammatoires [285-287]. En fait, les concentrations élevées des marqueurs pro-inflammatoires observées au début de la grossesse semblent diminuer progressivement jusqu'à la fin de la grossesse, pour ensuite réaugmenter, en préparation à l'accouchement [36]. De plus, le gain de tissu adipeux associé à la grossesse ainsi que le statut pondéral prégrossesse pourraient aussi influencer la sécrétion et la production d'adipocytokines pro-inflammatoires, comme l'IL-6 [288, 289]. L'évaluation des associations entre la qualité alimentaire et les marqueurs de l'inflammation durant la grossesse devrait donc se faire de façon prospective et prendre en considération le statut pondéral prégrossesse et le gain de poids gestationnel. L'étude de ces associations est importante, car comme il a été discuté au début de ce chapitre, l'état inflammatoire de bas grade en début de grossesse peut, en présence de certains facteurs de risque, comme une alimentation de moindre qualité, s'amplifier et être associé au développement de différentes complications prénatales [37, 39]. Le chapitre 10 présente une évaluation prospective des concentrations d'IL-6 et de CRP au cours des trimestres de la grossesse, en association avec le score d'adhésion à la diète méditerranéenne et l'indice inflammatoire alimentaire.

3.4.2. Marqueurs de l'homéostasie du glucose

Il a été mentionné au début de ce chapitre que la grossesse est associée avec une résistance à l'insuline qui peut, dans certaines conditions, évoluer en un diabète gestationnel [43, 44]. Outre une glycémie et des concentrations d'insuline altérées, plusieurs marqueurs ont été associés à la résistance à l'insuline en période gestationnelle, tel que la leptine et l'adiponectine [45, 290]. Ces deux adipocytokines sont impliquées dans les mécanismes liés à l'homéostasie du glucose, mais aussi dans la régulation des sensations de faim et de satiété. En fait, les concentrations de leptine sont proportionnelles à la masse adipeuse, reflétant ainsi les réserves énergétiques d'un individu et

induisant une sensation de satiété sur le long terme [291]. Des concentrations élevées de leptine ont été observées en situation de résistance à l'insuline, comme l'obésité et la grossesse [43, 291]. Les concentrations d'adiponectine, quant à elles, sont inversement proportionnelles au statut pondéral et sont associées à une meilleure sensibilité à l'insuline [291, 292]. Contrairement à la leptine, les concentrations d'adiponectine diminuent en contexte gestationnel, ce qui va de pair avec la diminution de la sensibilité à l'insuline associée à la grossesse [43, 291]. Les concentrations de leptine et d'adiponectine sont également associées à des états pro- et anti-inflammatoires, respectivement [291].

Vu les liens existants entre les concentrations de leptine et d'adiponectine et la résistance à l'insuline et l'inflammation, certains auteurs se sont intéressés à leurs associations potentielles avec l'alimentation. Une meilleure adhésion à la diète méditerranéenne a entre autres été associée à des concentrations plus élevées d'adiponectine et plus faibles de leptine dans des populations non enceintes [293, 294]. Des apports en nutriments ou aliments spécifiques, comme les fibres et les légumes ont également été corrélés inversement aux concentrations de leptine de femmes japonaises [295]. Durant la grossesse, une étude effectuée auprès de femmes enceintes avec un IMC prégrossesse normal a observé une diminution moins importante (en pourcentage) des concentrations d'adiponectine, du 1er au 3e trimestre chez les femmes qui présentaient l'adhésion la plus élevée à la diète méditerranéenne [296]. D'autres études ont quant à elles observé des associations entre des modèles alimentaires ou des nutriments liés à une qualité alimentaire moindre, et des concentrations plus élevées de leptine, et plus faibles d'adiponectine [297-300]. Cependant, aucune des études mentionnées ci-dessus n'a caractérisé ces associations à chaque trimestre de la grossesse. Parallèlement à ce qui a été mentionné plus tôt par rapport aux marqueurs inflammatoires, il est possible que les mécanismes physiologiques naturels associés à la grossesse, le gain de tissu adipeux ainsi que le statut pondéral prégrossesse influencent les associations entre l'alimentation et les concentrations maternelles de leptine et d'adiponectine. Par exemple, les femmes enceintes ayant un IMC prégrossesse plus élevé et qui gagnent plus poids durant leur grossesse ont peut-être une augmentation plus marquée de leurs concentrations de leptine au cours des trimestres de la grossesse. Les variables pondérales devraient donc être prises en considération lors de l'évaluation des associations entre la qualité alimentaire des femmes enceintes et leurs concentrations de leptine et d'adiponectine. C'est d'ailleurs ce qui a été fait dans le cadre des travaux présentés au chapitre 10.

En résumé, les liens existants entre l'alimentation et les variables de la santé sont complexes, surtout durant la période prénatale, où s'installent de nombreux changements anatomiques, métaboliques et psychologiques. Il est aussi possible que l'étude des associations entre l'alimentation et la santé prénatale ait été affectée par une évaluation imprécise ou incomplète des apports et du statut nutritionnel des femmes enceintes. Ainsi, et en considérant tous les éléments discutés dans ce chapitre, les travaux inclus dans la présente thèse visent à caractériser prospectivement les apports et la qualité alimentaires d'un échantillon de femmes enceintes québécoises, en comparaison avec les recommandations en vigueur ainsi qu'en association avec certains marqueurs de la santé métabolique. Il s'agit, à notre connaissance, de la première étude ayant évalué l'alimentation de femmes enceintes québécoises en utilisant un design prospectif et en considérant les variables physiologiques, démographiques et comportementales qui pourraient influencer, ou être influencées par, les habitudes alimentaires durant la grossesse. Cette caractérisation prospective apparaît comme essentielle pour identifier des cibles d'interventions nutritionnelles et de promotion des saines habitudes de vie spécifiques aux femmes enceintes québécoises. L'objectif général et les sous objectifs de cette thèse ainsi que les hypothèses qui y sont associées sont présentés en détail au prochain chapitre.

Chapitre 2 – Objectifs et hypothèses

Cette thèse avait comme **objectif général** d'évaluer de façon quantitative et qualitative les apports et la qualité alimentaires durant la grossesse ainsi que d'identifier les variables physiologiques, sociodémographiques et comportementales qui leur sont associées.

Hypothèse générale. Les apports et la qualité alimentaires augmentent au cours des trimestres, et une meilleure qualité alimentaire est associée avec un profil métabolique favorable durant la grossesse.

Les objectifs spécifiques qui sont présentés ci-dessous ont ensuite été définis pour réaliser l'objectif général de la présente thèse.

Objectif spécifique 1. Répertorier les études ayant mesuré la dépense énergétique durant la grossesse et examiner la concordance avec les apports énergétiques recommandés.

Hypothèse 1. Les études rapportent une augmentation de la dépense énergétique totale et au repos durant la grossesse, mais cette augmentation est moins importante que ce qui est suggéré dans les recommandations d'apports énergétiques pour les femmes enceintes.

Objectif spécifique 2. Caractériser les apports nutritionnels durant la grossesse.

Sous-objectif spécifique 2.1. Évaluer prospectivement les apports nutritionnels des femmes enceintes en association avec les recommandations.

Sous-objectif spécifique 2.2. Mesurer prospectivement les concentrations de 25(OH)D et examiner les facteurs qui les influencent.

Hypothèse 2. Les apports en énergie et nutriments ainsi que les concentrations de 25(OH)D augmentent au cours des trimestres, et une majorité de femmes ont des apports alimentaires insuffisants en vitamine D. La prise de suppléments améliore l'atteinte des recommandations en vitamine D et est associée aux concentrations en 25(OH)D.

Objectif spécifique 3. Caractériser la qualité alimentaire pendant la période prénatale.

Sous-objectif spécifique 3.1. Évaluer prospectivement la qualité alimentaire des femmes enceintes, et les facteurs qui y sont associés.

Sous-objectif spécifique 3.2. Comparer la qualité alimentaire des femmes enceintes avec celle de femmes 1) en âge de procréer et 2) désirant devenir enceinte.

Hypothèse 3. La qualité alimentaire augmente au cours des trimestres et varie selon le statut pondéral prégrossesse, la présence de nausées et de vomissements, l'âge et le niveau d'éducation. La qualité alimentaire des femmes enceintes est plus élevée que celle de femmes en âge de procréer et qui planifient devenir enceintes.

Objectif spécifique 4. Évaluer les attitudes face au gain de poids gestationnel en association avec l'IMC prégrossesse et les comportements alimentaires durant la grossesse.

Hypothèse 4. Les femmes ayant un IMC prégrossesse à l'intérieur des limites recommandées rapportent des attitudes positives face au gain de poids gestationnel, par rapport aux femmes avec un surpoids et une obésité. Des attitudes positives envers le gain de poids gestationnel sont associées à des comportements alimentaires plus sains et à un score plus élevé d'alimentation intuitive.

Objectif spécifique 5. Caractériser l'évolution de la leptine, l'adiponectine, l'IL-6 et la CRP durant la grossesse et examiner leurs associations avec l'alimentation.

Sous-objectif spécifique 5.1. Caractériser les changements dans les concentrations d'IL-6, de CRP, de leptine et d'adiponectine au cours des trimestres et selon l'IMC prégrossesse.

Sous-objectif spécifique 5.2. Évaluer les associations entre la qualité alimentaire, mesurée par l'indice inflammatoire alimentaire et l'adhésion à la diète méditerranéenne, et les concentrations d'IL-6, de CRP, de leptine ainsi que d'adiponectine.

Hypothèse 5. Les concentrations d'IL-6, de CRP et de leptine augmentent tandis que les concentrations d'adiponectine diminuent au cours des trimestres de la grossesse. Ces changements sont plus marqués chez les femmes avec un IMC prégrossesse plus élevé. À chaque trimestre, l'indice inflammatoire alimentaire est corrélé aux concentrations d'IL-6, de CRP et de leptine et inversement associé aux concentrations d'adiponectine; et vice-versa pour l'adhésion à la diète méditerranéenne.

Le prochain chapitre présente un résumé des méthodes utilisées pour réaliser ces objectifs et répondre aux hypothèses formulées ci-haut.

Chapitre 3 – Méthodes

Cette thèse présente des travaux de recherche ayant utilisé des données recueillies au sein de trois cohortes distinctes : ANGE (Apports Nutritionnels durant la GrossessE), ANGE-Contrôle (Apports Nutritionnels durant la GrossessE – Cohorte contrôle) et PREDISE (PREDicteurs Individuels, Sociaux et Environnementaux). Ces cohortes sont décrites brièvement dans la présente section. Pour faciliter la compréhension de la méthodologie, un tableau résumé des différentes mesures effectuées au sein de chacune des cohortes est présenté à la fin de cette section.

Description des cohortes

Cohorte ANGE

Quatre-vingt-six femmes enceintes recrutées d'avril 2016 à mai 2017 au CHU de Québec - Université Laval (CRCHUL) et résidant dans la région de la Capitale-Nationale ont été incluses dans le projet ANGE. Le recrutement s'est effectué via diverses publicités (exemples : courriel aux employés du CHU de Québec, courriel aux étudiants et employés de l'Université Laval, annonces dans les réseaux sociaux, etc.). Les femmes de moins de 18 ans et ayant un âge gestationnel supérieur à 11 semaines de grossesse au moment du recrutement ont été exclues. Les femmes atteintes d'une maladie chronique déjà diagnostiquée (diabète de type 1 et 2, maladie rénale, maladies inflammatoires et auto-immunes) ont aussi été exclues. Le projet était constitué d'un volet Web (questionnaires à compléter à domicile) et de cinq visites au CRCHUL. Sept femmes ont abandonné le projet en raison d'une fausse couche (n=3) ou de l'incapacité de consacrer du temps à l'étude (n=4). Ainsi, l'échantillon final du projet ANGE comprend 79 femmes pour lesquelles nous avons des données nutritionnelles et biochimiques à chacun des trimestres. Les données recueillies au sein de la cohorte ANGE ont été utilisées dans le cadre des travaux présentés aux chapitres 5 à 10.

Cohorte ANGE-Contrôle

En date du 8 décembre 2021, le projet ANGE-Contrôle est toujours en cours et a recruté, depuis juin 2017, 326 femmes de la région de la Capitale-Nationale désirant devenir enceintes dans la prochaine année. Similairement au projet ANGE, le recrutement s'est fait via diverses publicités (exemples : courriel aux employés du CHU de Québec, courriel aux étudiants et employés de l'Université Laval,

annonces dans les réseaux sociaux, etc.). Les femmes de moins de 18 ans et/ou atteintes d'une maladie chronique déjà diagnostiquée (ex. diabète de type 1 et 2, maladies inflammatoires et auto-immunes) ont été exclues de cette cohorte. Seulement des données Web ont été recueillies (questionnaires à compléter à domicile) au sein de cette cohorte. Des 326 femmes initialement recrutées, 28 sont devenues enceintes durant le projet, quatre n'ont pas complété l'ensemble des questionnaires Web et quatre autres ont abandonné en raison d'un manque de temps à accorder au projet. Les travaux présentés au chapitre 8 de cette thèse ont analysé les apports et la qualité alimentaire de 55 femmes provenant de la cohorte ANGE-Contrôle.

Cohorte PREDISE

Le projet PREDISE visait à mesurer l'adhésion aux recommandations visant la saine alimentation chez des adultes francophones de la province de Québec. Le recrutement a été effectué d'août 2015 à avril 2017 dans cinq régions administratives du Québec (Estrie, Saguenay-Lac-Saint-Jean Capitale-Nationale/Chaudière-Appalaches, Montréal et Mauricie) par une firme de recherche et d'enquête utilisant une méthode d'appels téléphoniques aléatoires. Le recrutement a été conçu afin que les participants représentent la population adulte francophone de chaque région en fonction du sexe et de l'âge. Les individus présentant une forme de malabsorption intestinale ont été exclus du projet, de même que les femmes enceintes et allaitantes. Des données Web (questionnaires à compléter à domicile), anthropométriques et biochimiques furent recueillies dans le cadre de ce projet. Parmi les 1849 participants initialement recrutés, 1147 hommes et femmes âgés entre 18 et 65 ans ont complété les questionnaires Web du projet [184]. De cet échantillon, 92 femmes non enceintes et non allaitantes étaient âgées entre 18 et 40 ans et vivaient dans la région de Chaudière-Appalaches/Capitale-Nationale. Les données alimentaires recueillies auprès d'un sous-échantillon de 55 femmes en âge de procréer de la cohorte PREDISE (sélectionnées parmi les 92 mentionnées ci-haut) ont été analysées dans le cadre des travaux présentés au chapitre 8.

Cueillette de données

Les données alimentaires des trois cohortes décrites ci-haut ont été obtenues grâce aux deux à trois rappels de 24h Web complétés à chaque trimestre chez les participantes de la cohorte ANGE, puis à un seul moment chez les participantes des cohortes ANGE-Contrôle et PREDISE. Les données recueillies par les rappels de 24h ont permis de calculer différents indices de qualité alimentaire, qui

seront décrits aux chapitres 7, 8 et 10. Pour les participantes des cohortes ANGE et ANGE-Contrôle, un questionnaire Web sur la prise de suppléments alimentaires a également été complété. Ensuite, les participantes des trois cohortes ont complété d'autres questionnaires Web permettant d'évaluer les variables sociodémographiques et la pratique d'activité physique. Les participantes du projet ANGE-Contrôle ont eu à compléter un questionnaire additionnel sur leur état de santé. Les données de taille et de poids prégrossesse rapportées dans ce questionnaire ont permis de calculer l'IMC des femmes de la cohorte ANGE-Contrôle. Finalement, les participantes du projet ANGE ont complété des questionnaires Web supplémentaires portant sur les symptômes associés à la grossesse (nausées, vomissements, préférences alimentaires) les attitudes et comportements face au gain de poids gestationnel (*Pregnancy Weight Gain Attitude Scale*) ainsi que les comportements alimentaires (le *Three-Factor Eating Questionnaire* et l'*Intuitive Eating Scale-2*).

Des visites en centre de recherche ont eu lieu dans le cadre des projets PREDISE et ANGE. Lors des visites du projet PREDISE, des mesures anthropométriques ont été effectuées et ont permis d'évaluer, entre autres, l'IMC. L'IMC prégrossesse des participantes du projet ANGE a quant à lui été calculé en utilisant le poids prégrossesse auto-rapporté, puis la taille mesurée lors de la première visite du projet. Des prélèvements sanguins à jeun ont été effectués à chaque trimestre de grossesse, au sein de la cohorte ANGE, et ont été utilisés pour évaluer les concentrations de 25(OH)D, leptine, adiponectine, IL-6 et CRP, entre autres.

Tableau 1. Caractéristiques et mesures effectuées au sein des différentes cohortes

	ANGE	ANGE-Contrôle[1]	PREDISE[1]
Nombre de participantes	**79**	**290**	**92**
Statut	Enceintes	Non enceintes planifiant une grossesse	Non enceintes
Poids prégrossesse (ou actuel)	Auto-rapporté	Auto-rapporté	Mesuré
Taille	Mesurée	Auto-rapportée	Mesurée
Questionnaires complétés[2]			
Rappel de 24h	9 (3 par trimestre)	3	3
Suppléments	3 (1 par trimestre)		
Variables sociodémographiques	1	1	1
Activité physique	3 (1 par trimestre)	1	1
Symptômes de la grossesse	1	-	-
TFEQ	3 (1 par trimestre)	-	-
IES-2	3 (1 par trimestre)	-	-
PWGAS	1	-	-
État de santé général	-	1	-
Biomarqueurs (nombre de mesures)			
Dosage 25(OH)D	3 (1 par trimestre)		
Dosage leptine	3 (1 par trimestre)		
Dosage adiponectine	3 (1 par trimestre)		
Dosage IL-6	3 (1 par trimestre)		
Dosage CRP	3 (1 par trimestre)		

[1]Seulement 55 femmes par cohorte ont été appariées aux femmes de la cohorte ANGE et incluses dans les analyses présentées au chapitre 8. La taille d'échantillon présentée correspond au nombre total de femmes en âge de procréer dans la région de Chaudière-Appalaches/Capitale-Nationale.

[2]Seuls les questionnaires analysés dans le cadre des travaux inclus dans la présente thèse sont mentionnés. D'autres questionnaires ont été complétés par les différentes cohortes.

Abréviations : ANGE, Apports Nutritionnels Durant la Grossesse; ANGE-Contrôle, Apports Nutritionnels Durant la Grossesse – Cohorte Contrôle; IES-2, Intuitive Eating Scale-2; PREDISE, PREdicteurs des Déterminants Individuels, Sociaux et Environnementaux de la saine alimentation; PWGAS, Pregnancy Weight Gain Attitude Scale; TFEQ, Three-Factor Eating Questionnaire; 25(OH)D, 25-hydroxyvitamine D.

Chapitre 4 – Energy expenditure during pregnancy: a systematic review

Résumé

Cette revue a répertorié les études prospectives qui ont mesuré la dépense énergétique au repos (DÉR) ou totale (DÉT) pendant la grossesse. Quatre bases de données ont été consultées pour identifier les publications pertinentes jusqu'au 14 novembre 2019. Toutes les études mesurant la DÉR ou la DÉT plus d'une fois pendant la grossesse ont été incluses. Deux auteurs ont indépendamment examiné 4852 références. Au total, 32 études ont été retenues. Bien que plusieurs études aient rapporté une augmentation de la DÉR ou de la DÉT au cours de la grossesse, l'amplitude de cette augmentation était très variable d'une étude à l'autre. Les participantes étudiées étaient généralement caucasiennes et de poids normal. Plusieurs études n'ont pas rapporté des covariables importantes telles que l'IMC et l'adéquation du gain de poids gestationnel. Plus d'études longitudinales sont nécessaires pour quantifier l'augmentation de la dépense énergétique au cours des trimestres de la grossesse.

Title page

Title: Energy expenditure during pregnancy: a systematic review

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Keywords: energy expenditure, energy intake, energy needs, energy requirements, pregnancy

Abstract

Context: Contrary to nutritional guidelines, accumulating evidence shows that pregnant women's energy intakes remain stable throughout trimesters. Although pregnant women may eat below their needs or underreport their energy intakes, it is also relevant to question how energy requirements – estimated through measurements of energy expenditure (EE) – change throughout pregnancy.

Objective: This review examined prospective studies that measured EE during pregnancy, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Data sources: PubMed/MEDLINE, Web of Science, Embase, and CINAHL databases were searched to identify relevant publications up to November 14, 2019.

Study selection: All studies that measured EE prospectively and objectively during pregnancy were included in this systematic review. Two authors independently screened 4852 references. A total of 32 studies were included in the final analysis.

Data extraction: One author extracted data and assessed the risk of bias, and a second author did so for a random sample of studies (n = 7; 22%).

Data analysis: Increases in resting EE ranged from 0.5% to 18.3% (8–239 kcal), from 3.0% to 24.1% (45–327 kcal), and from 6.4% to 29.6% (93–416 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively. Increases in total EE ranged from 4.0% to 17.7% (84–363 kcal), from 0.2% to 30.2% (5–694 kcal), and from 7.9% to 33.2% (179–682 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively. Participants were mainly of normal weight, although many studies did not report important covariates such as prepregnancy body mass index and gestational weight gain adequacy.

Conclusions: Additional high-quality longitudinal studies (ie, with multiple objective measurements of EE in all periods of pregnancy while considering important confounding variables, like gestational weight gain) are required.

Introduction

Pregnancy represents a crucial period in a woman's life owing to, among other things, the numerous physiological changes the mother undergoes to ensure optimal fetal growth and development.[1,2] In fact, to account for the increased maternal energy expenditure (EE) due to the mother's weight gain and the development of maternal and fetal tissues, the dietary reference intakes recommend a daily increase of 340 and 452 kcal in energy intake (EI) in the first and third trimesters, respectively.[3] These additional EIs should support the mother's increasing EE and allow the accumulation of energy stores during pregnancy.[3,4] Nevertheless, it should be noted that the dietary reference intake recommendations are based on a limited number of studies that all took place before 2000[5–19] and on a theoretical model developed by Hytten and Chamberlain in 1991.[20] It is therefore possible that the resulting EI recommendations do not reflect the needs of pregnant women nowadays, who are generally older,[21] have more sedentary behaviors, and have different body compositions than the populations studied at the time these recommendations were being developed.[22–24] The EI recommendations have not been revised since then, even though the guidelines for gestational weight gain (GWG) were updated in 2009 to better represent the needs of women from all prepregnancy weight categories.[25]

Furthermore, other authors have observed, through longitudinal studies, little to no augmentation in EI across trimesters of pregnancy, which is in contradiction to current recommendations.[26–29] One systematic review evaluating studies that measured EI throughout pregnancy also found no prospective increase in EI even though women gained a significant amount of weight during their pregnancy.[30] In fact, excessive gestational weight gain (GWG) is now highly prevalent, affecting 1 in 2 women during pregnancy[31,32] – a finding that is in contradiction with the lack of increase in EI observed by other authors. Indeed, since EI correlates with GWG,[33] it is contradictory to observe reports of stable EI and excessive GWG at the same time. Furthermore, although numerous systematic reviews and meta-analysis have investigated the complex associations between EI and GWG,[30,33–36] very few studies have investigated the other component of energy balance during pregnancy: energy expenditure. Thus, because contradictory results are reported in regards to EI and GWG, it is relevant to question the extent to which resting energy expenditure (REE) and total, 24-hour energy expenditure (TEE) increase during pregnancy. In fact, existing reviews on the topic have either examined the same studies or data on which the EI recommendations are based,[37,38] or are focused solely on basal

metabolism[39] or respiratory quotient.[40] Moreover, there are various methods for measuring EE, all with different limitations, thus making it difficult to compare studies that measure EE during pregnancy. Therefore, the present systematic review aimed to examine the variability in energy expenditure during pregnancy. Observational and intervention studies that prospectively measured REE and/or TEE in pregnant women were reviewed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Appendix S1).[41]

Methodology

The present systematic review was achieved based on a predefined protocol (not registered). The database search strategy was designed by an experienced scientific librarian and the final search – of the MEDLINE, EMBASE, CINAHL and Web of Science databases – was conducted on November 14, 2019. There was no publication year limit, but only articles published in English and French were reviewed. The complete search strategy for all databases is provided in Appendix S2.

Titles and abstracts were first reviewed by 2 independent reviewers. The study selection process was performed using Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). All records presenting studies among pregnant women (or women in the preconception period) that reported or mentioned objective measurements of REE or TEE were selected for full-text review. The selected full-text records were reviewed by the same 2 independent reviewers. Full-text articles were included if the selection criteria matched (see below). For titles and abstracts as well as full-text screening, a third reviewer was contacted in cases of disagreement between the 2 independent reviewers. The PICOS (population, intervention or exposure, comparison, outcome, and study design) selection criteria are presented in Table 1. The comparison criteria were not applicable to the present systematic review.

Systematic reviews, conference abstracts, books, guidelines, case reports, and case studies were excluded from this review. Randomized controlled trials and intervention studies were also excluded, on the basis that any intervention could impact a pregnant woman's EE. However, those studies were selected for qualitative analysis if they included a control group (no intervention) for which detailed information on EE measurement was provided. Moreover, after full-text screening, studies restricted to nonpregnant women, adolescents, and/or participants with diagnosed medical conditions were excluded. Other exclusion criteria were REE or TEE that was (1) not measured, (2) measured only

once, (3) estimated using questionnaires or diaries, and (4) estimated with nonvalidated accelerometers or other devices.

Data were extracted by one reviewer using a predesigned template, and the following information was extracted: general study characteristics (author[s], journal, year of publication, study design, geographic setting, and sample size); EE measurement method(s); timing of EE assessment(s); summary results (participant characteristics, mean values of REE/TEE, mean GWG and adherence to GWG guidelines, etc.); measurement of dietary information; control of participants' diet; and adjustment(s) of EE for covariates, and if so, for which covariates. A second reviewer extracted data from a randomly selected sample (n = 7, 22%) of included studies to ensure the adequacy of the data extraction. Quality assessment of the included studies was performed simultaneously with data extraction, using the Effective Public Health Practice Project's quality assessment tool for quantitative studies.[42] That tool is considered to be adequate for use in systematic reviews of observational studies and its quality assessment is based on (1) representativeness of study population, (2) study design, (3) inclusion of relevant confounders, (4) blinding of personnel/participants, (5) validity of measurement methods, and (6) report of dropouts/withdrawals.[42,43] In brief, one reviewer assigned scores to the 6 subcategories of the quality assessment tool for all articles, and a different reviewer did the same with a random sample of selected articles (n = 7; 22%). There was 86% concordance in the scores assigned by both reviewers. A study could be classified as strong (no subcategories had been assigned the "weak" score), moderate (one subcategory had been assigned the "weak" score), or weak (2 or more subcategories had been assigned the "weak" score)

Results

Of the 4852 records identified, 288 full-text articles were assessed for eligibility, of which 32 studies were included for qualitative analysis (Figure 1). Summaries of the included studies that measured REE and TEE are presented in Table 2[8,11,12,14,15,17,44–66] and Table 3[4,6,8,11,12,26,47,62,] respectively. Mean values of REE were not reported in one of the studies (results presented in graphs only) and the sole author of the study was not reachable (deceased).[52] Nevertheless, that study was included because it met all the inclusion criteria. Timing of EE measurement is presented as pregnancy periods (early, mid- and late pregnancy) rather than pregnancy trimesters because many studies either (1) did not have the same classification criteria for trimesters of pregnancy or (2) did not take into consideration the fact that for the same measurement period, participants were in 2 different trimesters of pregnancy. For

example, one study reporting on mean REE included women that were in both the first and second trimesters (range: 0–20 wk).[56] That measurement was therefore classified as being in "early pregnancy" rather than in the first trimester.

Characteristics of the studies

All included studies used a prospective design. Twenty-four studies measured REE[14,15,17,44–46,48–61,63–66] and the other 8 either measured TEE only[4,6,26] or a combination of REE and TEE.[8,11,12,47,62] The majority of studies were published before 2000 (n = 18, 56%), were from Europe and North America (n = 24, 75%), and had ≤20 participants (n = 18, 56%).

Timing and methods of measurement

On average, studies reported 4 measurements (range: 2–11 measurements). Nine studies measured EE during preconception and early, mid-, and late pregnancy,[6,12,17,47,52,53,58,62,63] similarly to 14 other studies that did the same but with no preconception measurement.[11,14,15,26,46,49–51,54–57,65,66] Durnin[52] measured REE in 162 women at 10 different timepoints throughout pregnancy and once in the preconception period, but no mean REE values were reported by the authors (results presented in graphs only). The ventilated open-circuit system and doubly labeled water were found to be the most frequently used methods for measuring REE (59%)[12,14,45,46,48–51,55–59,61,63,64,66] and TEE (63%),[4,8,11,12,47] respectively.

Resting energy expenditure

Figure 2 shows the changes in REE throughout pregnancy for the included studies. Increases in REE ranged from 0.5% to 18.3% (8–239 kcal) between early and mid-pregnancy, from 3.0% to 24.1% (45–327 kcal) between mid- and late pregnancy, and from 6.4% to 29.6% (93–416 kcal) between early and late pregnancy. The median increases in REE were 5.3% (72 kcal), 9.9% (153 kcal), and 18.0% (252 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively. The greatest differences in REE were observed by Kopp-Hoolihan et al,[12] who reported increases of 18.3% (239 kcal), 9.5% (147 kcal), and 29.6% (387 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively, after measuring REE at five different timepoints in 10 American pregnant women. Inversely, Illingworth et al,[57] who measured REE at four different timepoints in 7 Scottish women, observed the smallest increase in REE throughout pregnancy: 3.3% (48 kcal), 3.0% (45 kcal),

and 6.4% (93 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively. More recently, Bugatto et al[46] measured REE in 21 normal and 14 overweight Spanish pregnant women and observed increases of 0.9% (12 kcal), 19.0% (264 kcal), and 20.0% (276 kcal) in normal-weight women and increases of 12.1% (209 kcal), 8.9% (173 kcal), and 22.1% (382 kcal) in overweight women between early and mid-, mid- and late, and early and late pregnancy, respectively. All 3 studies used a ventilated open-circuit system to measure REE.[12,46,57]

Total energy expenditure

Changes in TEE throughout pregnancy, for the included studies, are presented in Figure 3. Increases in TEE ranged from 4.0% to 17.7% (84–363 kcal) between early and mid-pregnancy, from 0.2% to 30.2% (5–694 kcal) between mid- and late pregnancy, and from 7.9% to 33.2% (179–682 kcal) between early and late pregnancy, respectively. The median increases in TEE were 6.2% (144 kcal), 7.1% (170 kcal), and 12.0% (290 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively. Similarly to what they observed for REE, Kopp-Hoolihan et al[12] reported the greatest increases in TEE throughout pregnancy: 17.7% (364 kcal), 13.2% (318 kcal), and 33.2% (682 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively. The smallest increases in TEE were reported by Goldberg et al,[11] who measured TEE 4 times and observed differences of 4.6% (70 kcal), 5.4% (92 kcal), and 10.3% (162 kcal) between early and mid-, mid- and late, and early and late pregnancy, respectively. In a recent study by Most et al,[4] TEE was measured in early and late pregnancy in 54 obese pregnant American women and was found to increase by 9.1% (247 kcal), 12.0%, (320 kcal) and 12.4% (319 kcal) in women with inadequate, recommended, and excessive GWG, respectively. Kopp-Hoolihan et al,[12] Goldberg et al,[11] and Most et al all[4] measured TEE using the doubly labeled water method.

Prepregnancy energy expenditure

In general, studies observed small increases, and even decreases, in REE and TEE between the preconception and early-pregnancy periods (range: −3.3% to 7.9% or −41 to 112 kcal for REE, and −7.1% to 1.2% or −158 to 24 kcal for TEE). For example, Spaanderman et al[64] measured REE in 12 women, using a ventilated open-circuit, in preconception and at 4 early-pregnancy timepoints and observed changes in REE ranging from −4.7% to 2.6% (−70 to 40 kcal) that were all not statistically significant. Similar findings were observed by de Groot et al,[6] who measured TEE in 10 women in

preconception and in each trimester using a metabolic chamber and found an increase of 1.2% (24 kcal) between preconception and early pregnancy.

Quality assessment of studies

The majority of studies (59.4%) were classified as being of moderate quality[8,11,14,15,17,26,45,48–52,57–59,61,62,64,66] and 5 and 8 studies were classified as being of strong and weak quality, respectively. Women included in the 32 studies were predominantly Caucasian: seven studies comprised Caucasians only,[6,11,17,46,49,50,63] 5 studies reported a proportion of Caucasian women varying between 50% and 91%, and 6 studies had no Caucasian participant.[14,44,54,62,65,66] The 14 remaining studies were conducted in Europe, North America, and Oceania and did not explicitly specify the ethnicity of their participants.[8,12,15,48,51–53,56–61,64] Among the 23 studies that reported the mean prepregnancy BMI of their sample, 5 studies[4,26,46,55,61] reported a mean prepregnancy BMI above the "normal weight" threshold of 24.9 kg/m^2 and the other 18 studies[6,8,11,12,15,47,48,50,51,54,56–60,62–64] reported mean prepregnancy BMIs that ranged from 20.8 to 24.1 kg/m^2. The study by Most et al[4] was the only one that included solely obese pregnant women (n = 54), and the studies by Bugatto et al[46] and Butte et al[47] were the only 2 studies that categorized their participants based on their prepregnancy BMI. Four studies provided their participants' diet for a set number of days (range: 7–14 d) in order to minimize the impact of EI and macronutrient distribution on the measurement of EE.[6,48,53,61] Moreover, 10 studies assessed their participants' usual dietary habits[8,11,12,14,26,45,52,55,59,65] and 6 studies assessed usual physical activity level.[45,51,52,55,61,65] Almost all studies (87.5%) reported the mean or median GWG of their participants, but only 4 mentioned the proportion of their participants whose GWG fell under, within, or above the recommended guidelines. Among those 4 studies, the proportion of women whose GWG fell above the recommended guidelines ranged from 10% to 67%.[4,47,51,55] Furthermore, 12 studies (37.5%) observed that the increases in REE/TEE were not statistically significant after adjustment for a weight variable (ie, prepregnancy BMI, GWG, fat mass, or fat-free mass).[8,11,14,15,44,45,47,49,56,57,60,66]

Discussion

This systematic review aimed to examine observational studies with prospective and objective measurements of EE during pregnancy. In the present review, the majority of studies were published before 2000 and included mainly Caucasian and normal-weight pregnant women. This review showed that REE and TEE increase during pregnancy, mainly from early to late and from mid- to late pregnancy.

Smaller increases were observed between pre- and early pregnancy as well as between early and mid-pregnancy. There is, however, a great variability in the extent to which REE and TEE increase throughout pregnancy. Moreover, inconsistencies were observed in the measurement and reporting of important covariates, such as prepregnancy BMI, GWG, usual dietary intakes, and physical activity level. The present review thus highlights the need for additional prospective studies of high quality – that is, with multiple measurements of REE or TEE in all periods of pregnancy (early, mid-, and late), using validated and objective measurement methods (doubly labeled water for TEE and ventilated open-circuit for REE), among a diverse population of pregnant women, while considering important confounding variables such as prepregnancy BMI and GWG.

The studies reviewed demonstrated that REE increased by 8–239 kcal (median 72 kcal) and by 93–416 kcal (median 252 kcal) between early and mid-, and between early and late, pregnancy, respectively. It is complex to compare those increases with the current EI recommendations for pregnant women because (1) the increases reported by the reviewed studies represent REE measured at specific timepoints only, whereas the recommendations for EI represent whole trimesters, and (2) those recommendations are supposed to reflect increases in TEE (ie, REE in combination with thermogenesis and physical activity).[3] In studies that measured TEE, TEE increased by 84–363 kcal (median 144 kcal) and by 179–682 kcal (median 290 kcal), between early and mid-, and between early and late, pregnancy, respectively. Based on the median increases in TEE (144 and 290 kcal), half of the studies that measured TEE reported increases that were below the EI recommendations of an additional 340 and 452 kcal/d in the second and third trimesters, respectively.[3] However, it should be mentioned that a comparison of measurements of TEE with EI recommendations needs to be interpreted with caution, as pregnant women are not supposed to be in energy balance, since energy is required for, and spent on, fat storage, placenta development, and changes in blood constituents and volume as well as for supporting fetal development. Nevertheless, since prospective measurements of REE and TEE do take into account pregnancy weight gain, questioning the justification behind the EI recommendations remains relevant.[3,20]

As recently mentioned by Most et al,[67] the studies that form the foundation for the EI recommendations estimated the energy cost of GWG based on all participants, without considering each woman's adherence to GWG guidelines. Therefore, the inclusion of participants with excessive GWG, for example, has likely caused overestimation of the EI requirements, simply because such participants

deposited more energy than they needed to, and, overall, larger body size leads to greater EE.[67] In the present review, although most studies measured and reported their participants' mean GWG, only 4 studies reported the proportion who adhered to or exceeded the GWG guidelines.[4,47,51,55] This could be explained by the fact that most of the reviewed studies were published before the publication of the new GWG guidelines in 2009.[25] Still, studies published before 2009 could have compared participants' GWG with the previous guidelines,[68] but most did not. The 4 studies that reported their participants' adherence to GWG guidelines reported proportions of excessive GWG that ranged from 10% to 67%. Even though the other studies did not report their participants' adherence to GWG guidelines, it can be hypothesized that the prevalence of excessive GWG was probably variable from one study to another. This could, in part, explain the large variability observed in the extent of the increases in REE and TEE, since body weight is associated with EE. In summary, since approximately half of the energy cost of pregnancy is associated with the development of maternal tissues (fat mass, breast tissues, uterus, and placenta),[20] it is crucial that EI recommendations be based on measurements recorded among women with adequate GWG. Future studies should consider adherence to GWG guidelines when measuring TEE and REE during pregnancy, in order to avoid the overestimation of energy requirements associated with the development of maternal tissues.

The proportion of women entering pregnancy with overweight/obesity has increased since 2006, when EI recommendations were published. In fact, among American women of childbearing age, the overweight and obesity prevalence increased from 22.8% in 1976 to 53.5% in 2014,[69] which may explain why most studies included in the present review – mainly published before 2000 – reported a mean prepregnancy BMI corresponding to a normal weight. Moreover, although it has been said that EI recommendations should be population-specific and based on observations made in healthy, normal-weight women,[37] it could be argued that for a measure with such high variability as EE, women from all weight categories should not be studied as if they were in one single group. In fact, as observed by Bugatto et al,[46] who measured REE in normal (n = 21) and overweight women (n = 14) throughout pregnancy, the increase in REE from mid- to late pregnancy was twice as high in normal vs. overweight women (19.0 vs 8.9%). Bugatto et al[46] explained their results, in part, by the higher lipid oxidation observed in overweight vs. normal-weight women, which is in accordance with the findings of other reports on lipolysis during pregnancy.[70] It could thus be hypothesized that, owing to the fact that overweight and obese women have more adipose tissue to oxidize, their energy metabolism, and therefore energy requirements, may differ from that of normal-weight women who rely more on

carbohydrate oxidation.[46] In fact, by wanting to recognize the different energy requirements of overweight and obese women, the American College of Obstetricians and Gynecologists acknowledged that overweight and obese pregnant women may not require as many additional calories as pregnant women of normal weight.[71] However, no specific EIs were explicitly recommended.[71] Additional studies are necessary to better understand the mechanisms governing energy metabolism, and requirements, of overweight and obese pregnant women.

Another similar systematic review by de Oliveira Fonseca Sally et al[39] was published in Portuguese in 2013, and their database search was conducted in 2010. Their objective was to review fluctuations in basal metabolic rate during pregnancy and they found, based on the 37 studies they reviewed, that increases in basal metabolic rate ranged between 8% and 35%.[39] However, that particular review included studies that were cross-sectional (one measurement of basal metabolic rate only) and studies that used physical activity questionnaires to measure the basal metabolic rate. In addition to having included articles published after 2010 (n = 8), the present review differs from the one conducted by Sally Ede et al[39] firstly by the inclusion of studies that measured TEE as well as REE, secondly by including only cohort studies in which participants were compared to themselves, and thirdly by adding an inclusion criterion about the objective measurement of REE and TEE, which excluded certain studies (EE estimated with questionnaires and accelerometers) but probably increased, ultimately, the accuracy of the observations. Nevertheless, this review has some limitations, the main one being that no meta-analysis was carried out, because of the heterogeneity in the studied populations, timing of measurements, and measurement methods. Thus, the present review could not quantify the increase in REE and TEE during pregnancy. Another limitation is that only articles written in French and English were included, which could have limited the generalizability of the results, since high-quality studies from developing countries, or countries where women are of smaller stature (eg, Japan), for example, may have been excluded. Moreover, since studies among pregnant women with a serious medical condition were excluded from the present review, the observations made cannot be generalized to pregnant women with, for example, gestational diabetes mellitus. Further studies are necessary to assess changes in EE among populations of pregnant women with altered metabolic profiles

Conclusion

It is clear that there is an increase in REE and TEE throughout pregnancy and particularly toward the end of pregnancy. However, the extent to which REE and TEE are increased is highly variable, and

the majority of studies reported increases in TEE that were below the EI recommendations for pregnant women. Increases in REE and TEE also appear to be associated with prepregnancy weight status as well as with GWG. Future studies investigating EE during pregnancy should therefore do so in relation to the participants' adherence to GWG guidelines. Because of the heterogeneity of the reviewed studies, it is difficult to obtain a precise overview of the situation in all pregnant women. Therefore, it is not possible to conclude to what extent EIs should be increased during pregnancy, even though this was not the purpose of this review. Nevertheless, the results of this review highlight the need to revise the current recommendations in EI during pregnancy, in order to make them more appropriate for overweight and obese women, since these are the individuals who are more at risk of excessive GWG.

Declarations

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Author contributions: All authors made substantial contributions to the conception and design of the manuscript, and all critically revised a first draft of the manuscript for important intellectual content. All authors contributed to the elaboration of the review protocol. C.S. and A.L. were the 2 independent reviewers in charge of titles and abstracts as well as full-text review. A.-S.M. acted as the third reviewer. Data extraction and quality assessment of the included studies was done by C.S. (all studies) and A.L. (22% of studies), under the supervision of A.-S.M. C.S. conducted primary statistical analyses of the data with the help of A.-S.M., A.L., S.O., B.F.-B., and F.H. All authors participated in the interpretation of data. All authors gave their approval of the manuscript's final version to be published and therefore take public responsibility for the content of the manuscript. Finally, all authors agreed to be accountable for all aspects of the work.

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Tables

Table 1. PICOS criteria, energy expenditure during pregnancy : a systematic review

	Selection criteria
Population	Women with singleton pregnancies
Intervention/exposure	Time (pregnancy)
Comparison	Not applicable
Outcome	Energy expenditure variability
Study design	Cohort studies
	Case-control studies
	Intervention studies

PICOS, Population, Intervention or exposure, Comparison, Outcome, and Study design.

Table 2. Summary of studies that measured resting energy expenditure

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Banerjee et al., 1971 (Singapore) [44]	**Sample size**: 11 **Age**: not reported **Pre-pregnancy BMI**: not reported **Ethnicity**: All participants were Asian	**Two timepoints:** 2nd and 3rd trimester (weeks not specified)	Portable respirometer	**Median REE (kcal/day)** Mid-pregnancy: 1310 Late pregnancy: 1440 **Change (%)** 9.9; *p* not reported
Berggren et al., 2015 (USA) [45]	**Sample size**: 11 **Age (median)**: 29.0 years (range: 27.0 – 36.0) **Pre-pregnancy BMI (median)**: 23.8 kg/m^2 (range: 19.2 – 31.4) **Ethnicity**: 91% Caucasian and 9% Other	**Two timepoints**: Pre and late (34-36 wks) pregnancy	Ventilated open-circuit system	**Median REE (kcal/day)** Pre: 1457 34-36 wks: 1743 **Change (%)** 19.6; *p*=0.003
Bugatto et al., 2017 (Spain) [46]	**Sample size:** 35 (21 normal weight, NW and 14 overweight, OW) **Age (mean): NW:** 29.3 years (SD: 4.6); **OW:** 31.4 years (SD: 3.1) **Pre-pregnancy BMI (mean): NW:** 21.4 kg/m^2 (SD: 1.5); **OW:** 32.9 kg/m^2 (SD: 5.9) **Ethnicity:** All women were Caucasian	**Seven timepoints**: Early (12 and 16 wks), mid- (20, 24 and 28 wks) and late (32 and 36 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** NW - OW 12 wks: 1378 - 1729 24 wks: 1390 - 1938 36 wks: 1654 - 2111 **Change (%)** NW - OW 12 to 24 wks: 0.9 - 12.1; *p* not reported 12 to 36 wks: 20.0; *p*<0.001 - 22.1; *p*=0.03 24 to 36 wks: 18.9 - 8.9; *p* not reported
Butte et al., 2004 (USA) [47]	**Sample size**: 63 (17 UW, 34 NW and 12 OW) Age (mean) **UW**: 30.8 years (SD: 3.9); **NW**: 30.3 years (SD: 4.3); **OW**: 31.2 years (SD: 4.5) Pre-pregnancy BMI (mean) **UW**: 18.9 kg/m^2 (SD: 0.8); **NW**: 22.1 kg/m^2 (SD: 1.5); **OW**: 28.8 kg/m^2 (SD: 2.6) **Ethnicity**: 78% Caucasian, 9.5% African American, 9.5% Hispanic and 3% Asian	**Five timepoints:** Pre, early (9 wks), mid- (22 wks) and late (36 wks) and postpartum (27 wks after delivery)	Metabolic chamber	**Mean REE (kcal/day)** UW – NW - OW Pre: 1201- 1323 - 1505 9 wks: 1234 - 1350 - 1600 22 wks: 1330 - 1413 - 1693 36 wks: 1573 - 1673 - 2016 **Change (%)** UW – NW - OW Pre to 9 wks: 2.7 - 2.0 - 6.3 Pre to 22 wks: 10.7 - 6.8 - 12.5 Pre to 36 wks: 31.0 - 26.5 - 34.0 9 to 22 wks: 7.8 - 4.7 - 5.8 9 to 36 wks: 27.5 - 23.9 - 26.0 22 to 36 wks: 18.2 - 18.4 - 19.1; *p* not reported

Table 2. Summary of studies that measured resting energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Catalano et al., 1998 (USA) [48]	**Sample size**: 5 **Age (median)**: 31.8 years (SD: 5.5) **Pre-pregnancy BMI** (median): 20.8 kg/m^2 (SD: 2.3) **Ethnicity**: Not reported	**Three timepoints:** Pre, early (12-14 wks) and late (34-36 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** Pre: 1402 12-14 wks: 1513 34-36 wks: 1886 **Change (%)** Pre to 12-14 wks: 7.9; NS Pre to 34-36 wks: 34.5; p=0.0001 12-14 to 34-36 wks: 24.7; p=0.0001
Cikrikci et al., 1999 (Turkey) [49]	**Sample size**: 24 **Age (mean)**: 28.8 years (SD: 4.8) **Pre-pregnancy BMI**: 24.0 kg/m^2 (SD: 1.9) **Ethnicity**: All women were Caucasian	**Three timepoints:** 1st, 2nd and 3rd trimesters (weeks not specified)	Ventilated open-circuit system	**Mean REE (kcal/day)** 1st trimester: 1245 2nd trimester: 1382 3rd trimester: 1524 **Change (%)** 1st to 2nd: 11.0; p<0.01 1st to 3rd: 22.4; p<0.01 2nd to 3rd: 10.3; p<0.001
Damjanovic et al., 2009 (Serbia) [50]	**Sample size**: 31 **Age (mean)**: 24.8 years (SD: 5.7) **Pre-pregnancy BMI**: Not reported **Ethnicity**: All women were Caucasian	**Three timepoints:** Early (12 wks), mid- (26 wks) and late (36 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** 12 wks: 1404 26 wks: 1479 36 wks: 1564 **Change (%)** 12 to 26 wks: 5.3; p<0.001 12 to 36 wks: 11.4; p<0.001 26 to 36 wks: 5.7; p not reported
Denize et al., 2019 (Canada) [51]	**Sample size**: 10 **Age (mean)**: 31.9 years (SD: 3.7) **Pre-pregnancy BMI** (mean): 22.1 kg/m^2 (SD: 1.9) **Ethnicity**: Not reported	**Three timepoints:** Early (15.4±0.9 wks), mid- (26.4±1.1 wks) and late (35.3±1.1 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** 15 wks: 2124 26 wks: 2304 35 wks: 2506 **Change (%)** 15 to 26 wks: 8.5; p not reported 15 to 35 wks: 18.0; p=0.06 26 to 35 wks: 8.9; p not reported

Table 2. Summary of studies that measured resting energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Durnin et al., 1991 (Scotland) [52]	**Sample size**: 162 **Age (mean)**: 28.0 years (range: 20.0 - 30.0) **Pre-pregnancy BMI** (mean): Not reported **Ethnicity**: Not reported	**Eleven timepoints:** Pre, early (between 1-20 wks), mid- (between 21-28) and late (between 29-40) pregnancy	Douglas bags	No increase from pre to 16 wks of pregnancy, then a steady increase, up to +400 kcal/day close to term. (No mean or *p* reported, sole author impossible to contact)
Emerson et al., 1972 (USA) [53]	**Sample size**: 10 **Age (mean)**: 22.8 years (range: 19.0 - 31.0) **Pre-pregnancy BMI:** Not reported **Ethnicity**: Not reported	**Seven timepoints:** Pre, early (0-20 wks), mid- (24 and 28 wks) and late (32, 36 and 38-41 wks) pregnancy	Douglas bags	**Mean REE (kcal/day)** Pre: 1470 0-20 wks: 1488 28 wks: 1590 38-41 wks: 1753 **Change (%)** Pre to 0-20 wks: 1.2 Pre to 28 wks: 8.2 Pre to 38-41 wks: 19.3 0-20 to 28 wks: 6.9 0-20 to 38-41 wks: 17.8 28 to 38-41 wks: 10.3; *p* not reported
Eto et al., 2018 (Japan) [54]	**Sample size**: 103 **Age (mean)**: 33.7 years (SD: 5.7) **Pre-pregnancy BMI** (mean): 21.8 kg/m^2 (SD: 3.4) **Ethnicity**: All women were Asian	**Four timepoints:** Early (up to 15 wks), mid- (16 – 27 wks), late (28 wks to delivery) pregnancy and postpartum (4-5 wks after delivery)	Portable respirometer	**Mean REE (kcal/day)** 0-15 wks: 1461 16-27 wks: 1491 ≥ 28 wks: 1644 **Change (%)** 0-15 to 16-27 wks: 2.0; NS 0-15 to ≥ 28 wks: 12.1; $p<0.05$ 16-27 to ≥ 28 wks: 10.3; $p<0.05$
Forsum et al., 1992 (Sweden) [8]	**Sample size**: 22 **Age (mean)**: 29.0 years (SD: 4.0) **Pre-pregnancy BMI** (mean): 22.3 kg/m^2 (SD 3.1) **Ethnicity**: Not reported	**Three timepoints:** Pre, early (16-18 wks) and late (30 wks) pregnancy	Douglas bags	**Mean REE (kcal/day)** Pre: 1340 16-18 wks: 1435 30 wks: 1651 **Change (%)** Preto 16-18 wks: 7.1; NS Pre to 30 wks: 23.2; $p<0.001$ 16-18 to 30 wks: 15.1; *p* not reported

Table 2. Summary of studies that measured resting energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Goldberg et al., 1993 (England) [11]	**Sample size**: 12 **Age (mean)**: 28.8 years (SD: 3.3) **Pre-pregnancy BMI (mean)**: 23.0 kg/m^2 (SD: 3.3) **Ethnicity**: All women were Caucasian	**Four timepoints:** Early (12 wks), mid- (18 and 24 wks) and late (30 wks) pregnancy[c]	Metabolic chamber	**Mean REE (kcal/day)** 12 wks: 1490 24 wks: 1582 30 wks: 1652 **Change (%)** 12 to 24 wks: 6.2 12 to 30 wks: 4.4 24 to 30 wks: 10.9; *p* not reported
Hagobian et al., 2015 (USA) [55]	**Sample size**: 16 **Age (mean)**: 30.3 years (SD: 3.8) **Pre-pregnancy BMI** (mean): 25.2 kg/m^2 (SD: 3.6) **Ethnicity**: 81% Caucasian and 19% Hispanic	**Three timepoints:** Early (12-16 wks), mid- (24-26 wks) and late (32-34 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** 12-16 wks: 1458 24-26 wks: 1580 32-34 wks: 1830 **Change (%)** 12-16 to 24-26 wks: 8.4; $p<0.05$ 12-16 to 32-34 wks: 25.5; $p<0.05$ 24-26 to 32-34 wks: 15.8; $p<0.05$
Hronek et al., 2011 (Czech Republic) [56]	**Sample size**: 31 **Age (mean)**: 29.2 years (SD: 3.6) **Pre-pregnancy BMI** (mean): 21.2 kg/m^2 (SD: 3.0) **Ethnicity**: Not reported	**Four timepoints:** Early (0-20 wks), mid- (21-29 wks) and late (30-36 and 37-39 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** 0-20 wks: 1407 21-29 wks: 1493 37-39 wks: 1655 **Change (%)** 0-20 to 21-29 wks: 6.1 0-20 to 37-39 wks: 17.6 21-29 to 37-39 wks: 10.9; overall $p<0.0001$
Illingworth et al., 1987 (Scotland) [57]	**Sample size**: 7 **Age (mean)**: 28.2 years (SD: 2.9) **Pre-pregnancy BMI**: Not reported **Ethnicity**: Not reported	**Four timepoints:** Early (12-15 wks), mid- (25-28 wks), late (34-36 wks) pregnancy and after cessation of lactation.	Ventilated open-circuit system	**Mean REE (kcal/day)** 12-15 wks: 1457 25-28 wks: 1506 34-36 wks: 1550 **Change (%)** 12-15 to 25-28 wks: 3.4 12-15 to 34-36 wks: 6.4 25-28 to 34-36 wks: 2.9; *p* not reported

Table 2. Summary of studies that measured resting energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Kopp-Hoolihan et al., 1999 (USA) [12]	**Sample size**: 10 **Age (mean)**: 29.1 years (SD: 5.0, range) **Pre-pregnancy BMI** (mean): 23.1 kg/m^2 (SD: 2.1) **Ethnicity**: All women were Caucasian	**Five timepoints:** Pre, early (8-10 wks), mid- (24-26 wks), late (34-36 wks) pregnancy and 4-6 wks postpartum	Ventilated open-circuit system	**Mean REE (kcal/day)** Pre: 1315 8-10 wks: 1306 24-26 wks: 1545 34-36 wks: 1693 **Change (%)** Pre to 8-10 wks: -0.7 Pre to 24-26 wks: 17.5 Pre to 34-36 wks: 28.7 8-10 to 24-26 wks: 18.3 8-10 to 34-36 wks: 29.6 24-26 to 34-36 wks: 9.6; *p* not reported
Lof et al., 2005 (Sweden) [58]	**Sample size**: 22 **Age (mean)**: 29.0 years (SD: 3.0) **Pre-pregnancy BMI** (mean): 23.0 kg/m^2 (SD 3.0) **Ethnicity**: Not reported	**Six timepoints:** Pre, early (8, 14 wks), mid- (20 wks) and late (32, 35 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** Pre: 1299 8 wks: 1325 20 wks: 1373 35 wks: 1718 **Change (%)** Pre to 8 wks: 2.0; NS Pre to 20 wks: 5.7; NS Pre to 35 wks: 32.3; $p<0.001$ 8 to 20 wks: 3.6; *p* not reported 8 to 35 wks: 29.7; *p* not reported 20 to 35 wks: 25.1; *p* not reported
Martin et al., 2001 (Australia) [59]	**Sample size**: 8 **Age (mean)**: 32.0 years (SD: 1.0) **Pre-pregnancy BMI**: Not reported **Ethnicity**: Not reported	**Three timepoints:** Mid- (19±1 wks), late (36±1 wks) pregnancy and postpartum (16 wks after delivery)	Ventilated open-circuit system	**Mean REE (kcal/day)** 19 wks: 1416 36 wks: 1590 **Change (%)** 12.3; $p<0.05$

Table 2. Summary of studies that measured resting energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Nagy et al., 1983 (USA) [60]	**Sample size**: 5 **Age (mean)**: 25.0 years (SD: 3.0) **Pre-pregnancy BMI:** Not reported **Ethnicity**: Not reported	**Four timepoints:** Mid- (15-25 wks) and late (25-30, 30-35, 35-40 wks) pregnancy	Metabolic chamber	**Mean REE (kcal/day)** 15-25 wks: 1454 25-30 wks: 1483 30-35 wks: 1613 35-40 wks: 1656 **Change (%)** From 2.0 to 13.9; p<0.05 between 15-25 and 35-40
Okereke et al., 2004 (USA) [61]	**Sample size**: 8 **Age (mean)**: 31.6 years (SD: 3.4) **Pre-pregnancy BMI** (mean): 26.2 kg/m^2 (SD: 4.5) **Ethnicity**: Not reported	**Three timepoints:** Pre, early (12-14 wks) and late (34-36 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** Pre: 1488 12-14 wks: 1600 34-36: 1897 **Change (%)** Pre to 12-14 wks: 7.5; NS Pre to 34-36 wks: 27.5; *p*=0.0001 12-14 to 34-36 wks: 18.6; NS
Piers et al., 1995 (India) [14]	**Sample size**: 18 **Age (mean)**: 29.6 years (SD: 5.2) **Pre-pregnancy BMI**: Not reported **Ethnicity**: All participants were Asian (Indian)	**Three timepoints:** Early (12 wks), mid- (24 wks) and late (34 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** 12 wks: 1226 24 wks: 1347 34 wks: 1478 **Change (%)** 12 to 24 wks: 9.9; *p*<0.05 12 to 34 wks: 20.6; *p*<0.05 24 to 34 wks: 9.7; *p*<0.05
Poppitt et al., 1993 (Gambia) [62]	**Sample size**: 9 **Age (mean)**: 26.2 years (SD: 7.1) **Pre-pregnancy BMI** (mean): 21.4 kg/m^2 (SD: 2.1) **Ethnicity**: All women were African	**Four timepoints:** Pre, mid- (18, 24 wks) and late (30, 36 wks) pregnancy[d]	Metabolic chamber	**Mean REE (kcal/day)[d]** Pre: 1244 18 wks: 1224 30 wks: 1306 **Change (%)** Pre to 18 wks: -1.6 Pre to 30 wks: 5.0 18 to 30 wks: 6.7; *p* not reported

Table 2. Summary of studies that measured resting energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Prentice et al., 1989 (England) [15]	**Sample size:** 8 **Age (mean)**: 29.3 years (SD: 4.5) **Pre-pregnancy BMI** (mean): 23.1 kg/m^2 (SD) **Ethnicity**: Not reported	**Three timepoints:** Mid- (18, 24 wks) and late (30 wks) pregnancy[e]	Metabolic chamber	**Mean REE (kcal/day)** 18 wks: 1466 24 wks: 1529 30 wks: 1647 **Change (%)** 18 to 24 wks: 4.3 18 to 30 wks: 12.3 24 to 30 wks: 7.7; *p* not reported
Spaaij et al., 1994 (Netherlands) [63]	**Sample size**: 26 **Age (mean)**: 30.0 years (SD: 3.9) **Pre-pregnancy BMI** (mean): 21.8 kg/m^2 (SD: 2.4) **Ethnicity**: Not reported	**Four timepoints:** Pre, early (13 wks) mid- (24 wks) and late (35 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** Pre: 1323 13 wks: 1381 24 wks: 1499 35 wks: 1619 **Change (%)** Pre to 13 wks: 4.4; NS Pre to 24 wks: 13.3; $p<0.05$ Pre to 35 wks: 22.4; $p<0.05$ 13 to 24 wks: 8.5; $p<0.05$ 13 to 35 wks: 17.2; $p<0.05$ 24 to 35 wks: 8.0; $p<0.05$
Spaanderman et al., 2000 (Netherlands) [64]	**Sample size**: 12 **Age (mean)**: 29.0 years (SD: 3.0) **Pre-pregnancy BMI**: 23.0 kg/m^2 (SD: 3.0) **Ethnicity**: Not reported	**Five timepoints:** Pre and early (6, 8, 10 and 12 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** Pre: 1496 6 wks: 1536 8 wks: 1451 10 wks: 1486 12 wks: 1426 Change (%) From -4.7 to 2.6%; all non significant

Table 2. Summary of studies that measured resting energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was REE measured?	How was REE measured?	Change in REE[b]
Tuazon et al. 1987 (Philippines) [65]	**Sample size**: 40 **Age (mean)**: 23.8 years (SD: 3.4) **Pre-pregnancy BMI**: Not reported **Ethnicity**: All participants were Asian	**Five timepoints:** Early (11-16 wks) mid- (17-22, 23-28 wks), late (29-34, 35-40 wks) pregnancy and postpartum (6, 12 wks after delivery)	Doublas bags	**Mean REE (kcal/day)** 11-16 wks: 1196 23-28 wks: 1292 35-40 wks: 1411 **Change (%)** 11-16 to 23-28 wks: 8.0 11-16 to 35-40 wks: 18.0 23-28 to 35-40 wks: 9.2; no *p* reported
van Raaij et al., 1989 (Netherlands) [17]	**Sample size**: 23 **Age**: Not reported (only for total sample, not the 23 pregnant women) **Pre-pregnancy BMI**: Not reported **Ethnicity**: All participants were Caucasian	**Five timepoints:** Pre, early (4-8, 10-14 wks) mid- (22-26 wks) and late (34-38 wks) pregnancy	Doublas bags	**Mean REE (kcal/day)** Pre: 1452 10-14 wks: 1503 22-26 wks: 1541 34-38 wks: 1742 **Change (%)** Pre to 10-14 wks: 3.5; NS Pre to 22-26 wks: 6.1; NS Pre to 34-38 wks: 20.0; $p<0.001$ 10-14 to 22-26 wks: 2.5; NS 10-14 to 34-38 wks: 15.9; NS 22-26 to 34-38 wks: 13.0; NS
Willommet et al., 1992 (Gambia) [66]	**Sample size**: 9 **Age (mean)**: 23.0 (SD 3.0) **Pre-pregnancy BMI**: Not reported **Ethnicity**: All women were African	**Three timepoints:** Early (11 wks), mid- (23 wks) and late (33 wks) pregnancy	Ventilated open-circuit system	**Mean REE (kcal/day)** 11 wks: 1253 23 wks: 1325 33 wks: 1426 **Change (%)** 11 to 23 wks: 5.7; $p<0.05$ 11 to 33 wks: 13.8; $p<0.01$ 23 to 33 wks: 7.6; $p<0.05$

[a]Sample size and characteristics refer to the pregnant women (with no medical condition) for which all data was available.

[b]For studies with more than one REE/TEE measurement by pregnancy or prenatal period, only one measurement by period is presented, in order to lighten the table.

[c]Only the presented timepoints included all 12 pregnant women.[11]

[d]Only the 3 presented timepoints included all 9 pregnant women. [62]

[e]Only the presented timepoints included all 8 pregnant women.[15]

Abbreviations: NS, not significant; NW, normal weight; OW, overweight; pre, preconception; REE, resting energy expenditure; SD, standard deviation; TEE, total energy expenditure; UW, underweight.

Table 3. Summary of studies that measured total energy expenditure

Authors, year (country)	Sample characteristics[a]	When was TEE measured?	How was TEE measured?	Change in TEE[b]
Abeysekara et al., 2016 (Australia) [26]	**Sample size**: 26 **Age (mean)**: 29.9 years (SD 4.0) **Pre-pregnancy BMI (mean)**: 25.4 kg/m^2 (SD: 4.3) **Ethnicity**: 58% Caucasian, 31% Asian, 12% Other	**Three timepoints**: Early (12-14 wks), mid- (24-26 wks) and late (34-36 wks) pregnancy	Accelerometer (Sensewear Armband) worn during 24 hours.	**Mean TEE (kcal/day)** 12-14 wks: 2276 24-26 wks: 2451 34-36 wks: 2455 **Change (%)** 12-14 to 24-26 wks: 7.6; NS 12-14 to 34-36 wks: 7.9; *p*=0.003 24-26 to 34-36 wks: 0.2; NS
Butte et al., 2004 (USA) [47]	**Sample size**: 63 (17 UW, 34 NW and 12 OW) **Age (mean)** **UW**: 30.8 years (SD: 3.9); **NW**: 30.3 years (SD: 4.3); **OW**: 31.2 years (SD: 4.5) **Pre-pregnancy BMI (mean)** **UW**: 18.9 kg/m^2 (SD: 0.8); **NW**: 22.1 kg/m^2 (SD: 1.5); **OW**: 28.8 kg/m^2 (SD: 2.6) **Ethnicity**: 78% Caucasian, 9.5% African American, 9.5% Hispanic and 3% Asian	**Five timepoints:** Pre, early (9 wks), mid- (22 wks) and late (36 wks) and postpartum (27 wks after delivery)	**REE** with metabolic chamber and **TEE** with doubly labelled water	**Mean TEE (kcal/day) UW – NW - OW** Pre: 2348 - 2434 - 2940 22 wks: 2272 - 2520 - 2887 36 wks: 2439 - 2693 - 3020 **Change in TEE (%) UW – NW - OW** Pre to 22 wks: -3.2 - 3.5 - -1.8 Pre to 36 wks: 3.9 - 10.6 - 2.7 22 to 36 wks: 7.4 - 6.9 - 4.6; overall *p*=0.02
de Groot et al., 1994 (Netherlands) [6]	**Sample size**: 10 **Age (mean)**: 28.4 years (SD: 2.5) **Pre-pregnancy BMI (mean)**: 21.3 kg/m^2 (SD: 3.0) **Ethnicity**: All women were Caucasian	**Four timepoints:** Pre, early (12 wks), mid- (23 wks) and late (34 wks) pregnancy	Metabolic chamber	**Mean TEE (kcal/day)** Pre: 2065 12 wks: 2089 23 wks: 2172 34 wks: 2378 **Change (%)** Pre to 12 wks: 1.2; NS Pre to 23 wks: 5.2; *p*<0.05 Pre to 34 wks: 15.2; *p*<0.05 12 to 23 wks: 4.0; NS 12 to 34 wks: 13.8; *p*<0.05 23 to 34 wks: 9.5; *p*<0.05

Table 3. Summary of studies that measured total energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was TEE measured?	How was TEE measured?	Change in TEE[b]
Forsum et al., 1992 (Sweden) [8]	**Sample size**: 22 **Age (mean)**: 29.0 years (SD: 4.0) **Pre-pregnancy BMI (mean)**: 22.3 kg/m^2 (SD 3.1) **Ethnicity**: Not reported	**Three timepoints:** Pre, early (16-18 wks) and late (30 wks) pregnancy	Doubly labelled water	**Mean TEE (kcal/day)** Pre: 2488 16-18 wks: 2297 30 wks: 2990 **Change in TEE (%)** Pre to 16-18 wks: -7.7; NS Pre to 30 wks: 20.2; $p< 0.05$ 16-18 to 30 wks: 30.2; *p* not reported
Goldberg et al., 1993 (England) [11]	**Sample size**: 12 **Age (mean)**: 28.8 years (SD: 3.3) **Pre-pregnancy BMI (mean)**: 23.0 kg/m^2 (SD: 3.3) **Ethnicity**: All women were Caucasian	**Four timepoints:** Early (12 wks), mid- (18 and 24 wks) and late (30 wks) pregnancy[c]	Doubly labelled water	**Mean TEE (kcal/day)** 12 wks: 2430 24 wks: 2625 30 wks: 2679 **Change in TEE (%)** 12 to 24 wks: 8.0; *p* not reported 12 to 30 wks: 10.2; *p* not reported 24 to 30 wks: 2.1; *p* not reported
Kopp-Hoolihan et al., 1999 (USA) [12]	**Sample size**: 10 **Age (mean)**: 29.1 years (SD: 5.0, range) **Pre-pregnancy BMI (mean)**: 23.1 kg/m^2 (SD: 2.1) **Ethnicity**: All women were Caucasian	**Five timepoints:** Pre, early (8-10 wks), mid- (24-26 wks), late (34-36 wks) pregnancy and 4-6 wks postpartum	Doubly labelled water	**Mean TEE (kcal/day)** Pre: 2208 8-10 wks: 2050 24-26 wks: 2414 34-36 wks: 2732 **Change in TEE (%)** Pre to 8-10 wks: -7.2 Pre to 24-26 wks: 9.3 Pre to 34-36 wks: 23.7 8-10 to 24-26 wks: 17.8 8-10 to 34-36 wks: 33.3 24-26 to 34-36 wks: 13.2; *p* not reported

Table 3. Summary of studies that measured total energy expenditure (*continued*)

Authors, year (country)	Sample characteristics[a]	When was TEE measured?	How was TEE measured?	Change in TEE[b]
Most et al., 2019 (USA) [4]	**Sample size**: 54 (10 INA, 8 REC and 36 EXS) **Age (mean)** **INA**: 29.2 years (SD: 1.3); **REC**: 25.0 years (SD: 1.7); **EXS**: 27.7 years (SD: 0.8) **Pre-pregnancy BMI**: All women were obese at 15 wks **Ethnicity**: 52% Caucasian, 41% African American, 7% Other	**Two timepoints:** Early (13-16 wks) and late (35-37 wks) pregnancy	Doubly labelled water	**Mean TEE (kcal/day) INA – REC - EXS** 13-16 wks: 2719 - 2664 - 2563 35-37 wks: 2966 - 2984 - 2882 **Change in TEE (%) INA – REC - EXS** 9.1 - 12.0 - 12.4; *p* not reported
Poppitt et al., 1993 (Gambia) [62]	**Sample size**: 9 **Age (mean)**: 26.2 years (SD: 7.1) **Pre-pregnancy BMI (mean)**: 21.4 kg/m^2 (SD: 2.1) **Ethnicity**: All women were African	**Four timepoints:** Pre, mid- (18, 24 wks) and late (30, 36 wks) pregnancy[d]	Metabolic chamber	**Mean TEE (kcal/day)** Pre: 1533 36 wks: 1612 (Other TEE timepoints not reported) **Change in TEE (%)** Pre to 36 wks: 5.2; *p*=0.64

[a]Sample size and characteristics refer to the pregnant women (with no medical condition) for which all data was available.

[b]For studies with more than one REE/TEE measurement by pregnancy or prenatal period, only one measurement by period is presented, in order to lighten the table.

[c]Only the presented timepoints included all 12 pregnant women.[11]

[d]Only the preconception and 36-week value were presented in the paper and included all women.[62]

Abbreviations: EXS, excessive gestational weight gain; INA, inadequate gestational weight gain; NS, not significant; NW, normal weight; OW, overweight; pre, preconception; REC, recommended gestational weight gain; REE, resting energy expenditure; SD, standard deviation; TEE, total energy expenditure; UW, underweight.

Figures

1. PRISMA flowchart

2. Change in resting energy expenditure throughout pregnancy. Each data point represents the mean value of energy expenditure reported by studies that measured resting energy expenditure. Means from the same study are linked by the same line. Full grey colored lines and dotted black lines represent the studies for which the participants' mean pre-pregnancy BMI was below 25 kg/m^2 and equal or over 25 kg/m^2, respectively.

3. Change in total energy expenditure throughout pregnancy. Each data point represents the mean value of energy expenditure reported by studies that measured total energy expenditure. Means from the same study are linked by the same line. Full grey colored lines and dotted black lines represent the studies for which the participants' mean pre-pregnancy BMI was below 25 kg/m^2 and equal or over 25 kg/m^2, respectively.

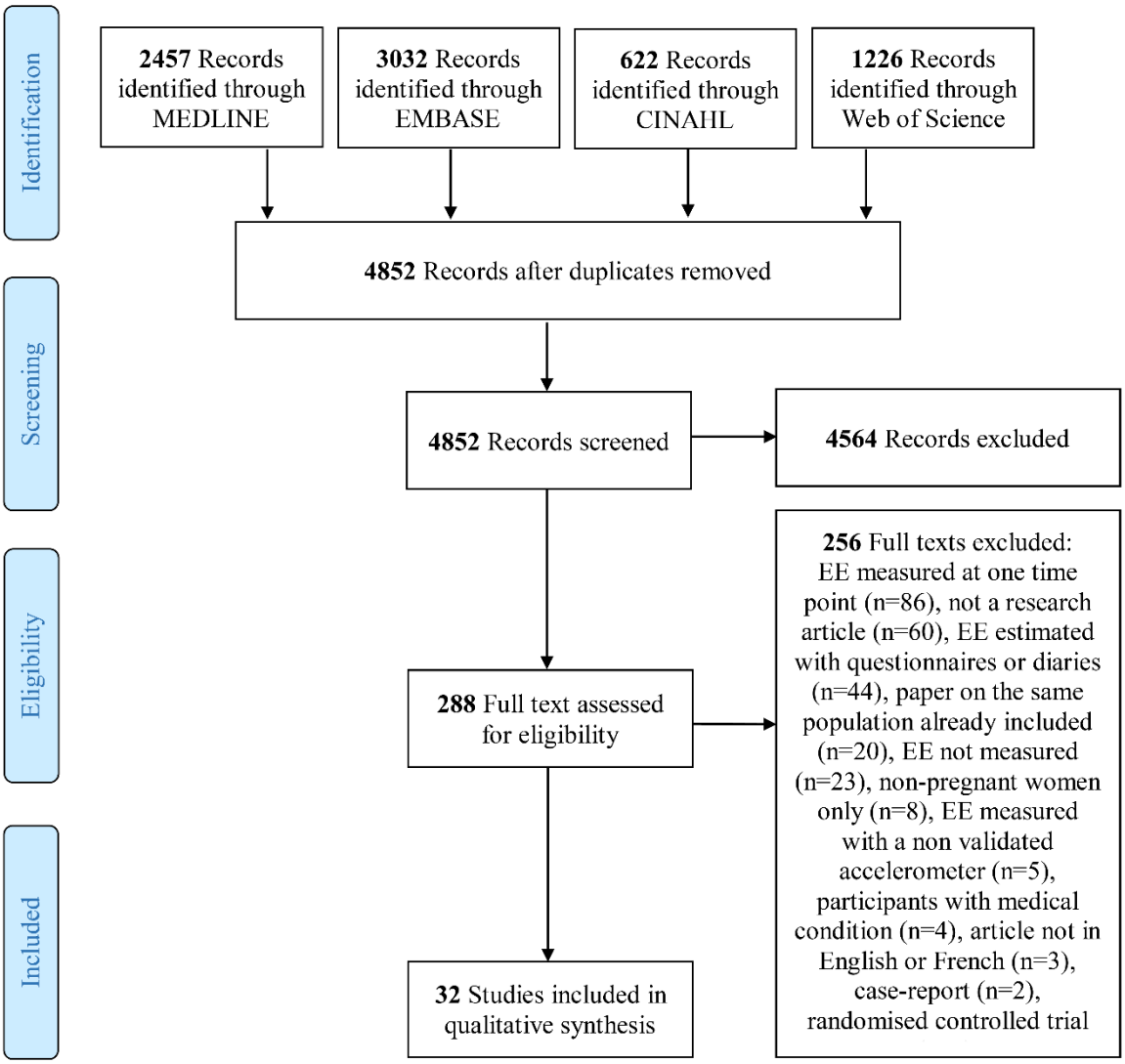

Figure 1. PRISMA flowchart

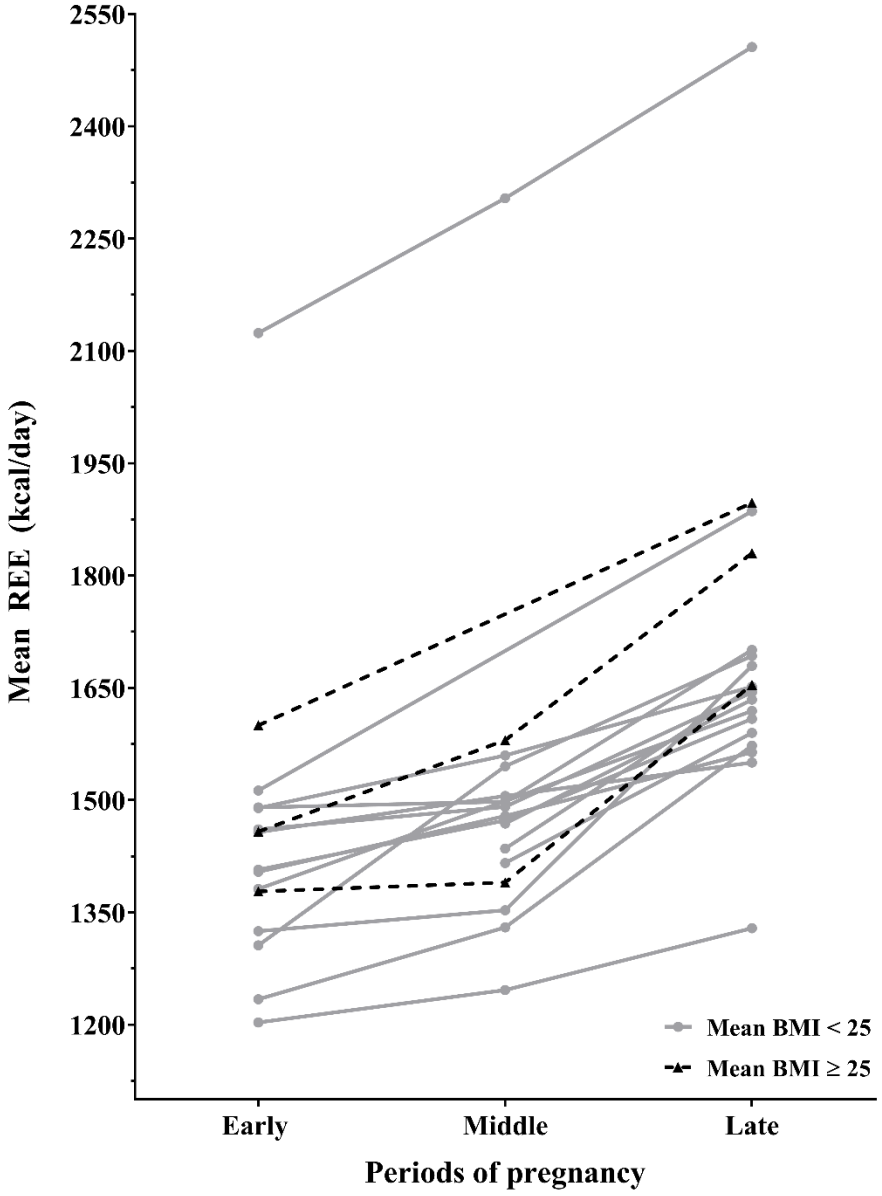

Figure 2. Change in resting energy expenditure throughout pregnancy

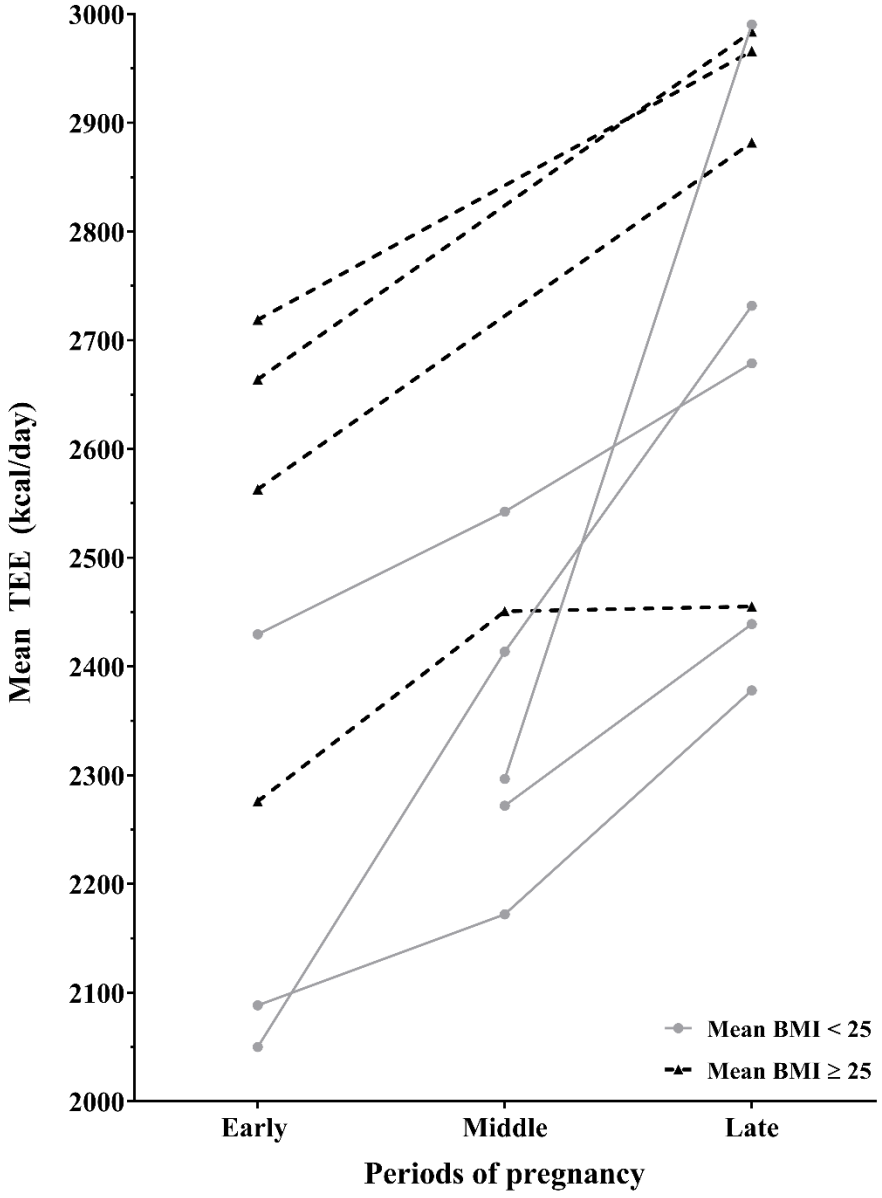

Figure 3. Change in total energy expenditure throughout pregnancy

Supporting information

Appendix S1. Search strategies used on November 14th, 2019

a. MEDLINE

Major topics	Search terms
Energy	'Energy Metabolism' OR 'energy adj5 expenditure*' OR 'exp Calorimetry' OR 'calorimetr*' OR 'exp Basal Metabolism' OR 'basal adj5 metaboli*' OR 'dlw' OR '((doubly or double) adj5 (labeled or labelled) adj5 water*)' OR '(energy adj2 metabolism)'
	AND
Pregnancy	'exp pregnancy' OR '(pregnancy or pregnancies or pregnant)' OR '(maternal* or gestational*)
	AND
Humans	'exp humans' OR 'women' OR 'patients' OR '(woman* OR women* OR human OR humans OR patient OR patients)'
	NOT
Animals	'exp animals' OR 'not exp humans'

b. EMBASE

Major topics	Search terms
Energy	'energy metabolism'/de OR 'energy expenditure'/exp OR 'calorimetry'/exp OR 'metabolic rate'/exp OR 'basal metabolism'/exp OR 'doubly labeled water technique'/exp OR 'energy' NEAR/2 'metabolism' OR 'energy' NEAR/5 'expenditure*' OR ((doubly OR double) NEAR/5 (labeled OR labelled) NEAR/5 water*) OR 'dlw' OR 'calorimetr*'
	AND
Pregnancy	'pregnancy'/exp OR 'pregnant woman'/exp OR 'pregnancy' OR 'pregnancies' OR 'pregnant' OR 'maternal' OR 'gestational'
	AND
Humans	'human'/exp OR 'patient'/exp OR 'woman*' OR 'women*' OR 'human' OR 'humans' OR 'patient' OR 'patients'
	NOT
Animals	'animal'/exp NOT 'human'/exp

c. CINAHL

Major topics	Search terms
Energy	(MH "Energy Metabolism") OR (MH "Calorimetry") OR (MH "Basal Metabolism+") OR (MH "Doubly Labeled Water Technique") OR 'energy N2 metabolism' OR 'energy N5 expenditure*' OR 'basal N5 metaboli*' OR '((doubly OR double) N5 (labeled OR labelled) N5 (water*))' OR 'dlw' OR 'calorimetr*'
	AND
Pregnancy	(MH "Pregnancy+") OR 'pregnancy' OR 'pregnancies' OR 'pregnant' OR (MH "Expectant Mothers") OR (MH "Maternal Nutritional Physiology+") OR 'gestational' OR 'maternal'

d. Web of Science

Major topics	Search terms
Energy	'(energy NEAR/5 metabolism)' OR '(energy NEAR/5 expenditure*)' OR 'calorimetr*' OR '(basal NEAR/5 metaboli*)' OR '((doubly OR double) NEAR/5 (labeled OR labelled) NEAR/5 water*)' OR 'dlw'
	AND
Pregnancy	'pregnan*' OR 'maternal' OR 'gestational'
	AND
Humans	'women*' OR 'woman*' OR 'human' OR 'humans' OR 'patient' OR 'patients'

Appendix S2. PRISMA 2009 Checklist, energy expenditure during pregnancy: a systematic review

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1 and 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5 and Table 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4 and supplement
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4-5

Appendix S2. PRISMA 2009 Checklist, energy expenditure during pregnancy: a systematic review (*continued*)

Section/topic	#	Checklist item	Reported on page #
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6 and Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A

Appendix S2. PRISMA 2009 Checklist, energy expenditure during pregnancy: a systematic review (*continued*)

Section/topic	#	Checklist item	Reported on page #
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13-14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

Chapitre 5 – Trimester-specific dietary intakes in a sample of French-Canadian pregnant women in comparison with national nutritional guidelines

Résumé

Cette étude visait à évaluer l'adhésion des femmes enceintes aux recommandations nutritionnelles actuelles. Soixante-dix-neuf femmes enceintes ont complété, à chaque trimestre, trois rappels de 24 heures et un questionnaire sur l'utilisation de suppléments. Les apports alimentaires, avec et sans suppléments, ont été comparés aux recommandations. Contrairement à la recommandation d'augmenter les apports énergétiques aux deuxième et troisième trimestres, ces derniers sont demeurés stables au cours des trimestres. En incluant les suppléments, la majorité des femmes atteignaient les recommandations en micronutriments, mais des proportions considérables de femmes avaient des apports insuffisants en vitamine D (20%) et excessifs en acide folique (80%). En somme, les femmes enceintes n'augmentent pas leurs apports énergétiques aux deuxième et troisième trimestres et, bien que les suppléments augmentent les apports en micronutriments, il existe toujours un risque d'apports inadéquats en vitamine D et en acide folique.

Title page

Title: Trimester-specific dietary intakes in a sample of French-Canadian pregnant women in comparison with national nutritional guidelines.

Full reference: Savard C, Lemieux S, Weisnagel SJ, Fontaine-Bisson B, Gagnon C, Robitaille J, Morisset A-S. Trimester-Specific Dietary Intakes in a Sample of French-Canadian Pregnant Women in Comparison with National Nutritional Guidelines. Nutrients, 2018; 10(6):768.

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Keywords: pregnancy; dietary intakes; energy intakes; supplements; dietary reference intakes (DRIs)

Abstract

Diet during pregnancy greatly impacts health outcomes. This study aims to measure changes in dietary intakes throughout trimesters and to assess pregnant women's dietary intakes in comparison with current Canadian nutritional recommendations. Seventy-nine pregnant women were recruited and completed, within each trimester, three Web-based 24-h dietary recalls and one Web questionnaire on supplement use. Dietary intakes from food, with and without supplements, were compared to nutritional recommendations throughout pregnancy. Energy and macronutrient intakes remained stable throughout pregnancy. A majority of women exceeded their energy and protein requirements in the first trimester, and fat intakes as a percentage of energy intakes were above recommendations for more than half of the women in all trimesters. Supplement use increased dietary intakes of most vitamins and minerals, but 20% of women still had inadequate total vitamin D intakes and most women had excessive folic acid intakes. This study showed that pregnant women did not increase their energy intakes throughout pregnancy as recommended. Furthermore, although prenatal supplementation reduces the risk of inadequate intake for most micronutrients, there is still a risk of excessive folic acid and insufficient vitamin D intake, which needs further investigation.

Introduction

Pregnancy is a critical period during which the pregnant woman's diet must provide enough nutrients to ensure optimal fetal development as well as to sustain the mother's physiological needs. In fact, in addition to the metabolic demand associated with the fetus' growth, rises in blood volume, extracellular liquids, adipose tissue, and placental weight all lead to an increase in the mother's dietary requirements [1,2]. Consequently, as recommended by the Institute of Medicine and Health Canada, daily pre-pregnancy energy intakes should be increased by 340 and 452 kcal in the second and third trimesters, respectively, in order to create a positive energy balance [3,4]. Likewise, pregnant women should increase their protein intakes in the second and third trimesters, but no specific recommendation exists for carbohydrates and fats during pregnancy [3].

Higher energy intakes should allow pregnant women to meet their higher essential fatty acid, dietary fiber, folic acid, iron, vitamin D, calcium, vitamin B12, and vitamin C requirements [3,4]. However, previous research highlighted various dietary inadequacies, namely folate, iron, vitamin B12, and vitamin D insufficiencies [5,6,7] thus suggesting that pregnant women may have difficulty meeting their higher micronutrient requirements through diet alone [5]. Moreover, since inadequate folate and iron status during pregnancy has been associated with numerous adverse health outcomes [8,9,10], Health Canada recommends that pregnant women should take, on a daily basis, a multivitamin that contains at least 400 µg of folic acid and 16–20 mg of iron [4]. There are currently no specific recommendations in terms of supplementation for other micronutrients. The use of a multivitamin combined with the increase in total energy intakes is probably sufficient to allow pregnant women to fill other micronutrient requirements [11].

Dietary intakes should be examined throughout pregnancy in order to detect potential excesses or deficiencies in macro- and micronutrients associated with adverse pregnancy outcomes [12,13,14]. However, to date, few studies have assessed pregnant women's dietary intakes by considering both food and supplement sources, and even fewer have done so in each trimester of pregnancy [15,16,17,18,19,20]. To our knowledge, no study assessed trimester-specific adequacy to current nutritional Canadian recommendations. This study aimed to: (1) measure changes in energy and macronutrient intakes across trimesters; and (2) assess pregnant women's dietary intakes in comparison with current Canadian nutritional recommendations.

Materials and methods

Study Population

Eighty-six (86) pregnant women recruited from April 2016 to May 2017 at the CHU de Québec—Université Laval (Québec City, QC, Canada) were included in the ANGE (Apports Nutritionnels durant la GrossessE) project. Women younger than 18 years old and with a gestational age greater than 11 weeks of pregnancy at the time of recruitment were excluded. Women with a previously diagnosed severe medical condition (i.e., type 1 or type 2 diabetes, renal disease, inflammatory and autoimmune disorders) were also excluded. Our final sample included 79 women for whom we have nutritional data in all trimesters. The ANGE project was approved by the CHU de Québec—Université Laval Research Center's Ethics Committee and participants gave their informed written consent at their first visit to the research center.

The Automated Web-Based 24-h Recall (R24W)

In the first (range: 8.4–14.0 weeks), second (range: 19.3–28.3 weeks), and third (range: 31.9–37.7 weeks) trimesters of pregnancy, each participant was asked to complete a total of three Web-based 24-h dietary recalls, using the R24W (Rappel de 24h Web; 24h dietary recall) platform, on two weekdays and one weekend day (total of nine dietary recalls throughout pregnancy). The development of the R24W has been previously described [21]. Briefly, the R24W uses a sequence of questions inspired by the United States Department of Agriculture (USDA) Automated Multiple Pass Method (AMPM) [22]. The application sends automatic emails on randomly chosen dates to remind the participants to complete the recall. Participants were required to watch a mandatory tutorial video prior to their first recall. The database includes 2865 food items that are linked to the Canadian Nutrient File [23] to enable automatic extraction of nutrient values. Participants can report an unlimited number of meals and snacks for a 24-h period. Pictures depicting multiple portion sizes with corresponding units and/or volume are available for more than 80% of all food items. After selecting a food item, participants must choose the picture that best represents the amount of food eaten. In addition, systematic questions are asked about frequently forgotten food items including toppings, condiments, fats, snacks, and drinks. The R24W was previously validated in pregnant women for each trimester [24]. All food items were automatically coded using the 2015 version of the Canadian Nutrient File [23] and data for energy and 22 nutrients were analyzed.

Supplement Use

Information regarding dietary and prenatal supplement use was obtained through a Web questionnaire administered within each trimester. Participants had to identify their supplement (e.g., brand name, type of supplement, specific nutrient, etc.), and provide its drug identification number (DIN), its measurement unit (e.g., tablets, drops, grams, milliliters, etc.), the dosage, and the frequency at which the reported dose was taken. Participants could enter as many as 10 dietary supplements. The Health Canada Licensed Natural Health Product Database [25] as well as companies' product labels and websites were used to collect the nutritional information of all supplements entered by participants. If information was missing or was incomplete for any of the supplements' characteristics, a research assistant contacted the participant to obtain the missing information. We assessed supplement use by compiling types of supplements used (multivitamins or single-nutrient supplements) and the number of users for each type of supplement.

Estimated Energy and Protein Requirements

Pre-pregnancy body weight was self-reported and height was measured at baseline to calculate pre-pregnancy BMI. Participants completed the validated French version of the Pregnancy Physical Activity Questionnaire (PPAQ) [26,27] within each trimester. Physical activity levels (PALs) were determined by ranking the participants according to the total amount of time they engaged in moderate and high-intensity activities (minutes/day). According to the Institute of Medicine (IOM) guidelines for the general adult population (which includes pregnant women) [3], participants were either considered sedentary (less than 30 min of moderate-intensity activity), low-active (30 to 60 min of moderate-intensity activity), active (60 to 180 min of moderate-intensity activity or 30 to 60 min of high-intensity activity) or very active (more than 180 min of moderate-intensity activity or more than 60 min of high-intensity activity). Estimated energy requirements (EERs) were calculated for each trimester by using pre-pregnancy weight, age, height, and physical activity coefficient corresponding to the PAL determined by the PPAQ [3]. An additional 340 kcal and 452 kcal were respectively added to the second and third trimester EERs [3]. Daily protein requirements were calculated as 1.1 g/kg of pre-pregnancy weight for the first 20 weeks of pregnancy, to which 25 g of protein per day was added for the remaining 20 weeks of pregnancy [3].

Other Variables

Gestational age (weeks of gestation) was confirmed by ultrasound conducted at the CHU de Québec—Université Laval in the first trimester. A Web-based self-administered questionnaire was completed by all participants either in the first (n = 62) or in the second (n = 24) trimester to collect information on economic and socio-demographic characteristics.

Statistical Analyses

within each trimester, means and standard deviations for energy and macro- and micronutrient intakes as well as the percentage of energy from carbohydrates (% carbohydrates), fat (% fat), and proteins (% proteins) were calculated from the three 24-h dietary recalls. Total micronutrient intakes were calculated by combining intakes from supplements and intakes from food sources only (derived from the dietary recalls). We then compared total energy and nutrient intakes and intakes from food sources only with dietary reference intakes (DRIs) by calculating proportions of women that had intakes below the estimated average intakes (EARs) and above the upper intake limit (UL), as applicable [28]. Folate intakes as dietary folate equivalent (DFE) were compared to the EAR (520 µg), and only synthetic forms of folic acid (i.e., fortified foods and supplements) were compared to the UL for folic acid (1000 µg), as the UL for folic acid applies only to synthetic forms [3]. Similarly, only niacin and magnesium intakes from supplements were compared to the UL for these nutrients, as their respective UL only applies to intakes from supplements [3]. Energy intakes (EIs) were compared with EERs, and protein, carbohydrate, and fat intakes as percentages of energy were compared with the acceptable macronutrient distribution range (AMDR) [3]. Proportions of women with values below or above the EERs or AMDR were calculated. Protein intakes (g/day) were also compared to estimated protein requirements, as previously described [3]. Finally, repeated measures ANOVA was performed to assess variations in energy, macro- and micronutrient intakes across trimesters. All statistical analyses were performed in JMP version 13 (SAS Institute Inc., Cary, NC, USA).

Results

Participant characteristics are presented in Table 1. Of the 86 pregnant women recruited, seven were lost to follow-up, mainly due to miscarriage or lack of time to devote to the project. Therefore, results include 79 pregnant women with a mean age of 32.1 ± 3.7 years and an average pre-pregnancy BMI

of 25.7 ± 5.8 kg/m^2. The majority of participants were Caucasian (97.5%), had a university degree (78.5%), an annual household income of C$80,000 or more (63.3%), and were multiparous (64.6%).

Supplement use

Prenatal multivitamins were used by a majority of pregnant women (86.1%, 84.8%, and 78.5% in the first, second, and third trimesters, respectively) and folic acid supplements were the most commonly reported single-nutrient supplements (data not shown). Among women that did not take a multivitamin, the most reported single nutrient taken was folic acid for all trimesters (data not shown). Furthermore, among participants taking two supplements, the most reported single nutrients combined with a multivitamin were folic acid (50.0%) vitamin D (40.0%), and iron (44.4%) in the first, second, and third trimesters, respectively (data not shown). Small proportions (<10%) of women reported taking vitamin D, iron, and omega-3 as single-nutrient supplements throughout pregnancy (data not shown). In the third trimester, women who reported taking no supplement were significantly younger than the women who were taking at least one supplement (30.3 ± 3.8 years old vs. 32.6 ± 3.5 years old, $p = 0.0236$; data not shown).

Energy, Macronutrients, and Dietary Fiber

Table 2 shows trimester-specific energy intakes and macronutrient intakes as percentages of energy intake derived from the dietary recalls in comparison with EERs and AMDRs. No significant difference was observed for energy, protein, carbohydrate, or lipid intakes across trimesters. However, a significant increase in SFAs and a decrease in PUFAs as percentages of energy intakes were observed across trimesters (Table 2). Macronutrient intakes (grams per day) derived from the R24Ws and proportions of women that reported intakes above or below the corresponding DRIs are shown in Table 3. Mean energy intakes exceeded EERs in the first trimester (2294.3 ± 487.2 vs. 2122.4 ± 265.9 kcal; $p = 0.006$), but were below EERs in the third trimester (2234.6 ± 476.1 vs. 2492.2 ± 216.8 kcal; $p < 0.0001$). Protein intakes as a percentage of energy were within the acceptable distribution range (10–35%) in all trimesters but exceeded estimated requirements (1.1 g/kg) in the first trimester (96.7 ± 20.7 vs. 70.0 ± 8.6 g/day; $p < 0.0001$) for almost all participants (94.9% of them). In all trimesters, a majority of women reported fat intakes that were above the acceptable distribution range as a percentage of energy intakes. Inversely, carbohydrate intakes as percentages of energy were below the acceptable

distribution range for more than 20% of participants for each trimester. Dietary fiber intakes were also below the DRI of 14 g/1000 kcal in all trimesters for more than 85% of participants.

Vitamins and Minerals

Micronutrient intakes derived from the R24Ws (food sources only) and proportions of women that reported intakes above or below the corresponding DRIs are shown in Table 4. A high prevalence of inadequate intakes was observed for vitamin D (93.7%, 83.5%, 78.5%), iron (88.6%, 89.9%, 94.9%), and folate (58.2%, 60.8%, 68.4%) in all trimesters, when only food sources were considered (Table 4). Vitamin B6 intakes were below the EAR for 36.7%, 32.9%, and 38.0% of women in the first, second, and third trimesters, respectively. Smaller proportions of women reported, throughout pregnancy, inadequate intakes of magnesium, vitamin A, calcium, and zinc. Vitamin C intakes were inadequate for 22.8% of participants in the second trimester but only for 4.1% and 10.1% of women in the first and third trimesters, respectively. Repeated measures ANOVA showed significant decreases in dietary intakes of vitamin C and manganese, as well as significant increases in dietary calcium and vitamin B12 intakes across trimesters (Table 4). In all trimesters, a majority of pregnant women reported sodium intakes that were above the UL of 2300 mg.

As shown in Table 5, when food sources and dietary supplements were combined, the proportion of women with adequate micronutrient intakes increased. With the exception of folate, vitamin D, and iron, less than 15% of our participants had total micronutrient intakes below the EAR, in all trimesters. Total intakes of folic acid and sodium were above the UL for a majority of women, and more than a third of participants had total iron intakes above the UL for all trimesters. The significant decrease observed for vitamin C and manganese, as well as the significant increase in calcium intakes persisted after the addition of intakes from supplements (Table 5).

Discussion

Our prospective assessment of pregnant women's dietary intakes revealed a stability in energy and macronutrient intakes across trimesters. Most women exceeded their estimated requirements in terms of energy and protein in the first trimester but reported energy intakes below their needs later in pregnancy. We also found that diet alone may not be sufficient to provide adequate intakes for all micronutrients. Besides, when only food sources were considered, insufficient intakes of dietary fiber, vitamin D, folate, and iron were observed for a majority of women. Supplement use considerably

improved the adequacy of micronutrient intakes among the pregnant women in our study sample, although excessive intakes were observed for iron, folic acid, and sodium.

Although it is recommended for pregnant women to increase their caloric intake as the pregnancy progresses [3], we found that there was a stability in energy intakes throughout pregnancy. Likewise, Abeysekera et al. [29] and Talai Rad et al. [30] as well as Moran et al. [18] found no significant changes in longitudinal caloric intakes of pregnant women. A prospective study by Vioque et al. conducted among Spanish pregnant women even observed a significant decrease in energy intakes (from the first to the third trimester) measured by a food frequency questionnaire (FFQ) [31]. Moreover, a recent meta-analysis of 18 studies by Jebeile et al. [32] reported little to no change in energy intake during pregnancy, which is in line with the stability we observed across trimesters. In light of their observations, Jebeile et al. [32] questioned the current caloric recommendations during pregnancy, suggesting they may be too high, but this affirmation should be further explored through studies that will focus on energy metabolism during pregnancy.

Although no variation in energy and macronutrient intakes was observed, most women exceeded their EER and EPR in the first trimester, in contrast with the third trimester, where a majority of women reported energy intakes below their EER. Kubota et al. [15] reported partially similar results, as they observed dietary intakes in the third trimester that were 900 kcal below the official Japanese recommendations. Since we do not have pre-pregnancy nutritional data, it is unknown whether the caloric excess observed is related to pregnancy itself or if it was already present before pregnancy. Augustine et al. [33] suggested that the process of «eating for two» associated with pregnancy occurs before the actual metabolic demand affects the mother. According to them, hormone-induced increase in dietary intakes early on in pregnancy could represent an adaptive response to the upcoming metabolic demand [33]. This could partially explain why our sample exceeded their EERs and EPRs as early as in the first trimester. The higher protein intakes observed in the first trimester also suggest that foods rich in protein (e.g., meat, dairy, legumes, etc.) may have contributed to the energy excess observed in early pregnancy, but this should be further investigated. Moreover, the questionnaire used to calculate PAL, the PPAQ, has been known to overestimate PAL in a small cohort of pregnant women [34]; therefore, the EERs calculated within each trimester may have been overestimated. The use of a more precise method to measure our sample's PAL (e.g., an accelerometer), could have attenuated the gap between EIs and EERs in the third trimester but could have increased it in the first trimester.

In parallel with the energy and protein excess observed in the first trimester, we found that, in all trimesters, more than half of our study sample reported fat intakes as percentages of energy that exceeded the acceptable range of 20–35%. These results are similar to those of Dubois et al. [11] in which a third of the 1533 pregnant women studied had total fat intakes as a percentage of energy above the recommended range. Furthermore, a meta-analysis by Blumfield et al. [19] also found that studies set in Western regions reported mean fat intakes (as percentages of energy intakes) of 35.0% to 37.1% among pregnant women, in accordance with our results. Moreover, in our study, 20.3% to 24.1% of participants reported carbohydrate intakes as a percentage of energy below the recommendations, which is also similar to other North American studies [19]. However, the literature is still incomplete and unclear on the roles that each macronutrient plays in pregnant women's health [35]. Further research is therefore necessary to assess the impact of inadequate macronutrient intakes on maternal and fetal outcomes.

The suboptimal dietary intakes of fiber, vitamin D, folic acid, and iron observed in pregnant women from our study seem to be in line with the results of various authors [11,18,36,37,38,39]. Our results combined with those of other epidemiological studies thus suggest that food fortification policies and the use of a multivitamin during pregnancy are still necessary to reduce the risk of inadequate intake of micronutrients. In fact, our study showed that the use of dietary supplements greatly improved the adherence to micronutrient recommendations, as approximately 75% of all participants had total intakes above the EAR for all micronutrients. Dubois et al. [11] as well as Fayyaz et al. [40] reported similar results, especially regarding total iron and folate intakes. The insufficient intakes of dietary fiber observed in our study are in accordance with what Dubois et al. [11] reported, however, the relevance of these results and the impact of inadequate fiber intakes during pregnancy should be further investigated.

Most of our participants were supplement users and prenatal multivitamins were the most prevalent supplement taken by our study sample. It is important to mention that, although Health Canada recommends a prenatal multivitamin that contains 400 µg of folic acid and 16–20 mg of iron, close to all prenatal multivitamin supplements taken by our participants contained 1000 to 5000 µg of folic acid and 27 to 35 mg of iron (data not shown). Consequently, a majority of participants exceeded the UL for folic acid (1000 µg) in all trimesters and more than a third exceeded the UL for iron (45 mg) in the first and second trimesters. Dubois et al. [11] obtained similar results as they found that 90.4% and 32.4%

of their participants had excessive folic acid and iron intakes, respectively, when dietary supplements were taken into account. Increased iron and folic acid intakes are indicated for women with conditions such as iron-deficiency anemia (iron) or for pregnant women at higher risk of giving birth to children with neural tube defects (folic acid) [41,42]. In our study, we do not have information regarding the number of women that were prescribed an iron supplement to prevent or to treat an iron-deficiency anemia. It is therefore impossible to know if the excessive iron intakes observed among our participants were due to anemia prevention or treatment. Moreover, it is important to mention that other nutrients, namely calcium, might decrease iron absorption, and thus observed total intakes of iron may not reflect the real iron status of our participants [43]. For these reasons, our results should be combined with direct assessment of iron status to evaluate the adequacy of our participant's iron intakes. Furthermore, results from a recent Canadian study suggest that although fortification policies improved the population's dietary intakes of folic acid, supplement users may be at risk of folic acid overconsumption [44]. To date, the implications of high folic acid intakes on pregnancy and prenatal health outcomes are not well understood and should therefore be further investigated [40,45,46].

Along with iron and folate, vitamin D was found to be one of the nutrients for which diet alone was insufficient to provide adequate intakes. The prevalence of inadequate intakes did decrease when dietary supplements were taken into account, but more than 20% of participants sill had total vitamin D intakes that were below the EAR, in all trimesters. Similar inadequacies were reported by Aghajafari et al. [37], as they found that 44% of their sample (n = 537 pregnant women) reported total vitamin D intakes (diet and supplements) that did not meet the Recommended Dietary Allowance (RDA) of 600 IU. Furthermore, despite the fact that more than half of their participants reported adequate daily vitamin D intakes (≥600 IU), Aghajafari et al. found that 20% of them were vitamin D-insufficient, according to the Endocrine Society and Osteoporosis Canada's definition of 75 nmol/L circulating 25-hydroxyvitamin D. [47,48]. Moreover, Hollis et al. [49] conducted a double-blind randomized clinical trial in 494 pregnant women and found that a vitamin D supplementation of 4000 IU/day was the most effective in achieving vitamin D sufficiency, in comparison with 400 and 2000 IU/day. In our study, prenatal multivitamins taken by pregnant women contained, depending on the brand of the multivitamin, between 250 and 600 IU of vitamin D (data not shown). This may not be adequate, according to Hollis et al. [49], to complement dietary intakes of all pregnant women. Nevertheless, evidence regarding vitamin D supplementation during pregnancy is not currently sufficient to support definite clinical recommendations, and the results of Hollis et al. should be interpreted with caution [50]. It would also

be necessary to combine dietary assessment (food and supplements) with direct measurement of vitamin D status (i.e., circulating 25(OH)D) and sun exposure in order to accurately evaluate vitamin D adequacy during pregnancy [11,51].

To our knowledge, this is the first study to prospectively assess whether or not pregnant women met current Canadian nutritional recommendations. The use of a validated Web-based 24 h recall combined with a Web questionnaire on supplement use generated detailed information on dietary and total intakes during pregnancy. However, our study has some limitations, namely regarding the small size and the lack of representativeness of our study sample, since most pregnant women enrolled were Caucasians and of a higher socioeconomic status. The nutritional inadequacies observed among our study sample may therefore be greater among less educated and lower-income pregnant women. Nutritional adequacy of pregnant women of lower socioeconomic status should be further investigated. However, despite our small sample size, our results highlight the need for more prospective, population-based studies regarding pregnant women's dietary intakes, especially among lower income, less educated populations. Finally, our study did not measure circulating 25(OH)D in addition to iron and folate status, which limited our adequacy assessment of pregnant women's vitamin D, iron, and folate intakes.

Conclusions

In summary, we observed that, contrary to current recommendations, there was a stability in dietary intakes across trimesters, and thus most women exceeded their energy and protein requirements in the first trimester and were had intakes below recommendations in the third trimester. The implications and possible causes of excessive energy and protein intakes in early pregnancy are not well documented and should be further investigated in association with gestational weight gain and other metabolic outcomes. The use of prenatal multivitamins and single nutrient supplements considerably improved iron, folate, and vitamin D adequacy, although excessive folic acid, iron, sodium, and niacin intakes were observed, and vitamin D inadequacies persisted for some pregnant women. Further research is needed to, firstly, evaluate the impact of high doses of folic acid on pregnancy and prenatal outcomes, and, secondly, to identify the dose of supplemental vitamin D necessary to achieve vitamin D sufficiency.

Declarations

Author Contributions: All authors made substantial contributions to the conception and design of the manuscript, and all critically revised a first draft of the manuscript for important intellectual content. C.S. collected the data under the supervision of A.-S.M. and conducted primary statistical analyses of the data with the help of J.R., S.L., S.J.W., B.F.-B., C.G., and A.-S.M. All authors participated in the secondary analyses and interpretation of data. All authors gave their approval of the manuscript's final version to be published and therefore take public responsibility for the content of the manuscript. Finally, all authors agreed to be accountable for all aspects of the work.

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Conflicts of Interest: The authors declare no conflict of interest.

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Tables

Table 1. Participants' characteristics (n = 79)

Variables	Mean ± SD or N (%)
Age (years)	32.1 ± 3.7
Weeks of gestation at baseline (weeks)	9.3 ± 0.7
Primiparous	28 (35.4)
BMI (kg/m^2)	25.7 ± 5.8
Underweight	2 (2.5)
Normal weight	43 (54.4)
Overweight	19 (24.1)
Obese	15 (19.0)
Ethnicity – Caucasian	77 (97.5)
Education	
High school	4 (5.0)
College	13 (16.5)
University	62 (78.5)
Household income	
< 40 000 $	5 (6.3)
40 000 – 59 999 $	10 (12.7)
60 000 – 79 999 $	13 (16.5)
80 000 – 99 999 $	17 (21.5)
≥ 100 000 $	33 (41.8)
Income missing	1 (1.2)
Physical activity level	
(Minutes of moderate and vigorous activity/day)	
1st trimester	60.5 ± 59.6
2nd trimester	45.9 ± 51.1
3rd trimester	35.2 ± 41.5

Table 2. Trimester-specific energy intakes and macronutrient intakes as percentage of energy intakes in comparison with dietary reference intakes

	1st trimester			2nd trimester			3rd trimester			
	Mean ± SD or AMDR range	%below AMDR or EER	%above AMDR or EER	Mean ± SD or AMDR range	%below AMDR or EER	%above AMDR or EER	Mean ± SD or AMDR range	%below AMDR or EER	%above AMDR or EER	*p*-value[a]
EER (kcal/d)	2122.4 ± 265.9	-	-	2403.4 ± 241.1	-	-	2492.2 ± 216.8	-	-	
Energy intake (kcal/d)	2294.3 ± 487.2	36.7	63.3	2320.2 ± 519.1	60.8	39.2	2234.6 ± 476.1	70.9	29.1	0.09
AMDR Protein	10 – 35	-	-	10 – 35	-	-	10 -35	-	-	-
Protein, E%	16.9 ± 2.5	0	0	17.3 ± 2.9	0	0	17.9 ± 3.3	0	0	0.14
AMDR Carbohydrate	45 – 65	-	-	45 – 65	-	-	45 – 65	-	-	-
Carbohydrate, E%	49.4 ± 4.7	20.3	0	48.3 ± 5.7	24.1	0	48.3 ± 5.5	24.1	0	0.27
AMDR Total fat	20 – 35	-	-	20 – 35	-	-	20 -35	-	-	-
Total fat, E%	35.1 ± 4.0	0	50.6	35.8 ± 4.9	0	55.7	35.5 ± 4.4	0	57.0	0.53
SFA, E%	12.8 ± 2.1	-	-	13.2 ± 2.9	-	-	13.5 ± 2.5	-	-	0.047
MUFA, E%	12.3 ± 2.1	-	-	12.6 ± 2.0	-	-	12.5 ± 2.1	-	-	0.49
PUFA, E%	7.1 ± 1.9	-	-	7.1 ± 2.0	-	-	6.5 ± 1.8	-	-	0.03

[a]p-value for repeated measures ANOVA performed to assess variations in energy and macronutrient intakes across trimesters; When no dietary reference intake was established for a nutrient, the « - » was used instead of a 0; AMDR, Acceptable Macronutrient Distribution Range; EER, Estimated Energy Requirements, calculated with the following formula: 354 – (6.91 x Age) + Physical activity coefficient x [(9.36 x Weight) + (726 x Height)], to which an additional 340 or 452 kcal were added in the 2nd and 3rd trimesters; AI, Adequate Intake.

Table 3. Trimester-specific macronutrient intakes in comparison with dietary reference intakes

	1st trimester			2nd trimester			3rd trimester			*p*-value [a]
	Mean ± SD	%below EPR or AI	%above EPR or AI	Mean ± SD	%below EPR or AI	%above EPR or AI	Mean ± SD	%below EPR or AI	%above EPR or AI	
EPR, g/d	70.0 ± 8.6	-	-	95.0 ± 8.6	-	-	95.0 ± 8.6	-	-	-
Protein, g/d	96.7 ± 20.7	5.1	94.9	99.1 ± 20.9	48.1	51.9	98.2 ± 22.0	43.0	57.0	0.64
Carbohydrate, g/d	283.3 ± 68.8	-	-	280.3 ± 70.9	-	-	270.1 ± 68.0	-	-	0.14
Total fat, g/d	89.6 ± 21.7	-	-	93.1 ± 27.5	-	-	88.6 ± 23.6	-	-	0.20
Dietary fiber, g/d	23.3 ± 7.0	96.2	3.8	23.9 ± 8.0	87.3	12.7	22.9 ± 6.7	89.9	10.1	0.50
ω-6 Linoleic acid, g/d	14.8 ± 5.4	-	-	14.5 ± 5.3	-	-	13.4 ± 5.3	-	-	0.07
ω-3 Linolenic acid, g/d	2.0 ± 0.7	-	-	2.0 ± 0.9	-	-	1.9 ± 0.9	-	-	0.38
Cholesterol, mg/d	297.2 ± 99.7	-	-	291.1 ± 91.7	-	-	288.1 ± 109.0	-	-	0.81

[a]p-value for repeated measures ANOVA performed to assess variations in macronutrient intakes across trimesters; When no dietary reference intake was established for a nutrient, the « - » was used instead of a 0; EPR, Estimated Protein Requirement (1.1g/kg or pre-pregnancy weight for the first half of pregnancy and 1.1g/kg of pre-pregnancy weight + 25g for the second half); AI, Adequate Intake.

Table 4. Trimester-specific micronutrient intakes from food alone in comparison with dietary reference intakes

			1st trimester			2nd trimester			3rd trimester			
	EAR	UL	Mean ± SD	%below EAR	%above UL	Mean ± SD	%below EAR	%above UL	Mean ± SD	%below EAR	%above UL	*p*-value[a]
Vitamin D, IU/d	400	4000	234.8 ± 119.0	93.7	0	261.2 ± 135.2	83.5	0	271.9 ± 150.2	78.5	0	0.11
Iron, mg/d	22	45	15.3 ± 4.8	88.6	0	15.8 ± 5.2	89.9	0	14.8 ± 4.2	94.9	0	0.09
Folate, µg DFE/d	520	-	516.2 ± 139.5	58.2	-	495.4 ± 143.3	60.8	-	490.1 ± 141.3	68.4	-	0.31
Folic acid, µg/d	-	1000	155.0 ± 65.5	-	0	146.8 ± 72.6	-	0	138.3 ± 72.1	-	0	0.17
Vitamin B_6, mg/d	1.6	100	1.8 ± 0.5	36.7	0	1.9 ± 0.5	32.9	0	1.8 ± 0.5	38.0	0	0.32
Magnesium, mg/d	290-300	350	381.2 ± 103.8	17.8	-	391.9 ± 108.9	19.0	-	386.2 ± 106.4	20.3	-	0.65
Vitamin A, µg RAE/d	550	3000	879.2 ± 305.9	13.9	0	906.4 ± 392.5	17.7	0	916.2 ± 398.4	17.7	0	0.71
Zinc, mg/d	9,5	40	12.5 ± 3.2	12.7	0	13.4 ± 3.2	8.9	0	13.2 ± 3.7	11.4	0	0.15
Calcium, mg/d	800	2500	1292.3 ± 381.8	10.1	0	1350.3 ± 515.9	13.9	2.5	1427.0 ± 506.0	6.3	1.3	0.02
Vitamin C, mg/d	70	2000	159.5 ± 66.7	5.1	0	137.9 ± 81.4	22.8	0	138.4 ± 66.6	10.1	0	0.01
Thiamin, mg/d	1.2	-	1.9 ± 0.6	5.1	-	1.9 ± 0.7	7.6	-	1.8 ± 0.8	7.6	-	0.40
Vitamin B_{12}, µg/d	2.2	-	4.8 ± 1.6	2.5	-	5.4 ± 2.4	3.8	-	5.6 ± 2.5	0	-	0.02
Riboflavin, mg/d	1.2	-	2.3 ± 0.6	1.3	-	2.4 ± 0.6	1.3	-	2.5 ± 0.8	0	-	0.07
Niacin, mg NE/d	14	35	45.7 ± 10.6	0	-	45.9 ± 9.2	0	-	45.0 ± 10.3	0	-	0.64
Pantothenic acid, mg/d	-	-	6.5 ± 1.8	-	-	6.5 ± 1.5	-	-	6.5 ± 1.6	-	-	0.98
Phosphorus, mg/d	580	3500	1616.4 ± 383.7	0	0	1660.3 ± 398.0	0	0	1673.7 ± 442.1	0	0	0.47
Sodium, mg/d	-	2300	3406.0 ± 889.8	-	94.9	3276. 0 ± 950.3	-	86.1	3199.0 ± 921.7	-	84.8	0.17
Manganese, mg/d	-	11	4.0 ± 1.5	0	1.3	4.3 ± 1.4	-	0	3.9 ± 1.3	-	0	0.005
Selenium, µg/d	49	400	135.7 ± 34.0	0	0	135.2 ± 32.1	0	0	131.8 ± 30.9	0	0	0.48
Copper, mg/d	0.8	10	1.5 ± 0.6	1.3	0	1.6 ± 0.6	1.3	0	1.5 ± 0.5	3.8	0	0.22

[a]p-value for repeated measures ANOVA performed to assess variations in micronutrient intakes across trimesters; When no EAR or UL was established for a nutrient, the « - » was used instead of a 0; EAR, estimated average requirement; UL, upper intake limit; DFE, dietary folate equivalent; NE, niacin equivalent.

Table 5. Trimester-specific total micronutrient intakes (including food sources and supplements) in comparison with dietary reference intakes

			1st trimester			2nd trimester			3rd trimester			
	EAR	UL	Mean ± SD	%below EAR	%above UL	Mean ± SD	%below EAR	%above UL	Mean ± SD	%below EAR	%above UL	*p*-value[a]
Vitamin D, IU/d	400	4000	632.2 ± 555.9	25.3	1.3	690.0 ± 538.4	21.5	1.3	689.4 ± 544.9	21.5	1.3	0.15
Iron, mg/d	22	45	38.2 ± 14.0	19.0	35.4	38.8 ± 13.8	19.0	38.0	41.0 ± 24.7	22.8	36.7	0.65
Folate, µg DFE/d	520	-	1777.0 ± 1221.4	7.6	-	1763.2 ± 1313.0	10.1	-	1617.6 ± 1212.2	16.5	-	0.29
Folic acid, µg/d	-	1000	1415.8 ± 1213.7	-	86.1	1412.6 ± 1313.4	-	83.5	1265.8 ± 1199.3	-	79.7	0.27
Vitamin B_6, mg/d	1.6	100	5.6 ± 3.9	8.9	0	5.8 ± 4.0	7.6	0	5.4 ± 4.0	8.9	0	0.29
Magnesium, mg/d	290-300	350	419.1 ± 108.4	8.9	0	431.9 ± 113.9	8.9	0	424.2 ± 110.8	11.4	0	0.62
Vitamin A, µg RAE/d	550	3000	1398.1 ± 574.4	7.6	0	1415.9 ± 674.8	7.6	0	1429.8 ± 635.5	7.6	0	0.91
Zinc, mg/d	9,5	40	20.4 ± 6.7	5.1	0	21.4 ± 6.6	2.5	0	21.0 ± 7.2	3.8	0	0.36
Calcium, mg/d	800	2500	1503.4 ± 370.6	2.5	0	1560.0 ± 551.4	6.3	5.1	1630.7 ± 524.4	2.5	6.3	0.04
Vitamin C, mg/d	70	2000	234.7 ± 79.1	1.3	0	215.7 ± 93.3	7.6	0	213.2 ± 71.0	2.5	0	0.04
Thiamin, mg/d	1.2	-	3.4 ± 1.3	2.5	-	3.5 ± 1.3	2.5	-	3.3 ± 1.4	2.5	-	0.31
Vitamin B_{12}, µg/d	2.2	-	11.0 ± 8.0	1.3	-	10.6 ± 5.7	0	-	10.1 ± 5.3	0	-	0.54
Riboflavin, mg/d	1.2	-	4.0 ± 1.4	1.3	-	4.1 ± 1.5	0	-	4.1 ± 1.5	0	-	0.80
Niacin, mg NE/d	14	35	60.1 ± 13.4	0	-	60.8 ± 12.8	0	-	59.3 ± 14.6	0	-	0.64
Pantothenic acid, mg/d	-	-	11.1 ± 3.2	-	-	11.1 ± 3.1	-	-	10.9 ± 3.1	-	-	0.86
Phosphorus, mg/d	580	3500	1618.0 ± 383.6	0	0	1665.7 ± 401.2	0	0	1673.7 ± 442.1	0	0	0.49
Sodium, mg/d	-	2300	3406.0 ± 889.8	-	94.9	3276. 0 ± 950.3	-	86.1	3199.0 ± 921.7	-	84.8	0.17
Manganese, mg/d	-	11	5.0 ± 1.9	-	1.3	5.3 ± 1.8	-	1.3	4.9 ± 1.6	-	0	0.04
Selenium, µg/d	49	400	151.2 ± 38.1	0	0	151.4 ± 39.2	0	0	147.6 ± 37.5	0	0	0.57
Copper, mg/d	0.8	10	2.6 ± 0.9	1.3	0	2.7 ± 1.0	1.3	0	2.5 ± 0.9	2.5	0	0.23

[a]p-value for repeated measures ANOVA performed to assess variations in micronutrient intakes across trimesters; When no EAR or UL was established for a nutrient, the « - » was used instead of a 0; EAR, estimated average requirement; UL, upper intake limit; NE, niacin equivalent; DFE, dietary folate equivalent.

Chapitre 6 – Longitudinal assessment of vitamin D status across trimesters of pregnancy

Résumé

Ce projet visait à : 1) évaluer les concentrations sériques de 25-hydroxyvitamine D (25(OH)D) en fonction de l'IMC prégrossesse et 2) examiner leurs associations avec l'apport en vitamine D des suppléments. Les 79 femmes enceintes ont complété, à chaque trimestre, un questionnaire sur l'utilisation de suppléments. Les concentrations sériques de 25(OH)D ont été mesurées par chromatographie liquide avec spectrométrie de masse en tandem. Aux premier et troisième trimestres, les concentrations de 25(OH)D des femmes avec un IMC ≥30 kg/m^2 étaient inférieures à celles ayant un IMC <25 kg/m^2. Toutefois, à partir du deuxième trimestre, leurs concentrations de 25(OH)D étaient majoritairement adéquates. L'apport en vitamine D des suppléments était le déterminant le plus important des concentrations de 25(OH)D, dans un modèle incluant l'IMC, la variation saisonnière, et l'activité physique. En résumé, la majorité des femmes avait des concentrations de 25(OH)D adéquates, ce qui soutient la pertinence de la prise d'une multivitamine prénatale.

Title page

Title: Longitudinal assessment of vitamin D status across trimesters of pregnancy

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Keywords: vitamin D, vitamin D status, pregnancy, 25(OH)D, 25-hydroxyvitamin D, vitamin D intake, supplements

Abstract

Background : The evolution of vitamin D status across pregnancy trimesters and its association with prepregnancy body mass index (ppBMI; in kg/m^2) remain unclear.

Objectives: We aimed to 1) assess trimester-specific serum total 25-hydroxyvitamin D [25(OH)D] concentrations, 2) compare those concentrations between ppBMI categories, and 3) examine associations between 25(OH)D concentrations, ppBMI, and vitamin D intake.

Methods: As part of a prospective cohort study, 79 pregnant women with a mean age of 32.1 y and ppBMI of 25.7 kg/m^2 were recruited in their first trimester (average 9.3 weeks of gestation). Each trimester, vitamin D intake was assessed by 3 Web-based 24-h recalls and a Web questionnaire on supplement use. Serum total 25(OH)D was measured by LC–tandem MS. Repeated-measures ANOVA was performed to assess the evolution of 25(OH)D concentrations across trimesters of pregnancy and comparisons of 25(OH)D concentrations between ppBMI categories were assessed by 1-factor ANOVAs. Stepwise regression analyses were used to identify determinants of 25(OH)D concentrations in the third trimester.

Results: Mean ± SD serum total 25(OH)D concentrations increased across trimesters, even after adjustments for ppBMI, seasonal variation, and vitamin D intake from supplements (67.5 ± 20.4, 86.5 ± 30.9, and 88.3 ± 29.0 nmol/L at mean ± SD 12.6 ± 0.8, 22.5 ± 0.8, and 33.0 ± 0.6 weeks of gestation, respectively; $P < 0.0001$). In the first and third trimesters, women with a ppBMI ≥30 had lower serum total 25(OH)D concentrations than women with a ppBMI <25 ($P < 0.05$); however, most had concentrations >40nmol/L by the second trimester. Vitamin D intake from supplements was the strongest determinant of third-trimester serum total 25(OH)D concentrations ($r2 = 0.246$, $\beta = 0.51$; $P < 0.0001$).

Conclusions: There was an increase in serum total 25(OH)D concentrations across trimesters, independent of ppBMI, seasonal variation, and vitamin D intake from supplements. Almost all women had serum total 25(OH)D concentrations over the 40- and 50-nmol/L thresholds, thus our study supports the prenatal use of a multivitamin across pregnancy.

Introduction

The prenatal period is associated with many physiological changes and adaptations that require adequate energy and nutrient intakes. Recommended intakes for almost all nutrients are increased relative to those for nonpregnant women of the same age (1, 2). In Canada, national dietary guidance recommends that all women who could become pregnant take a daily multivitamin containing 400 μg (0.4 mg) of folic acid (2). It is also recommended that pregnant women continue taking this supplement throughout pregnancy to help meet the needs for folic acid and other nutrients like iron. Although the multivitamin recommended for women of childbearing age would typically contain vitamin D, it is not specifically recommended to supplement vitamin D intake during pregnancy. Conversely, in the United Kingdom, the National Institute for Health and Care Excellence recommends that pregnant women and women planning a pregnancy take 400 international units (IU) vitamin D/d throughout pregnancy to ensure adequate vitamin D status (3). Supplemental intake of vitamin D during pregnancy is important to consider, because studies from Canada and elsewhere have reported sizable proportions of pregnant women (range: 18.9%–90%) falling below the daily Estimated Average Requirement (EAR) of 400 IU vitamin D/d (4–8). The EAR value was set in accordance with adequate serum 25-hydroxyvitamin D [25(OH)D] concentrations of 40 nmol/L (9).

Assessment of vitamin D status during pregnancy remains relevant considering that lower serum total 25(OH)D concentrations in pregnant women were previously associated with the development of gestational diabetes mellitus, pre-eclampsia, and preterm birth (10–14). Prenatal vitamin D status is also important for fetal bone mineralization and growth (15). It has also been suggested that Canadian pregnant women may be at greater risk of vitamin D deficiency, considering Canada's higher latitude and therefore reduced ultraviolet β (UVB) exposure, which is necessary for dermal synthesis of vitamin D (16, 17). Notably, the National Academy of Medicine, formerly known as the Institute of Medicine, recommends using serum total 25(OH)D concentration thresholds of 40 and 50 nmol/L for evaluating the vitamin D status of populations and individuals, respectively (9). Nevertheless, some studies still compare their population's serum total 25(OH)D concentrations with the individual threshold value of 50 nmol/L, which corresponds to an RDA of 600 IU/d. In fact, among Canadian cohort studies conducted over the last decade (16, 18–24), serum total 25(OH)D concentrations <50 nmol/L were observed in 2%–45.6% of pregnant women. This rather wide range may be explained by disparities in the timing of the assessment of serum total 25(OH)D concentrations, because some studies have

assessed vitamin D status in the first trimester and others did so in the second or third trimesters (25). However, too few studies have investigated the evolution of serum total 25(OH)D concentrations across trimesters of pregnancy to suggest that concentrations <50 or 40 nmol/L are more prevalent in one trimester than in another. Furthermore, among the studies that have assessed serum total 25(OH)D concentrations during pregnancy, very few used the gold-standard method of liquid chromatography tandem mass spectroscopy (LC-MS/MS), which provides more valid and precise measurements. Thus, previously measured concentrations of serum total 25(OH)D may be over- or underestimated because of the timing and/or the method of assessment.

Moreover, only 3 of the mentioned Canadian cohort studies compared serum total 25(OH)D concentrations among prepregnancy body mass index (ppBMI) categories (21, 22, 24). They either observed no difference (21, 22) or higher serum total 25(OH)D concentrations in women with lower compared with greater ppBMI (24). The consideration of ppBMI in the assessment of vitamin D status is important, because obesity and adiposity have been associated with lower serum total 25(OH)D concentrations (26, 27) and because a considerable proportion of women now enter pregnancy with a long-standing BMI in the overweight or obese range (28). Adults with obesity also often require larger doses of vitamin D to reach similar serum total 25(OH)D concentrations to adults with a BMI in the recommended range (29). Thus, considering that the evolution of serum total 25(OH)D concentrations throughout pregnancy remains unclear and that its association with ppBMI is equivocal, we aimed to 1) assess trimester-specific serum total 25(OH)D concentrations, 2) compare those concentrations between ppBMI categories, and 3) examine associations between 25(OH)D concentrations, ppBMI, and vitamin D intake from food and supplements. We hypothesized that 1) serum total 25(OH)D concentrations would increase significantly from the first to the third trimester of pregnancy, 2) women with a higher ppBMI would have lower 25(OH)D concentrations in all trimesters, and 3) 25(OH)D concentrations would be inversely associated with ppBMI but positively associated with vitamin D intakes from food and supplements.

Methods

Participants

The present study used data from the Apports Nutritionnels durant la Grossesse (ANGE) cohort, a prospective study conducted from April 2016 to May 2017 in Québec City, Canada that followed 79 pregnant women from their first to their third trimester of pregnancy (4). Women with twin pregnancies,

a severe medical condition (i.e., type 1 or type 2 diabetes, renal or liver disease, inflammatory and autoimmune disorders), and women younger than 18 y were excluded from the study. At each trimester, all participants completed various Web-based questionnaires described below and came to the Research Center for on-site visits. The ANGE study was conducted according to the Declaration of Helsinki guidelines and was approved by the Centre Hospitalier Universitaire de Québec-Université Laval Research Centre's Ethics Committee (reference number: 2016–2866) as well as by Health Canada's Research Ethics Board (reference number: 2019-032H). All women gave their informed written consent during their first on-site visit to the research center.

Vitamin D intake from dietary and supplemental sources

Dietary intakes of vitamin D were assessed by self-administered Web-based 24-h dietary recalls, through the Rappel de 24h Web (R24W) platform. Three dietary recalls were completed in each trimester (at 8.4–14.0, 19.3–28.3, and 31.9–37.7 weeks of gestation). The R24W has been described elsewhere (30, 31) and its use has been validated by our team among pregnant women (32). Briefly, on the day they receive the automatically generated e-mail, participants must report all foods and drinks consumed the day before (24-h period). All food items included in the R24W database are linked to the 2015 Canadian Nutrient File (33), thus enabling the automatic extraction of nutritional information. Daily servings of milk and alternatives, according to the 2007 version of Canada's Food Guide (34), were automatically calculated by the R24W platform. A new version of Canada's Food Guide was published in 2019 (35), but the 2007 version of Canada's Food Guide (34) was used in the present study because it was the dietary guidance in use when the participants completed the recalls. Examples of milk and alternatives servings include 250 mL of milk or plant-based beverages fortified with vitamin D, 175 g of yogurt or kefir, and 50 g of cheese (34). The dietary vitamin D intakes reported in the present study represent sums of vitamin D intakes from all food sources averaged for the 3 recalls per trimester as well as the 9 recalls completed over pregnancy, when referring to trimester-specific and mean dietary intakes of vitamin D, respectively.

Participants also had to complete, in each trimester, a Web-based questionnaire on supplement use, as previously described (4). In brief, women were asked if they were currently taking a supplement and, if so, they reported its brand name and drug identification number or natural health product number, the dose they were taking, as well as the frequency of use. The amount of vitamin D in all reported supplements was collected either from Health Canada's Licensed Natural Health Product

Database (36) or from the companies' product labels or websites. Total vitamin D intake from supplements was evaluated as trimester-specific amounts and subsequently as an average representation of the whole pregnancy (mean of the 3 trimesters). Based on the most common doses of vitamin D reported by participants, mean supplement intake of vitamin D was also categorized as <250, 250–399, 400–599, and ≥600 IU/d.

Vitamin D status

Fasting blood samples were drawn at each trimester (9.9–14.7, 20.7–25.3, and 31.6–34.6 weeks of gestation) and were centrifuged at 20ºC for 10 minutes with a force of 1500 RCF's to extract serum. All samples were stored at −80°C and were later sent to Health Canada's laboratory (Nutrition Research Division) for measurement of the serum total 25(OH)D concentrations by LC-MS/MS (Quattro Premier XE, Waters Limited). Internal standards were first mixed with 150 µL of either serum sample, quality control, or calibrator. All samples were mixed with solutions of ZnSO4 and methanol to denature and precipitate proteins and were then centrifuged at at 20ºC for 5 minutes with a force of 2000 RCF's. Vitamin D metabolites were separated from the supernatant by solid phase extraction. For each vitamin D metabolite, MS/MS quantitation and ion transitions were obtained. A calibration curve (5-point) was plotted according to the areas of ion peak quantitation and internal standard response. Lastly, vitamin D metabolites' concentrations in the samples were computed from the calibration curve equation according to their peak areas and adjusting for internal standard response. The Health Canada laboratory is certified by the Vitamin D Standardization Certification Program (VDSCP) as being traceable to the internationally recognized reference procedures for measurement of serum total 25(OH)D (37). Via the VDSCP, the overall accuracy of the method was −2.5% and the precision was 5.7% (2019–2020).

Other variables

Weeks of gestation were confirmed by ultrasound in the first trimester. Each woman's ppBMI was calculated by dividing her self-reported prepregnancy weight by her measured height squared (measured at 9.3 ± 0.7 weeks of gestation), and weight was subsequently measured during all on-site visits. Because only 2 women were categorized as underweight, ppBMI (in kg/m^2) was categorized as follows: <25, 25–29.9, and ≥30. Analyses were performed with and without those 2 women and it did not affect the interpretation of the data. Each trimester, participants completed the Web-based French version of the Pregnancy Physical Activity Questionnaire (38, 39), from which daily minutes of

moderate- and high-intensity physical activity were calculated. According to the DRIs (1), women were also categorized as sedentary (<30 min/d of moderate-intensity activity), low active (30–59 min/d of moderate-intensity activity), active (60–179 min/d of moderate- or 30–59 min/d of high-intensity activity), or very active (≥180 min/d of moderate- or ≥60 min/d of moderate- plus ≥60 min/d of high-intensity activity). Seasons at the time of blood sampling were defined as follows: spring (21 March–20 June), summer (21 June–20 September), fall (21 September–20 December), and winter (21 December–20 March). Strength of UVB rays at the time of sampling was defined as high (1 April–31 October) or low (1 November–31 March). Finally, sociodemographic variables were surveyed once through a self-administered Web-based questionnaire.

Statistical analyses

Means ± SDs and proportions were used to describe the participants. Chi-square tests and 1-factor ANOVAs were performed to compare baseline characteristics between ppBMI categories. Repeated-measures ANOVAs were used to assess differences in serum total 25(OH)D, 25-hydroxyergocalciferol [25(OH)D2], 25-hydroxycholecalciferol [25(OH)D3], and 3-epi-25-hydroxyvitamin D3 [3-epi-25(OH)D3] concentrations across trimesters, followed by Tukey's honestly significant difference (HSD) post hoc tests for specific differences. Those analyses were adjusted for season at the time of sampling, ppBMI, and vitamin D intake from supplements. One-factor ANOVAs were used to compare trimester-specific serum total 25(OH)D concentrations between ppBMI categories and, in 2 separate models, 25(OH)D concentrations were compared according to season and strength of UVB rays at the time of sampling (measured in weeks of gestation). Tukey's HSD post hoc tests were performed for specific differences. Associations between trimester-specific serum total 25(OH)D concentrations and ppBMI as well as trimester-specific physical activity and vitamin D intake were explored through Pearson's product-moment correlation. A 1-factor ANOVA was used to compare differences in third-trimester serum total 25(OH)D concentrations according to mean (all trimesters) intake of vitamin D from supplements. We chose the third-trimester concentrations because we believe these provide a better reflection of vitamin D intakes throughout the whole pregnancy, contrary to the first and second trimesters. Stepwise regression analyses were performed with the predictor variables of trimester-specific serum total 25(OH)D concentrations. Variables first entered in the stepwise regression were ppBMI, mean or trimester-specific intake of vitamin D from supplements, mean or trimester-specific intake of vitamin D from foods, mean or trimester-specific amount of daily physical activity, education level (university degree compared with no university degree), mother's age, primiparity (being pregnant with their first

child), household income, and season at the time of sampling. In that model, in order for season to be a dichotomic variable, summer and fall as well as winter and spring were combined, therefore resulting in a 2-seasonal period. A cutoff of $P < 0.25$ was used in the stepwise regression, in order to identify which variables could be retained in the model. Finally, chi-square tests were performed to compare proportions of women with serum total 25(OH)D concentrations <40, <50, and ≥125 nmol/L, the latter being associated with adverse effects (9), across ppBMI categories (<25 and ≥25). Fisher's exact test was used instead of the chi-square tests if cells had <5 values. Proportions of women at risk of vitamin D deficiency were not tested across ppBMI categories because only 3 had serum total 25(OH)D concentrations <30 nmol/L in the first trimester and none thereafter. Statistical analyses were performed with JMP version 14 (SAS Institute Inc.) and differences were considered statistically significant at $P < 0.05$. One participant had extreme values of 25(OH)D concentrations in all trimesters, thus all analyses were done with and without that participant, and her inclusion did not affect the interpretation of the data. The residuals of our analyses were all normally distributed, therefore we did not normalize any of our data

Results

Most of the 79 women of the ANGE cohort were Caucasian, multiparous, >30 y of age, sedentary, and had a ppBMI <25 (Table 1). Overall socioeconomic status was high, as shown by the proportion of women with a university degree and a household income ≥80,000 CAD. All but 5 individuals (6.3%) reported taking a vitamin D–containing supplement in ≥1 of the 3 trimesters. Vitamin D intakes from food and supplement sources did not vary among trimesters ($P = 0.11$ and 0.49, respectively), but daily servings of milk and alternatives increased over time ($P = 0.002$). Women from the 3 ppBMI categories did not differ in terms of age, primiparity, vitamin D intakes (food and supplements), physical activity level, education, and household income (data not shown).

Concentrations of serum total 25(OH)D, 25(OH)D2, and 25(OH)D3 all increased significantly across trimesters, even after adjustments for season at the time of sampling, ppBMI, and vitamin D intake from supplements (Table 2). Concentrations of 3-epi-25(OH)D3 did not vary across trimesters. Overall, 5 women had serum total 25(OH)D concentrations <40 nmol/L in the first trimester, compared with 2 women in the second and third trimesters (Supplemental Table 1). Proportions of women with serum total 25(OH)D concentrations <40 nmol/L were low and did not differ between ppBMI categories (Supplemental Table 1). A higher proportion of women with overweight and obesity had serum total

25(OH)D concentrations <50 nmol/L in the first trimester than for women with under- and normal weight, but these same proportions were similar, between ppBMI categories, in the second and third trimesters (Supplemental Table 1). One woman had serum total 25(OH)D concentrations ≥125 nmol/L in the first trimester, whereas 6 women were at or above that threshold in the second and third trimesters.

Women with under- and normal weight had significantly higher serum total 25(OH)D concentrations than women with overweight and obesity in the first trimester (Figure 1). Similarly, in the third trimester, women with under- and normal weight had higher serum total 25(OH)D concentrations than women with obesity. No differences were observed in serum total 25(OH)D concentrations among BMI categories in the second trimester. Serum total 25(OH)D concentrations in the first and second trimesters also differed according to season at the time of blood sampling, with higher concentrations observed when blood was drawn in summer or fall (Supplemental Table 2). Serum total 25(OH)D concentrations did not differ according to strength of UVB rays at the time of sampling (Supplemental Table 3).

In all trimesters of pregnancy, serum total 25(OH)D concentrations were inversely correlated with ppBMI ($P < 0.01$) and positively correlated with trimester-specific supplemental and total vitamin D intakes, even after adjustment for season at the time of sampling (Table 3). Total minutes of moderate- and high-intensity physical activity were only associated with serum total 25(OH)D concentrations in the second trimester. Positive correlations were also observed between serum total 25(OH)D concentrations and daily servings of milk and alternatives and vitamin D intakes from foods, but only in the third trimester.

Third-trimester serum total 25(OH)D concentrations by mean supplemental intake of vitamin D were analyzed because vitamin D intakes from supplements did not vary across trimesters (Figure 2). Women with a mean supplemental intake of vitamin D ≥600 IU/d had higher serum total 25(OH)D concentrations than women in the 3 other, lower categories of supplemental intake ($P < 0.001$). The median (IQR) supplemental intake of vitamin D in the ≥600 IU/d category was 667 IU/d (600–1000 IU/d) and the median (IQR) total (food and supplements) vitamin D intake was 1027 IU/d (869–1310 IU/d).

Vitamin D intake from supplements was identified as the most significant determinant of third-trimester serum total 25(OH)D concentrations (Table 4). The same analysis was performed for the other

trimesters and vitamin D intake from supplements was also identified as the most significant determinant of the first and second trimesters' serum total 25(OH)D concentrations (Supplemental Tables 4, 5). Other significant determinants of third-trimester serum total 25(OH)D concentrations included ppBMI and blood sampling done in winter/spring compared with summer/fall, in a model that also included minutes of physical activity, vitamin D intakes from foods, education level (university degree compared with no university degree), mother's age, primiparity, and household income.

Discussion

Using data from a prospective pregnancy cohort, we aimed to measure and compare trimester-specific concentrations of serum total 25(OH)D in pregnant women, as well as to compare those concentrations between ppBMI categories. We also examined the associations between serum total 25(OH)D concentrations, ppBMI, and vitamin D intakes measured by a validated repeated 24-h recall assessment of food and supplements. To our knowledge, this is the first French-Canadian study to do so. Serum total 25(OH)D, 25(OH)D2, and 25(OH)D3, but not 3-epi-25(OH)D3, increased across pregnancy, even after adjustment for ppBMI and season at the time of sampling. Very few women had serum total 25(OH)D concentrations below the thresholds of 40 and 50 nmol/L and above the limit of 125 nmol/L, indicating an overall adequate vitamin D status. Although women with obesity had significantly lower serum total 25(OH)D concentrations in the first and third trimesters than women with a ppBMI <25, at least 95% of them had serum total 25(OH)D concentrations that were within the target ranges in all trimesters. Serum total 25(OH)D concentrations were inversely associated with ppBMI in all trimesters, but more strongly so in the first. The supplemental intake of vitamin D was thus effective in improving vitamin D status among women of higher ppBMI. Vitamin D intake from supplements was positively correlated with serum total 25(OH)D concentrations in each trimester, unlike dietary vitamin D intakes, the latter reflecting the mean intakes reported by the three 24-h recalls completed at each trimester. Women who reported an average intake of ≥600 IU supplemental vitamin D/d had higher serum total 25(OH)D concentrations (all >50nmol/L) in the third trimester than women with lower intakes from supplements. Finally, mean intake of vitamin D from supplements was identified as the strongest determinant of third-trimester serum total 25(OH)D concentrations.

Other longitudinal studies around the world found that serum total 25(OH)D concentrations increased throughout pregnancy (40–48). In the present study, it could be argued that the use of multivitamins containing vitamin D by most of our sample in the first trimester is the main reason for the increase in

serum total 25(OH)D concentrations from the first to the second and third trimesters. Still, the observed increase in the present study remained significant even after adjustment for vitamin D intake from supplements. Moreover, some of the previously cited studies observed an increase in serum total 25(OH)D concentrations even though none of their participants reported taking a supplement containing vitamin D throughout their whole pregnancy (40, 43, 45). For example, a Brazilian study published in 2018 measured plasma 25(OH)D concentrations in 199 women and observed a significant increase, from (mean ± SD) 65.0 ± 17.7 nmol/L in the first to 84.1 ± 24.5 nmol/L in the third trimester, which is very similar to our concentrations, even though none of their participants took a supplement containing vitamin D (43). Another study by O'Riordan et al. (45), conducted in Ireland among 43 pregnant women, observed a similar increase in serum total 25(OH)D concentrations (from mean ± SD 39.2 ± 17.9 nmol/L in the first to 53.3 ± 28.4 nmol/L in the third trimester) among women that did not take any supplement throughout their pregnancy. However, those studies did not assess trimester-specific dietary intakes of vitamin D and the increase they observed might be due to seasonal variation and sun exposure. Still, it could be hypothesized that some physiological factors, in addition to supplemental vitamin D, could influence the variations in serum total 25(OH)D concentrations across trimesters. In fact, even though it has not yet been confirmed that pregnancy itself directly affects serum total 25(OH)D concentrations, it was previously reported that some metabolites and active forms of vitamin D, as well as vitamin-D binding protein, are increased in high-estrogen states like pregnancy (49). Further longitudinal analyses of serum total 25(OH)D concentrations in pregnant women should be conducted to better understand its fluctuations throughout pregnancy.

The observed increase in serum total 25(OH)D concentrations was significant, even after an adjustment for ppBMI. Notably, the proportion of women with overweight or obesity in our sample (43.1%) was similar to that of all Canadian women aged 20–34 y, which was ∼40% in 2018 (50). It would be in accordance with the current literature to assume that, because 43% of our sample had a higher BMI, we would have observed a greater prevalence of 25(OH)D concentrations <40nmol/L. However, that was not the case. In fact, although women with obesity had lower serum total 25(OH)D concentrations in the first trimester, most (93.3%) of them were above the suggested target of 40 nmol/L by the third trimester. Therefore, they likely entered the pregnancy with lower vitamin D status, but most of them took a multivitamin or a supplement, which correlated with increased serum total 25(OH)D in the third trimester. As mentioned in the Introduction, the inverse association between vitamin D status and ppBMI has been previously reported (51, 52). In our study, vitamin D intakes from

food as well as from supplements in pregnancy did not differ between women with obesity and women with normal weight. The lower first-trimester serum total 25(OH)D concentrations may reflect prepregnancy dietary intakes more so than an increased need. This is further supported by similar increments among all ppBMI categories across trimesters. Thus, women with a ppBMI ≥30 who take a multivitamin containing vitamin D appear to achieve adequate vitamin D status, indicating that supplementation during pregnancy is an effective strategy. Furthermore, our results suggest that an individual assessment of nutrient intake and risk of deficiency would be preferable, as opposed to recommending that all pregnant women with obesity should take additional vitamin D supplementation. This was also highlighted in a review of national guidelines for pregnant women with obesity (53).

Although most of our participants were of high socioeconomic status and reported taking a multivitamin and/or a single-nutrient supplement that contained vitamin D, 22% of women did not report taking a vitamin D–containing supplement in the first trimester. Some of those women started to take a multivitamin later on, but conversely, other women that did report taking a multivitamin in the first trimester stopped doing so in the second or third trimester. This is concerning, considering that Health Canada recommends that all pregnant women should take a multivitamin containing ≥0.4 mg folic acid and 16–20 mg Fe (2). Although Health Canada does not specify that the multivitamin should contain vitamin D, most multivitamins do. The promotion of multivitamin use among pregnant women has been successful in increasing folic acid intakes (54), but does require further improvements to ensure that women meet the EAR for vitamin D through diet and supplemental intakes consistently during pregnancy. Furthermore, there is no existing consensus on what dose of vitamin D should be contained in prenatal multivitamins.

Based on pregnancy cohorts in Canada, prenatal multivitamin vitamin D content typically varies from 250 to 600 IU/tablet (22). In our study, the median vitamin D content of the multivitamins was 400 IU/d, and only approached 600 IU/d by the second trimester in 25% of the women. Thus, most of our participants had an average supplemental intake of vitamin D that was <600 IU/d. Still, among the participants that did report an average vitamin D intake from supplements ≥600 IU/d, there was no evidence of inadequacy [0% had serum total 25(OH)D <50 and <40 nmol/L in the third trimester]. Similarly, Perreault et al. (22) found that most of their participants met or exceeded the target value of 50 nmol/L, and their mean total vitamin D intake was similar to ours. A recent randomized controlled trial by O'Callaghan et al. (55) found that Irish pregnant women receiving a daily supplement of 800 IU

vitamin D, in addition to their baseline vitamin D intake, maintained 25(OH)D concentrations ≥50 nmol/L during their pregnancy. Ireland's higher latitude, lack of mandated vitamin D–fortified foods, as well as the fact that their participants were mostly enrolled in the winter months and that more of them were vitamin D deficient at baseline may explain why, in their study, a dose >600 IU supplemental vitamin D/d was necessary to achieve and maintain sufficient 25(OH)D concentrations. In contrast, and as mentioned in the Introduction, recommendations from the United Kingdom state that pregnant women should take a vitamin D supplement of 400 IU/d throughout pregnancy (3). Furthermore, a recent meta-analysis of 30 trials from various countries found that taking a supplement of ≥601 IU/d compared with ≤600 IU/d made little to no difference on the risk of various pregnancy outcomes (pre-eclampsia, preterm birth, and low birth weight) (56). Similar findings were obtained when comparing ≥4000 IU/d with ≤3999 IU/d. In summary, the appropriate dosage of supplemental vitamin D during pregnancy has not been determined yet and appears to vary according to the outcomes studied as well as the setting (country). Still, in consideration of our results and those of other studies from Canadian regions or provinces, a daily supplemental intake of 600 IU vitamin D appears to be sufficient to achieve adequate concentrations of serum total 25(OH)D ≥50 nmol/L, when measured by LC-MS/MS.

The present study has many strengths, including the measurement of serum total 25(OH)D concentrations with a VDSCP-certified LC-MS/MS method. The prospective design of our study is also a considerable strength because it makes us the first study in Canada that we know of to assess serum total 25(OH)D concentrations in all trimesters of pregnancy. We also used multiple validated Web-based 24-h recalls in each trimester combined with a questionnaire on supplement use, allowing us to obtain detailed information on dietary and supplemental intakes of vitamin D, which was crucial in our study. Our study however has some limitations, namely the small size and the overall homogeneity of our sample in terms of ethnicity and socioeconomic status. This limits the generalizability of our findings; thus, our analyses should be replicated in pregnant women of various ethnic backgrounds and of lower socioeconomic status. Still, despite our small sample size, we were able to observe significant differences in vitamin D status with regards to ppBMI and supplemental intake of vitamin D. The fact that we used a self-reported weight to calculate the ppBMI of our participants, which could translate into an underestimation of actual ppBMI, is also a limitation of our study. Still, the reliability of women's self-reported weight has been previously demonstrated (57). Moreover, we did not collect detailed information regarding our participants' sun exposure habits, but we, like other authors (18, 20–24), considered seasonal variation in all our analyses. Our study is also limited by the fact that we did

not collect any preconception data regarding supplement use, nor did we draw our participants' blood in the preconception period, which would have informed us even more regarding the evolution of maternal vitamin D status. Finally, we did not include data regarding 24,25(OH)2D3, another vitamin D metabolite, which prevented us from further exploring its potential role in the prenatal period. The LC-MS/MS method used in this study did, however, separate the 3-epi-25(OH)D3 from the total 25(OH)D concentrations, which allowed us to bypass the issues caused by its interference.

In conclusion, serum total 25(OH)D concentrations increased from the first trimester to the second and third trimesters, regardless of ppBMI, season at the time of blood sampling, and supplemental intake of vitamin D. It is however not clear if the use of supplements containing vitamin D is the sole reason behind the increase in serum total 25(OH)D concentrations, and associations between vitamin D status and estrogen should be investigated. Although very few women had serum total 25(OH)D concentrations below the 40 and 50 nmol/L and above the 125 nmol/L thresholds, our study supports the prenatal use of a multivitamin across pregnancy. Additional studies are necessary to identify what dose of vitamin D is optimal, i.e., one that promotes an adequate vitamin D status while avoiding concentrations >125 nmol/L. Furthermore, because a considerable proportion of women were not taking any vitamin D–containing supplement in their first trimester, this study reiterates the importance of promoting the use of a daily multivitamin among pregnant women.

Declarations

Author's contributions: The authors' responsibilities were as follows—A-SM, SL, HAW, and CS: designed the research; A-SM, CS, and A-SP: conducted the research; CS, A-SP, and AB: analyzed the data; CS: wrote the first draft of the manuscript, with major contributions from all other authors; A-SM: had primary responsibility for the final content; and all authors: critically revised a first draft of the manuscript for important intellectual content and read and approved the final manuscript.

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Tables

Table 1. Baseline and trimester-specific characteristics of the sample[1]

Characteristic	First trimester	Second trimester	Third trimester
Age, y	32.1 ± 3.7		
Primiparous, n (%)	28 (35.4)		
Prepregnancy body mass index, kg/m^2	25.7 ± 5.8		
Underweight, n (%)	2 (2.5)		
Normal weight, n (%)	43 (54.4)		
Overweight, n (%)	19 (24.1)		
Obese, n (%)	15 (19.0)		
Ethnicity – Caucasian[2]	77 (97.5)		
Education			
High school	4 (5.0)		
College	13 (16.5)		
University	62 (78.5)		
Household income			
< 60,000 CAD	15 (19.0)		
60,000-79,999 CAD	13 (16.5)		
80,000-99,999 CAD	17 (21.5)		
≥ 100,000 CAD	33 (41.8)		
Income not disclosed	1 (1.2)		
Gestational age at sampling, pregnancy weeks	12.6 ± 0.8	22.5 ± 0.8	33.0 ± 0.6
Season of sampling			
Spring	24 (30.4)	12 (15.2)	15 (19.0)
Summer	26 (32.9)	26 (32.9)	15 (19.0)
Fall	21 (26.6)	25 (31.6)	28 (35.4)
Winter	8 (10.1)	16 (20.3)	21 (26.6)
Supplement use			
Multivitamin	61 (77.2)	62 (78.4)	61 (77.2)
Multivitamin only	57 (72.2)	58 (73.4)	58 (73.4)
Multivitamin and vitamin D	4 (5.1)	4 (5.1)	3 (3.8)
Vitamin D supplement only	1 (1.2)	0	0
No supplement containing vitamin D	17 (21.5)	17 (21.5)	18 (22.8)
Vitamin D intake, IU/day			
Dietary	235 ± 119	261 ± 135	272 ± 150
Supplemental	397 ± 531	427.8 ± 521	418 ± 517
Total	632 ± 556	690 ± 538	689 ± 545
Servings of milk and alternatives, servings/day[3]	2.5 ± 1.1	2.7 ± 1.4	3.0 ± 1.4
Physical activity level[4]			
Sedentary	40 (50.6)	52 (65.8)	54 (68.4)
Low active	14 (17.7)	9 (11.4)	11 (13.9)
Active and very active	25 (31.6)	18 (22.8)	14 (17.7)

[1]Values are presented as means ± standard deviations or frequencies (%), n=79. [2]Other ethnicities include: Middle-Eastern (n=1) and Venezuelan (n=1); [3]According to the 2007 version of Canada's Food Guide (e.g. cheese, yogurt, cows' milk, plant-based beverages fortified with vitamin D, etc.) [183]; [4]Physical activity level was determined by ranking participants according to the daily amount of time engaged in moderate and high-intensity activities: Sedentary, <30 min of moderate-intensity activity; Low active, 30-59 min of moderate-intensity activity; Active, 60-179 min of moderate- or 30-59 min of high-intensity activity; Very active, ≥180 min of moderate- or ≥60 min of moderate plus ≥60 min of high-intensity activity. The active and very active categories were combined due to small sample size.

Table 2. Comparison of pregnant women's serum total 25(OH)D, 25(OH)D2, 25(OH)D3, and 3-epi-25(OH)D3 concentrations across trimesters of pregnancy[1]

	First trimester (9.9–14.7 weeks)	**Second trimester** (20.7–25.3 weeks)	**Third trimester** (31.6–34.6 weeks)	***P* value**
$25(OH)D_2$, nmol/L[2]	1.8 ± 0.9[b]	2.2 ± 1.4[a]	2.9 ± 2.2[a]	<0.0001
$25(OH)D_3$, nmol/L	65.7 ± 20.6[b]	84.3 ± 30.9[a]	85.3 ± 28.9[a]	<0.0001
Total 25(OH)D, nmol/L	67.5 ± 20.4[b]	86.5 ± 30.9[a]	88.3 ± 29.0[a]	<0.0001
3-epi-$25(OH)D_3$, nmol/L[3]	3.0 ± 1.7	3.1 ± 2.4	3.8 ± 2.2	0.57

[1]Values are presented as means ± standard deviations, n=79; [2]$25(OH)D_2$ concentrations were under the detection limit of 3 nmol/L for 70, 60 and 44 participants in the 1st, 2nd and 3rd trimesters, respectively. In those cases, a value of 1.5 nmol/L was used. [3]3-epi-$25(OH)D_3$ concentrations were under the detection limit of 2.5 nmol/L for 31, 34 and 40 participants in the 1st, 2nd and 3rd trimesters, respectively. In those cases, a value of 1.25 nmol/L was used. All *P* values refer to repeated measures ANOVA adjusted for season at the time of sampling, prepregnancy body mass index and vitamin D intake from supplements. Labeled means in a row without a common letter differ, P <0.05. 25(OH)D, 25-hydroxyvitamin D; $25(OH)D_2$, 25-hydroxyergocalciferol; $25(OH)D_3$, 25-hydroxycholecalciferol; 3-epi-$25(OH)D_3$, 3-epi-25-Hydroxyvitamin D_3.

Table 3. Correlations between trimester-specific concentrations of pregnant women's serum total 25(OH)D, pre-pregnancy BMI and trimester-specific physical activity and dietary variables[1]

	First trimester		Second trimester		Third trimester	
	r	r_{adj}	r	r_{adj}	r	r_{adj}
ppBMI	-0.42**	-0.42***	-0.33**	-0.32**	-0.33**	-0.34**
Physical activity (minutes/day)	0.08	0.09	0.38**	0.40**	0.12	0.13
Vitamin D intake from foods	0.13	0.14	0.18	0.13	0.26*	0.27*
Vitamin D intake from supplements	0.53***	0.58***	0.57***	0.59***	0.52***	0.50***
Total intake of vitamin D	0.53***	0.59***	0.60***	0.60***	0.56***	0.55***
Daily servings of milk and alternatives	-0.06	-0.09	0.11	0.06	0.20	0.22*

[1]Values are Pearson's correlation coefficient (r) or the coefficient adjusted for season at the time of sampling (r_{adj}), n=79. *P <0.05, ** P <0.01, *** P <0.0001. 25(OH)D, 25-hydroxyvitamin D; ppBMI, prepregnancy body mass index.

Table 4. Stepwise regression analysis of pregnant women's third-trimester concentrations of serum total 25(OH)D[1]

	r^2 x 100	β (95% CI)	*P* value
Mean (all trimesters) intake of vitamin D from supplement (IU/day)	24.6	0.51 (0.25, 0,71)	<0.0001
Prepregnancy BMI (kg/m^2)	5.2	-0.23 (-0.44, 0.05)	0.009
Third trimester sampling done in winter/spring (vs summer/fall)[2]	4.2	-0.21 (-0.44, 0.02)	0.02
Mean (all trimesters) amount of physical activity (minutes/day)	2.7	0.17 (-0.07, 0.39)	0.06
University degree (vs no university degree)	1.5	-0.13 (-0.31, 0.12)	0.15
Total	37.6		

[1]β coefficients, r^2x100 and *P* values are not shown for variables that were not included in the regression model *(P* > 0.25*)* following the stepwise procedure. Other variables tested in the stepwise procedure were age, primiparity (being pregnant with first child), vitamin D intake from foods and household income. [2]Seasons at the time of blood sampling were defined as follows: winter/spring (December 21st to June 20th), summer/fall (June 21st to December 20th). 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index.

Figures

1. Comparison of pregnant women's trimester-specific concentrations of serum total 25(OH)D according to pre-pregnancy BMI categories (n=79). Symbols represent individual 25(OH)D concentrations, thick lines represent mean 25(OH)D concentrations for each ppBMI category. Overall *P* values refer to one-way ANOVAs performed to compare serum total 25(OH)D concentrations between ppBMI categories, for each trimester and after adjustment for season at the time of sampling. *Different from women with a ppBMI <25kg/m^2, *P* < 0.05. 25(OH)D, 25-hydroxyvitamin D; ppBMI, pre-pregnancy body mass index.

2. Comparison of pregnant women's third trimester serum total 25(OH)D concentrations according to their mean intake of vitamin D from supplements (n=79). Circles represent individual 25(OH)D concentrations, thick lines represent mean 25(OH)D concentrations for each supplement intake category. Solid black circles represent women that did not take any vitamin D-containing supplement throughout pregnancy. Overall *P* value refer to the one-way ANOVA used to compare third trimester serum total 25(OH)D concentrations according to mean supplement intake of vitamin D, after adjustment for season at the time of sampling and pre-pregnancy BMI. *Different from women with a mean supplement intake ≥600 IU/day, *P* < 0.05. 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index.

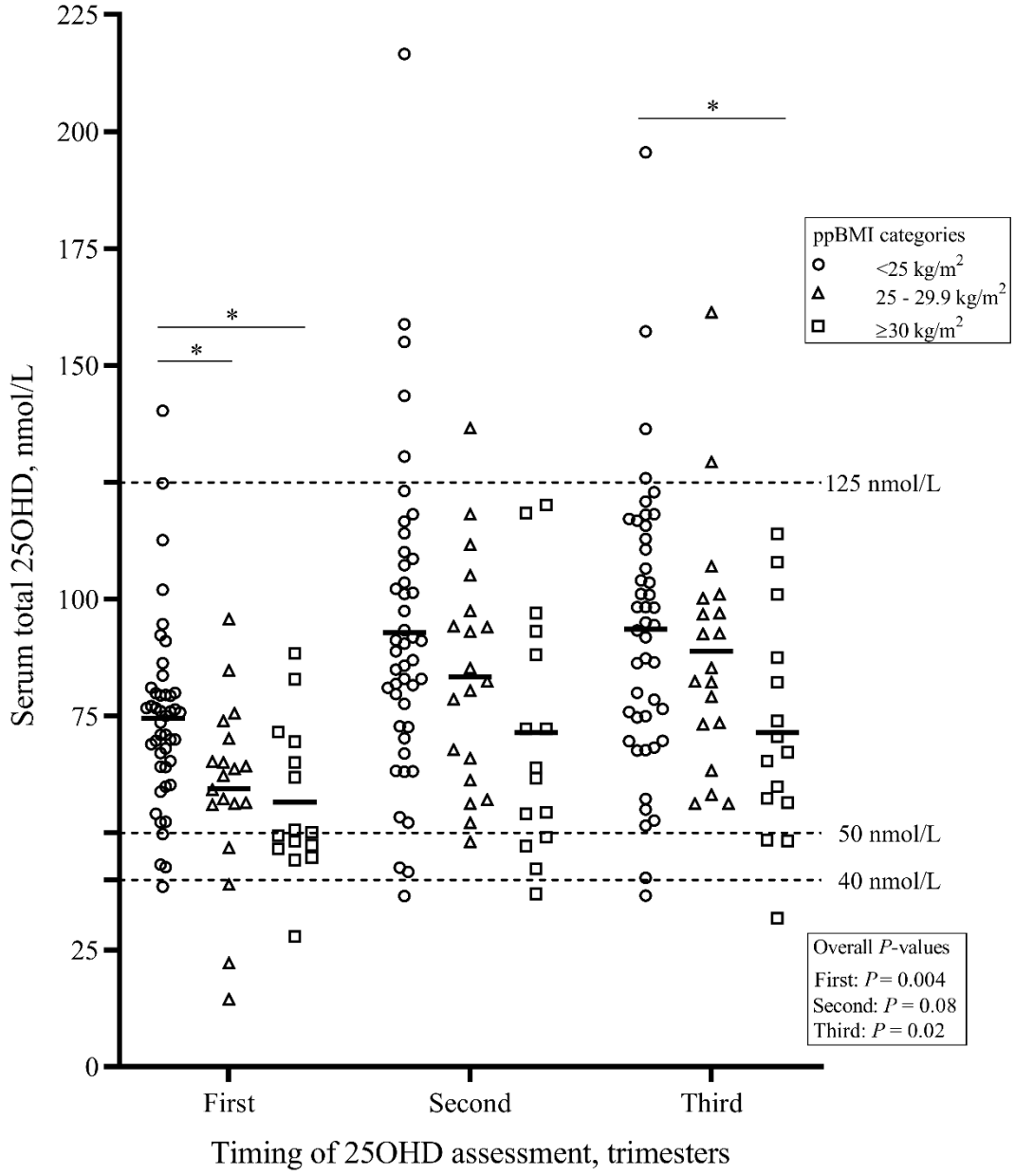

Figure 1. Comparison of pregnant women's trimester-specific concentrations of serum total 25(OH)D according to pre-pregnancy BMI categories (n=79)

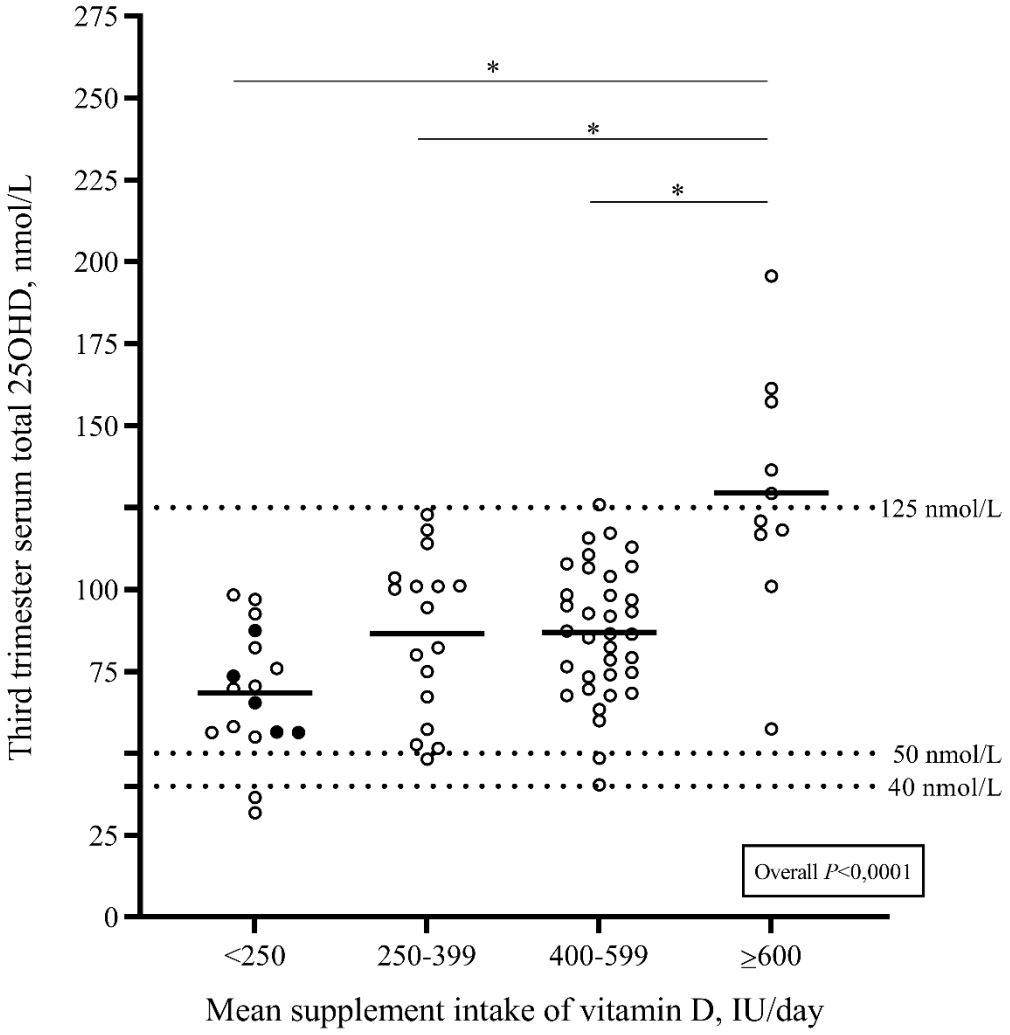

Figure 2. Comparison of pregnant women's third trimester serum total 25(OH)D concentrations according to their mean intake of vitamin D from supplements (n=79)

Supplementary data

Supplemental Table 1. Comparison of proportions of pregnant women with concentrations of serum total 25(OH)D below 40 and 50 nmol/L according to pre-pregnancy BMI[1]

	Below 50 nmol/L			Below 40 nmol /L		
	BMI < 25 kg/m^2 (n=45)	BMI ≥ 25 kg/m^2 (n=34)	*P* value	BMI < 25 kg/m^2 (n=45)	BMI ≥ 25 kg/m^2 (n=34)	*P* value
First trimester	4 (8.9)	11 (32.4)	0.02	1 (2.2)	4 (11.8)	0.08
Second trimester	3 (6.7)	5 (14.7)	0.24	1 (2.2)	1 (2.9)	0.84
Third trimester	2 (4.4)	3 (8.8)	0.43	1 (2.2)	1 (2.9)	0.84

[1]Values are presented as n (%), n=79. *P* values refer to the Chi-squared tests between the two BMI categories. Fisher's exact test was used if some cells had less than five values. 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index.

Supplemental Table 2. Pregnant women's trimester-specific concentrations of serum total 25(OH)D according to season at the time of sampling[1]

	Spring	Summer	Fall	Winter	*P* value
First trimester	63.1 ± 24.9 (n=24)	71.3 ± 11.4 (n=26)	73.3 ± 21.2 (n=21)	52.6 ± 19.9 (n=8)	0.04
Second trimester	67.2 ± 21.8[b] (n=12)	99.1 ± 35.7[a] (n=26)	89.4 ± 26.7[a,b] (n=25)	76.1 ± 25.4[a,b] (n=16)	0.009
Third trimester	87.2 ± 29.7 (n=15)	90.0 ± 28.1 (n=15)	96.2 ± 28.6 (n=28)	77.1 ± 27.9 (n=21)	0.15

[1]Values are presented as mean ± standard deviation in nmol/L, (number of women in each group), n=79. *P* values refer to one-way ANOVAs used to compare total 25(OH)D concentrations according to season at the time of sampling. Seasons at the time of blood sampling were defined as follows: spring (March 21st to June 20th), summer (June 21st to September 20th), fall (September 21st to December 20th) and winter (December 21st to March 20th). Labeled means in a row without a common letter differ, P <0.05. 25(OH)D, 25-hydroxyvitamin D.

Supplemental Table 3. Pregnant women's trimester-specific concentrations of serum total 25(OH)D according to strength of UVB rays at time of sampling[1]

	Sampling between April 1st and October 31st	Sampling between November 1st and March 31st	*P* value
First trimester	67.2 ± 19.0 (n=55)	68.1 ± 23.8 (n=24)	0.87
Second trimester	91.1 ± 32.4 (n=47)	79.8 ± 27.6 (n=32)	0.11
Third trimester	92.4 ± 30.5 (n=39)	84.3 ± 27.2 (n=40)	0.22

[1]Values are presented as mean ± standard deviation in nmol/L, (number of women in each group), n=79.
P values refer to one-way ANOVAs used to compare total 25(OH)D concentrations according to UVB exposure at the time of sampling. 25(OH)D, 25-hydroxyvitamin D; UVB, ultraviolet beta.

Supplemental Table 4. Stepwise regression analysis of pregnant women's first trimester concentrations of serum total 25(OH)D (n=79)[1]

	r^2x100	β (95% CI)	*P* value
First trimester intake of vitamin D from supplement (IU/day)	27.7	0.54 (0.14, 0.77)	<0.0001
First trimester sampling done in winter/spring (vs summer/fall)[2]	13.0	-0.37 (-0.58, -0.15)	<0.0001
Pre-pregnancy BMI (kg/m^2)	10.5	-0.33 (-0.54, -0.13)	<0.0001
First trimester physical activity (minutes/day)	1.9	0.14 (-0.11, 0.40)	0.08
Total	53.2		

[1]β coefficients, r^2 x 100 and *P* values are not shown for variables that were not included in the regression model (*P* > 0.25) following the stepwise procedure. Other variables tested in the stepwise procedure were age, primiparity (i.e. being pregnant with first child), vitamin D intake from foods, household income and education level. [2]Seasons at the time of blood sampling were defined as follows: winter/spring (December 21st to June 20th), summer/fall (June 21st to December 20th). 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index.

Supplemental Table 5. Stepwise regression analysis of pregnant women's second trimester concentrations of serum total 25(OH)D (n=79)[1]

	r^2x100	β (95% CI)	*P* value
Mean (first and second trimesters) intake of vitamin D from supplements (IU/day)	27.5	0.53 (0.14, 0.76)	<0.0001
Second trimester sampling done in winter/spring (vs summer/fall)[2]	9.0	-0.30 (-0.51, -0.13)	0.0002
Mean (first and second trimesters) amount of physical activity (minutes)	8.9	0.30 (0.07, 0.53)	0.0002
Pre-pregnancy BMI (kg/m^2)	4.7	-0.22 (-0.42, -0.01)	0.006
Total	50.2		

[1]β coefficients, r^2 x 100 and *P* values are not shown for variables that were not included in the final regression model (*P* > 0.25) following the stepwise procedure. Other variables tested in the stepwise procedure were age, primiparity (being pregnant with first child), vitamin D intake from foods, household income and education level. [2]Seasons at the time of blood sampling were defined as follows: winter/spring (December 21st to June 20th), summer/fall (June 21st to December 20th). 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index.

Chapitre 7 – Trimester-specific assessment of diet quality in a sample of Canadian pregnant women

Résumé

Les objectifs de cette étude étaient (1) d'examiner les changements dans la qualité de l'alimentation au cours des trimestres et (2) d'identifier les caractéristiques associées à la qualité de l'alimentation. Les 79 femmes enceintes ont complété, à chaque trimestre, trois rappels de 24 heures, à partir desquels le *Canadian Healthy Eating Index* (C-HEI) a été calculé, puis différents questionnaires sur les connaissances nutritionnelles et les données sociodémographiques. Bien que le score C-HEI total soit demeuré stable, une diminution significative des sous-scores « fruits et légumes », « gras insaturés » et « gras saturés » fut observée. Des scores C-HEI plus faibles ont été observés chez les femmes enceintes avec IMC≥25kg/m^2, de moins de 28 ans, sans diplôme universitaire, ayant de moins bonnes connaissances en nutrition et résidant en milieu urbain. En conclusion, la qualité alimentaire durant la grossesse demeure stable et pourrait être améliorée.

Title page

Title: Trimester-specific assessment of diet quality in a sample of Canadian pregnant women

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Keywords: diet quality; Healthy Eating Index; pregnancy; prenatal nutrition

Abstract

The present study aimed to (1) examine changes in diet quality throughout pregnancy and (2) identify maternal characteristics associated with trimester-specific diet quality. Pregnant women (n = 79) were recruited in their 1st trimester of pregnancy and completed, at each trimester, three web-based 24-hour dietary recalls, from which the Canadian Healthy Eating Index (HEI) was calculated. Physical activity, nutrition knowledge, and socio-demographic web-questionnaires were also completed. Although no variation in total HEI scores was observed across trimesters, we found an overall decrease in the following subscores: adequacy, total fruits and vegetables, unsaturated fats and saturated fats ($p < 0.05$). In the 1st trimester, overweight and obese pregnant women had a lower diet quality in comparison with normal-weight and underweight women (HEI scores: 63.1 ± 11.9 vs. 68.0 ± 9.3; $p = 0.04$). In the 3rd trimester, women younger than 28 years old, with no university degree, poorer nutrition knowledge and who reside in an urban setting, had a lower diet quality ($p < 0.05$). In conclusion, less educated, younger women who reside in an urban setting may be at a higher risk of poor diet quality in late pregnancy and could benefit from public health programs.

Introduction

Initiating and maintaining healthy eating behaviours is essential during pregnancy since poor maternal nutrition can adversely affect both the mother and her future child [1,2,3]. In the past, prenatal nutritional epidemiology was primarily concerned with the impact of malnutrition and nutritional deficiencies [4,5,6,7,8], but current literature is now increasingly interested in the overall quality of the maternal diet [9]. Combined assessment of maternal dietary intake and global diet quality would allow for (1) the detection of nutritional excesses and deficiencies, and (2) the identification of dietary patterns associated with adverse pregnancy outcomes [9]. For these reasons, various dietary patterns and diet quality indexes, such as the Healthy Eating Index (HEI) [10,11,12] were developed. Since then, greater diet quality during pregnancy has been associated with positive pregnancy outcomes [13]. A recent meta-analysis reported that a diet rich in fruits, vegetables, whole grains, and fish combined with lower intakes of red and/or processed meats and high-fat dairy products was associated with a lower risk of gestational diabetes [14]. Moreover, poorer diet quality during pregnancy has been associated with birthweight and neonatal adiposity [13,15]. However, in these studies, diet quality was not assessed at each trimester of pregnancy. It is important to address this gap in the literature, since diet during pregnancy may change and have different implications depending on the trimester during which diet is assessed [16,17]. In fact, during organogenesis, dietary intakes are more likely to play a role in the development of organs and systems, while during the fetal period, the diet would rather influence the growth and weight gain of the fetus as well as the mother's gestational weight gain [16,17,18]. For example, folic acid supplementation is recommended before and during early pregnancy in order to reduce the risk of neural tube defects [19]. However, little is known about the role of folic acid during the 2nd and 3rd trimesters, i.e., the fetal period, and a study by Wang et al. recently reported an association between folic acid supplementation after the 1st trimester and the risk of large-for-gestational-age birth [20].

According to national guidelines, pregnant women should increase their daily energy intake progressively, i.e., in the 2nd and 3rd trimesters, in order to account for the high metabolic demand related to the fetus' growth [21,22]. In Canada, pregnant women are advised to eat one to three additional servings from any of the four food groups (fruits and vegetables, grain products, milk and alternatives (yogurt, cheese, soy milk, almond milk, etc.), as well as meat and alternatives (red meat,

fish, poultry, grains, nuts, legumes, etc.)) of Canada's Food Guide (CFG), in order to increase their daily energy intake in the 2nd and 3rd trimesters [21].

Numerous studies have investigated pregnant women's dietary intakes from a quantitative point of view, i.e., by the assessment of specific or various nutrient intakes [23,24,25,26,27]. However, very few studies have investigated overall diet quality during pregnancy and its determinants. A previous Canadian study by Nash et al. identified immigration status, parity, physical activity, smoking habits, anxiety, marital status, and social support as variables that could significantly impact maternal diet quality [28]. The authors concluded that further research was necessary to investigate potential determinants of diet quality. Although Nash et al. identified determinants of overall diet quality during pregnancy, they did not examine trimester-specific determinants of diet quality [28].

To our knowledge, diet quality was not assessed prospectively among Canadian pregnant women and trimester-specific determinants of diet quality need to be further investigated. To address this gap in the literature, our study aimed (1) to examine changes in diet quality throughout pregnancy using the HEI and adherence to CFG and (2) to identify maternal characteristics associated with trimester-specific diet quality.

Materials and methods

Study Population

Eighty-six (86) pregnant women were recruited at the CHU de Québec—Université Laval (Québec City, Canada) to participate in the ANGE project (Apports Nutritionnels Durant la GrossessE). The study protocol has been previously described [29]. Briefly, women were included if they were at least 18 years of age, had a gestational age less than 11 weeks and were able to communicate in French. Women were excluded if they had an inflammatory or autoimmune disease and if they planned to deliver in birthing centers or hospital centers other than the CHU de Québec-Université Laval. The ANGE project was approved by the CHU de Québec—Université Laval Research Center's Ethical Committee (Reference number: 2016–2866) and participants gave their informed written consent at their first study visit to the research center (baseline visit). Seven women were lost at follow-up due to miscarriage (n = 3) or inability to devote time to the study (n = 4). Therefore, our final analyses include 79 pregnant women.

Nutritional Data Collection

Each participant was asked to complete a total of 9 web-based 24-h dietary recalls; 3 in the 1st trimester (range: 8.4–14.0 weeks), 3 in the 2nd trimester (range: 19.3–28.3 weeks), and 3 in the 3rd trimester (range: 31.9–37.7 weeks). At each trimester, dietary recalls were completed on two weekdays and one weekend day. The dietary recalls were completed using the R24W (Rappel de 24h Web) platform. The R24W has been previously described and was recently validated in pregnant women and in the general population [29,30,31]. Briefly, the R24W uses a sequence of questions adapted from the United States Department of Agriculture (USDA) Automated Multiple Pass Method (AMPM) [32]. The application sends automatic emails on randomly chosen dates to remind the participants to complete the recall. The database includes 2865 food items that are linked to the Canadian Nutrient File [33] to enable automatic extraction of nutrient values. Pictures depicting multiple portion sizes with corresponding units or volume are available for more than 80% of all food items. After selecting a food item, participants chose the picture that best represented the amount of food eaten. All food items were automatically coded using the 2015 version of the Canadian Nutrient File [33]. The number of servings for each CFG group was calculated automatically by the R24W platform [30,34]. To compare the number of servings of our study sample with CFG's recommendations, we used the recommended range of servings for non-pregnant adult women (for comparisons with 1st trimester servings), to which we added 2 and 3 additional servings, for comparisons with the 2nd and 3rd trimesters reported servings, respectively.

Healthy Eating Index

Diet quality was assessed using the 2007 version of the Canadian HEI (C-HEI) [35], which is automatically calculated by the R24W platform. The C-HEI is an adaptation of the HEI developed by Kennedy et al. [11] and its assessment relies on the number of servings reported by the participant, according to age and sex, as specified in the latest version of the CFG, which was published in 2007 [34,35]. Briefly, the Canadian HEI is comprised of eight adequacy components and three moderation components (see Table S1) [35]. For each component, points between 0 and the potential maximum score (5, 10, or 20) are assigned. An individual receives no points if they have failed to meet the criterion altogether, the maximum score is assigned if the criterion is met perfectly; and a proportional score is assigned if the reported intake falls between the two extremes. Scores are then added up for a maximum of 100 points, representing a perfect adherence to CFG. In this study, complex meals were

firstly decomposed into their main components. All food items and main components of complex dishes were then translated into CFG servings, from which HEI sub-scores are calculated [35]. Total HEI scores of each day (3 days per trimester) were computed and averaged by the R24W platform. The detailed information regarding the range of scores and scoring criteria is presented in Table S1. The HEI has been used by various authors to assess diet quality among pregnant women [36,37,38].

Supplement Use

A Web questionnaire administered at each trimester was completed by all participants in order to collect information on supplement use. Participants had to identify their supplement (e.g., brand name, type of supplement, specific nutrient, etc.), provide its drug identification number, its measurement unit (e.g., tablet, drop, gram, milliliter, etc.), its dose and the frequency at which the reported dose was taken (e.g., once a day, twice a week, etc.). We used the Health Canada Licensed Natural Health Product Database [39] as well as the companies' product labels and websites in order to collect the nutritional information of all supplements entered by participants. If information was missing or incomplete for any of the supplements' characteristics, a research assistant contacted the participant to obtain the missing information. Supplement use was assessed by compiling the types of supplement reported (multivitamin or single nutrient) and the number of users for each type of supplement.

Nutrition Knowledge

During their 1st trimester of pregnancy, participants completed a web-based self-administered questionnaire that assessed their general nutrition knowledge. The development of this questionnaire has been previously described and was validated among French-Canadian adults [40]. Questions are mainly related to the knowledge of CFG (e.g., number of servings recommended, and food items included in each food group), but some also assess general nutrition knowledge (e.g., agree/disagree 'All spices have a high sodium (salt) content'). Total score ranges from 0 to 13.5, 13.5 being the highest value given for knowledge of nutrition. In our analyses, participants were classified according to the median score of our sample. Women scoring equal to or above the median were considered as having a better nutrition knowledge.

Nausea, Vomiting and Food Preferences During Pregnancy

At each trimester, a web-based self-administered questionnaire regarding nauseous symptoms as well as food cravings and aversions was completed. If pregnant women reported having experienced nausea and/or vomiting, they were asked to specify how frequently these symptoms occurred. Finally, women were asked if they had experienced any food cravings and/or aversions since they became pregnant and if so, which foods were craved and/or disliked. All food items listed were analyzed by a registered dietitian and then divided into 9 food categories (see Results section). In our analyses, women were classified as having (yes) or not (no) reported nausea, vomiting, food cravings, and/or food aversions.

Other Variables

Pre-pregnancy BMI was calculated using self-reported pre-pregnancy weight and the height measured at the first study visit to the research center (baseline visit). Gestational age was confirmed by a dating ultrasound conducted at the CHU de Québec—Université Laval in the 1st trimester. Participants completed the validated web-based French version of the Pregnancy Physical Activity Questionnaire (PPAQ) [41,42] at each trimester. Physical activity level was determined by ranking participants according to the total amount of time they engaged in moderate and high-intensity activities (minutes/day). Women were either categorized as active (≥30 min/day) or less active (<30 min/day). Finally, participants completed a web-based self-administered questionnaire to collect information on economic and socio-demographic characteristics such as education level, annual income, and living environment. In this questionnaire, participants were asked whether they lived in an urban (in the city), suburban or rural (countryside) setting.

Statistical Analyses

Descriptive analyses were conducted to characterize the study population. Age was categorized according to the Canadian average age at first birth (28 years old) [43]. Pre-pregnancy BMI was divided in 2 categories to compare underweight/normal-weight women vs. overweight/obese women (<25 kg/m^2 and ≥25 kg/m^2). At each trimester, mean HEI scores (total and sub-scores) as well as the mean number of CFG servings were calculated from the three recalls. Repeated measures analyses of variance (MANOVA) were performed to assess variations, across trimesters, in diet quality, using the

two indicators described above (i.e., HEI and CFG servings). Pairwise comparisons were performed for components for which a significant variance was observed across trimesters. Further repeated measures analyses of variance were performed for total HEI score of subsamples of participants in order to compare variations in diet quality according to different maternal characteristics (i.e., age, primiparity, pre-pregnancy BMI, physical activity, multivitamin use, income, education, nutrition knowledge, living environment, reported food cravings/aversions, and nauseous symptoms). One-way analyses of variance (ANOVA) were used to compare trimester-specific HEI scores according to the maternal characteristics previously listed. Finally, stepwise regressions were performed with the predictor variables on trimester-specific HEI score. A cut point of $p < 0.25$ was used in the stepwise regression, in order to identify which variables could be entered in the model. The same maternal characteristics listed above were tested in the Stepwise procedure. For all statistical analyses, differences were considered to be statistically significant at $p \leq 0.05$ and $p \leq 0.10$ were considered as trends. Variables that were not normally distributed (Pre-pregnancy BMI, 1st trimester HEI score and physical activity in all trimesters) were transformed (Log10 or Boxcox) in order to perform analyses that require a normal distribution (Stepwise regression). All statistical analyses were performed using JMP version 13.2.1 (SAS Institute Inc., Cary, NC, USA).

Results

Participants' Characteristics

Participants' characteristics are presented in Table 1. Final analyses include 79 pregnant women recruited at 9.3 ± 0.7 weeks of pregnancy, aged 32.1 ± 3.7 years old on average and with a mean pre-pregnancy BMI of 25.7 ± 5.8 kg/m^2. Seventy-four (93.7%) of the women filled all nine dietary recalls. The five other women (6.3%) completed eight of the nine required R24W (data not shown). More specifically, two women missed one recall in the 1st trimester, two different women missed one recall in the 2nd trimester and another woman missed one recall in the 3rd trimester. Only two women (2.5%) were categorized as being underweight. The majority of participants were Caucasian (97.5%), multiparous (64.6%), resided in an urban/suburban area (89.8%), were university degree holders (78.5%), and had an annual household income of 80,000 Canadian dollars or more (63.3%). Physical activity decreased throughout pregnancy ($p = 0.0024$) and participants scored a mean of 9.6 ± 1.6 (range 5.1–12.8) out of 13.5 on the nutrition knowledge questionnaire. Most women (88.6%) reported nausea in the 1st trimester of pregnancy. Significantly fewer women reported nauseous symptoms in

the 2nd and 3rd trimesters (32.9% and 20.3%, respectively vs. 88.6% in the 1st trimester; p-value of MANOVA < 0.0001) and fewer participants reported having experienced vomiting throughout their pregnancy (31.7%, 19.0%, and 2.5% in the 1st, 2nd, and 3rd trimesters, respectively; p-value of MANOVA < 0.0001). Most women reported food cravings (55.7%) and aversions (63.3%) in their 1st trimester and these proportions decreased across trimesters (p = 0.0095 for cravings and p = 0.0001 for aversions; Table 1). Additional details on the frequency of nausea and vomiting symptoms and information regarding categories of foods craved and disliked are presented in Tables S2 and S3.

Supplement Use

Data on supplement use is presented in Table S4. A majority of women reported using prenatal multivitamins (86.1%, 84.8%, and 78.5% in the 1st, 2nd, and 3rd trimesters). Folic acid supplements were the most commonly reported single-nutrient supplements (data not shown). Only a small proportion (<10%) of women reported taking vitamin D, iron, and omega-3 as single-nutrient supplements throughout pregnancy (Table S4).

Adherence to Canada's Food Guide

Table 2 shows the adherence to CFG recommendations for each food group and subgroup throughout pregnancy. Average fruit and vegetable servings (6.4 ± 2.2 in the 1st, 6.1 ± 2.6 in the 2nd, and 5.8 ± 2.4 in the 3rd; p = 0.094) decreased throughout pregnancy and did not meet the minimum recommended number of servings of seven. Women were, on average, within the recommended ranges for the three other food groups. An increase in the number of servings throughout pregnancy was observed only for the 'milk and alternatives' food group. (2.5 ± 1.1, 2.7 ± 1.4, and 3.0 ± 1.4 in the 1st, 2nd and 3rd trimesters, respectively; p = 0.002).

Diet Quality throughout Pregnancy

Average HEI scores (total and subscores) are presented in Table 3. Total HEI scores did not significantly vary throughout pregnancy (65.8 ± 10.8 in the 1st, 65.0 ± 12.0 in the 2nd, and 62.9 ± 12.6 in the 3rd trimester; p = 0.075). In contrast, the adequacy sub-score significantly decreased across trimesters (47.2 ± 7.4, 46.4 ± 7.7, 44.7 ± 8.2; in the 1st, 2nd and 3rd trimesters, respectively; p = 0.016). Among the adequacy component, total vegetables/fruits as well as unsaturated fats sub-scores

significantly decreased throughout pregnancy ($p < 0.05$). Saturated fats sub-scores (part of the moderation component) also decreased throughout pregnancy ($p < 0.05$).

Pairwise comparisons for adequacy and unsaturated fats scores showed a significant decrease between the 1st and 3rd trimesters ($p < 0.05$) and between the 2nd and 3rd trimesters ($p < 0.05$), respectively. Total fruits and vegetables scores decreased between the 1st and 2nd trimesters ($p < 0.05$) and between the 1st and 3rd trimesters ($p < 0.05$). Finally, saturated fats scores decreased only between the 1st and 3rd trimesters ($p < 0.05$). When variations in diet quality were analyzed by maternal characteristics, the stability across trimesters previously observed was maintained, with the exception of a significant decrease in HEI scores in women who were less active in the 1st and 3rd trimesters, were living in an urban setting and who scored lower on the nutrition knowledge questionnaire (p-value of MANOVA < 0.05; data not shown).

Trimester-Specific Diet Quality

Figure 1 shows differences in trimester-specific HEI scores according to maternal characteristics. Higher pre-pregnancy BMI, lower maternal age, lower physical activity, lower education level, poorer nutrition knowledge and an urban living environment were all associated with poorer diet quality. However, as shown in Figure 1, the maternal characteristics associated with poorer diet quality varied across trimesters. No significant differences were observed in HEI scores of primiparous vs multiparous women and women who did or did not report nausea, food cravings, and aversions (data not shown). Women who did not report vomiting in the 1st trimester tended to have a lower HEI score compared to women that did report vomiting symptoms ($p = 0.098$; data not shown). Moreover, women that did not take a multivitamin in the 1st trimester tended to have a lower HEI score compared to women who did take one ($p = 0.0531$; data not shown).

Table 4 shows results of the stepwise regression of trimester-specific HEI to identify predictor variables. In the 1st trimester, reported vomiting ($r^2 = 0.10$; $\beta = 0.34$; $p = 0.003$), multivitamin use ($r^2 = 0.05$; $\beta = 0.23$; $p = 0.042$) and pre-pregnancy BMI ($r^2 = 0.04$; $\beta = -0.22$; $p = 0.047$) were identified as significant predictors of total HEI score, in a model that also included nutrition knowledge, living environment and education level. In the 2nd trimester, only physical activity ($r^2 = 0.07$; $\beta = 0.28$; $p = 0.012$) was a significant predictor of total HEI score, in a model that also included nutrition knowledge, reported vomiting and food cravings. Finally, in the 3rd trimester, only nutrition knowledge ($r^2 = 0.07$; $\beta =$

0.26; p = 0.017) was a significant predictor of total HEI score, in a model also including pre-pregnancy BMI, living environment and education level.

Discussion

Our research team recently published a trimester specific assessment of nutrient intakes in comparison with national dietary guidelines, in the same sample of pregnant women, but that paper did not assess overall diet quality during pregnancy [23]. This paper is therefore, to our knowledge, the first to assess trimester-specific diet quality and adherence to CFG in Canadian pregnant women, as well as identifying maternal characteristics associated with diet quality throughout pregnancy. In all trimesters, intake of fruits and vegetables did not meet the CFG recommended number of servings and decreased throughout pregnancy. In contrast, 'milk and alternatives' intake increased significantly across trimesters. Overall, total HEI score remained stable throughout pregnancy. Sub-scores of total fruits/vegetables and unsaturated fats significantly decreased throughout pregnancy. In the 1st trimester, overweight and obese women had poorer diet quality compared with normal-weight and underweight women. Later in pregnancy, women younger than 28 years old that were less active, residing in an urban setting, with no university degree, and poorer nutrition knowledge had lower HEI scores than older, more active, educated women with better nutrition knowledge who lived in the suburbs. The best predictors of poorer diet quality were (1) unreported vomiting, lack of multivitamin use, and higher pre-pregnancy BMI; (2) lower physical activity level; and (3) poorer nutrition knowledge, for the 1st, 2nd, and 3rd trimesters, respectively.

An overall decrease in maternal diet quality was observed by Moran et al. [36] in a study that assessed the HEI score of 301 overweight and obese Australian pregnant women at each trimester and at 4 months post-partum. Similarly, it has been suggested that women may change their diet after learning that they are pregnant, which could be explained by the fact that pregnancy itself is associated with a higher motivation to adopt healthy eating habits [44,45,46]. In the present study, since we did not assess pre-pregnancy diet, it is not possible to evaluate any diet changes between pre-pregnancy and early pregnancy. Nevertheless, a prospective study by Skreden et al. [47] observed an increase in the proportion of Norwegian pregnant women consuming fruits and vegetables daily or more frequently from pre-pregnancy to early (9–20 weeks) pregnancy. It could then be hypothesized that a decrease in motivation, from early to late pregnancy, could occur in certain women and therefore be associated with a decrease in overall diet quality as the pregnancy progresses. In our study, this could partly

explain the fact that the total fruits/vegetables, unsaturated and saturated fats sub-scores were higher in the 1st trimester compared with the 2nd and 3rd trimesters. However, changes in the motivation to maintain healthy eating habits during pregnancy should be further investigated in association with other determinants of diet quality. In addition, it would be interesting to assess diet quality after birth and/or during the breastfeeding period, in order to examine whether and how pregnancy impacts a woman's diet in the long-term.

In our study, overweight and obese pregnant women had, in the 1st trimester only, lower HEI scores compared to normal-weight and underweight women. Similarly, Shin et al. [48] assessed the HEI score of 795 American pregnant women once (various trimesters) and found an inverse association between pre-pregnancy BMI and maternal diet quality as well as nutritional biomarkers. Tsigga et al. [38] also found, using three dietary recalls once during pregnancy (trimester unspecified) among 100 Greek pregnant women, that overweight and obese women had a lower HEI score than their counterparts. Following these observations, it is relevant to mention that a poorer diet quality prior to pregnancy might contribute to a higher pre-pregnancy BMI. Consequently, it would be considered logical that, in our study, obese and overweight women had lower 1st trimester HEI scores. Once again, since we do not have any data regarding pre-pregnancy diet, we cannot verify these hypotheses. Nevertheless, our results combined with those of other authors suggest that women with a higher pre-pregnancy BMI are at higher risk of poorer diet quality during and after pregnancy and should therefore be monitored early on in pregnancy. However, in our study, pre-pregnancy BMI was not a significant predictor of diet quality in the 2nd and 3rd trimesters. It could then be hypothesized that diet quality is influenced by different factors in late pregnancy in comparison with early pregnancy. Moreover, given that overweight and obese pregnant women are at higher risk of gestational diabetes, hypertension disorders, and numerous other adverse pregnancy outcomes; their diet, especially in early pregnancy, should be monitored closely [49,50,51].

In the 2nd trimester, diet quality was lower in women younger than 28 years old, who were less active and had poorer nutrition knowledge. Differences in HEI scores related to age and nutrition knowledge persisted in the 3rd trimester where, additionally, women lacking a university degree, living in an urban setting (vs. the suburbs) also had lower diet quality. Similar differences were observed by Nash et al. [28], Rifas-Shiman et al. [52], Laraia et al. [53], who found that women who were younger, less educated, less physically active, and who lived within 500 m of fast-food restaurants and convenience

stores, had lower diet quality during pregnancy. Doyle et al. [54] observed similar associations and highlighted the need for more studies assessing diet quality in combination with environmental factors, as well as a consideration for pregnancy to be taken into account as a determinant factor itself. Although our results are in line with the literature, it is still important to further investigate diet quality during pregnancy in association with maternal, environmental, behavioural, and sociodemographic characteristics, in order to identify pregnant women at higher risk of nutritional inadequacies that could benefit the most from a nutritional intervention. Furthermore, in our study, maternal characteristics associated with poorer diet quality varied across trimesters, which suggest that diet quality may not be influenced by the same factors throughout pregnancy. Moreover, although some factors may help identify the women that are at higher risk of poorer diet quality, some of them are not necessarily modifiable (e.g., education level, living environment, age, etc.). Therefore, other modifiable factors (e.g., nutritional knowledge, physical activity level, etc.) could be targeted for nutritional interventions during pregnancy.

Stepwise regression analyses of HEI scores identified different predictors of diet quality depending on the trimesters. We found that the best predictors of poorer diet quality were: (1) the fact that women did not experience vomiting, lack of multivitamin use, and a higher pre-pregnancy BMI; (2) lower physical activity; and (3) poorer nutrition knowledge, for the 1st, 2nd, and 3rd trimesters, respectively. In comparison, Nash et al. [28] observed in their sample of 2282 Canadian pregnant women that the best determinants of greater diet quality were: being an immigrant residing in Canada for ≤5 years, marriage and multiparity, physical activity, lower anxiety levels, and greater social support from family. Apart from physical activity, our results differ from those of Nash et al. [28], possibly due to our small and homogenous sample. Support from family, anxiety levels, and marital status were not assessed in our study. Moreover, since only two of our participants were immigrants, we did not include this variable in our stepwise procedures. Nevertheless, the predictors identified in our study only explained a small proportion of the variability in diet quality (Total r^2 values of the models varied between 0.14 and 0.27). As previously mentioned, there are many factors that could contribute to maternal diet quality that were not included in our study [28,55,56]. Future studies should consider including environmental, psychosocial, socio-demographical as well as biological variables in multivariate models in order to obtain a more global picture of which variables best predict diet quality during pregnancy. In addition, as the best predictors of diet quality differed according to trimesters, it is important that diet quality be assessed prospectively, at each trimester.

Two major strengths of this study were its prospective design and its early enrollment of participants, allowing us to examine changes in diet quality throughout pregnancy. Moreover, the use of a validated web-based 24 h dietary recall generated detailed information on dietary intakes thus allowing a precise assessment of diet quality as well as the evaluation of adherence to CFG. Our study has some limitations, namely regarding the small size and the homogeneity of our sample; since most of the pregnant women who were enrolled were Caucasians and of a higher socioeconomic status. Still, even though our sample was highly educated and reported a high annual income, average intake of fruits and vegetables did not meet CFG's recommendations. We can hypothesize that less educated and lower-income women may be at a greater risk of poor diet quality and nutritional inadequacies. Our small sample size might also have attenuated the statistical significance of our results. Still, diet quality significantly differed between some subgroups. The variations we observed in some HEI sub-scores are possibly continuous throughout pregnancy, which we cannot confirm. For a better estimate and a more continuous evaluation of diet quality, additional R24Ws would have been needed. Yet, asking our participants to recall and report their dietary intakes for more than three days per trimester could have worsened compliance, participation rate, and potentially altered our results. In addition, it has been previously stated that three days are representative of a pregnant woman's usual diet [2,22]. Finally, our study did not assess important psychosocial factors like stress and anxiety that could have impacted on diet quality during pregnancy. Interactions between such factors and diet quality should be further investigated.

Conclusions

Overall diet quality did not vary throughout pregnancy, but sub-scores related to fruits and vegetables, unsaturated and saturated fats significantly decreased across trimesters. Although pregnancy is known to be a key period during which pregnant women are motivated to adopt healthy behaviors, it is possible that motivation decreases as pregnancy progresses, making it difficult for women to maintain the quality of their diet. Women who were overweight and obese had poorer diet quality in early pregnancy compared to normal-weight and underweight women. Our study also showed that women under 28 years of age, less educated, less active, and who live in an urban setting may be at a higher risk of poorer diet quality in late pregnancy. These women may benefit the most from interventions centered on healthy eating behaviors. Furthermore, variables associated with poorer diet quality varied across trimesters, which suggests that diet quality may not be influenced by the same factors throughout

pregnancy. Hence, highlighting the need to monitor diet quality at various points during pregnancy. Future studies should assess trimester-specific diet quality in association with environmental, psychosocial, biological, as well as socio-demographical factors.

Declarations

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Authors' Contributions: A.-S.M. formulated the research question and designed and carried out the study with C.S. C.S. collected the data under the supervision of A.-S.M. and conducted statistical analyses of the data with the help of S.L., É.C., J.R., and A.-S.M. All authors contributed to the analysis and interpretation of data. All authors made substantial contributions to the conception and design of the manuscript, and all critically revised a first draft of the manuscript for important intellectual content. All authors gave their approval of the manuscript's final version to be published and therefore take public responsibility for the content of the manuscript.

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Tables

Table 1. Participants' characteristics (n = 79)

Variables	Mean ± SD or N (%)		
	Baseline (1st trimester)	2nd trimester	3rd trimester
Age (years)	32.1 ± 3.7	-	-
Weeks of gestation at baseline (weeks)	9.3 ± 0.7	-	-
Primiparous	28 (35.4)	-	-
BMI (kg/m^2)	25.7 ± 5.8	-	-
Underweight	2 (2.5)	-	-
Normal weight	43 (54.4)	-	-
Overweight	19 (24.1)	-	-
Obese	15 (19.0)	-	-
Ethnicity – Caucasian[1]	77 (97.5)	-	-
Education			
High school	4 (5.0)	-	-
College	13 (16.5)	-	-
University	62 (78.5)	-	-
Household income			
< 60 000 $	15 (19.0)	-	-
60 000 – 79 999 $	13 (16.5)	-	-
80 000 – 99 999 $	17 (21.5)	-	-
≥ 100 000 $	33 (41.8)	-	-
Income missing	1 (1.2)	-	-
Living environment			
Urban	37 (46.8)	-	-
Rural	8 (10.1)	-	-
Suburbs	34 (43.0)	-	-
General nutrition knowledge (total score)[2]	9.6 ± 1.6	-	-
Physical activity level (minutes/day)[3]	60.5 ± 59.6	45.9 ± 51.1	35.2 ± 41.5
Reported nausea (yes)	70 (88.6)	26 (32.9)	16 (20.3)
Reported vomiting (yes)	25 (31.7)	15 (19.0)	2 (2.5)
Food cravings (yes)	44 (55.7)	33 (41.8)	25 (31.7)
Food aversions (yes)	50 (63.3)	28 (35.4)	17 (21.5)

[1]Other ethnicities were: Middle-Eastern (n=1) and Venezuelan (n=1); [2]Total score ranges from 0 to 13.5, assessed by the Nutrition Knowledge Questionnaire developed by Bradette-Laplante et al. (2017); [3]Sum of moderate- and vigorous-intensity physical activity assessed by the PPAQ.

Table 2. Servings of 2007 Canada's Food Guide food groups and subgroups throughout pregnancy

Food groups	Number of servings/day (or other)[1]						
	1st trimester		2nd trimester		3rd trimester		
	Recommended range[2]	Mean ± SD	Recommended range[3]	Mean ± SD	Recommended range[3]	Mean ± SD	*p*-value*
Fruits and vegetables	7-8	6.4 ± 2.2	7-10	6.1 ± 2.6	7-11	5.8 ± 2.4	0.094
Whole fruits	-	2.0 ± 1.1	-	2.0 ± 1.3	-	2.0 ± 1.2	0.8751
Green and orange vegetables	2	1.3 ± 0.8	2-4	1.2 ± 0.9	2-5	1.1 ± 0.8	0.3213
Grain products	6-7	6.1 ± 1.8	6-9	5.9 ± 1.8	6-10	5.7 ± 2.0	0.206
Whole grain products	3	1.5 ± 1.3	3-5	1.5 ± 1.3	3-6	1.6 ± 1.4	0.8683
Milk and alternatives	2	2.5 ± 1.1	2-4	2.7 ± 1.4	2-5	3.0 ± 1.4	0.002
Meat and alternatives	2	2.2 ± 0.9	2-4	2.2 ± 0.8	2-5	2.1 ± 0.8	0.740
Saturated fats (% daily EI)	-	12.8 ± 2.1	-	13.2 ± 2.9	-	13.5 ± 2.5	0.0472
Other foods (% daily EI)	-	22.2 ± 9.6	-	22.0 ± 9.5	-	22.1 ± 10.3	0.9694

[1]For specific information regarding serving sizes of each food group, please refer to CFG [183]; [2]Recommendations for non-pregnant adult women; [3]1st trimester recommendations + 2 portions; [3]1st trimester recommendations + 3 portions; EI: Energy intake; **p-value of the repeated measures analyses of variance performed across trimesters.

Table 3. Healthy Eating Index total and subscores throughout pregnancy

	1st trimester	2nd trimester	3rd trimester	*p*-value*
HEI				
Total	65.8 ± 10.8	65.0 ± 12.0	62.9 ± 12.6	0.075
Adequacy†	47.2 ± 7.4	46.4 ± 7.7	44.7 ± 8.2	0.016
Total vegetables and fruits	8.3 ± 2.0	7.7 ± 2.1	7.7 ± 2.2	0.018
Whole fruits	4.3 ± 1.5	4.1 ± 1.4	4.3 ± 1.4	0.778
Dark green and orange vegetables	3.5 ± 1.6	3.4 ± 1.6	3.0 ± 1.6	0.056
Total grain products	4.5 ± 0.7	4.4 ± 0.8	4.2 ± 0.9	0.123
Whole grains	2.4 ± 1.8	2.3 ± 1.7	2.4 ± 1.9	0.893
Milk and alternatives	8.9 ± 2.0	8.9 ± 2.1	9.1 ± 1.9	0.685
Meat and alternatives	8.7 ± 2.0	8.9 ± 1.9	8.6 ± 2.2	0.566
Unsaturated fats	6.6 ± 3.0	6.6 ± 3.4	5.4 ± 3.4	0.008
Moderation‡	18.6 ± 7.2	18.6 ± 7.9	18.2 ± 8.1	0.894
Saturated fats	4.0 ± 2.7	3.6 ± 3.1	3.1 ± 2.8	0.039
Sodium	4.4 ± 2.6	4.7 ± 2.8	5.0 ± 2.7	0.173
Other foods	10.2 ± 5.1	10.3 ± 5.2	10.2 ± 5.7	0.970

*p-value of the repeated measures analyses of variance performed across trimesters. †For adequacy components, 0 points for minimum intake or less, 5, 10 or 20 for maximum intake or more, and proportional for amounts between minimum and maximum. ‡For moderation components, 10 or 20 points for minimum intake or less, 0 points for maximum intake or more, and proportional for amounts between minimum and maximum.

Table 4. Stepwise regression analyses of trimester-specific HEI scores[a]

	1st trimester			2nd trimester			3rd trimester		
	r^2 x 100	β[b]	p-value	r^2 x 100	β	p-value	r^2 x 100	β	p-value
Vomiting (yes/no)	10.0	0.34	0.003	1.9	-0.14	NS	-	-	-
Multivitamin use (yes/no)	4.5	0.23	0.042	-	-	-	-	-	-
Pre-pregnancy BMI (kg/m^2)	4.2	-0.22	0.047	-	-	-	4.5	-0.20	NS
Nutrition knowledge (score)	3.5	0.21	NS	3.5	0.19	NS	6.8	0.26	0.017
Living environment[c]	3.3	0.32	NS	-	-	-	6.7	0.16	NS
University degree (yes/no)	1.7	0.14	NS	-	-	-	2.6	0.16	NS
Physical activity (min/day)	-	-	-	7.4	0.28	0.012	-	-	-
Food cravings (yes/no)	-	-	-	1.6	-0.13	NS	-	-	-
Total	27.3			14.4			20.6		

[a] β coefficients, r^2 x 100 and p-values are not shown for variables that were not included in the regression model (P > 0.25) following the stepwise procedure.

[b] β coefficients of the 1st trimester analyses represent the degree of change in BoxCox transformed HEI score, since this variable was not normally distributed in the 1st trimester.

[c] Living environment refers to living in the suburbs or in a rural setting, as opposed to an urban setting.

Figures

1. Trimester-specific diet quality according to maternal characteristics: (A) Age; (B) BMI; (C) Physical activity; (D) Education; (E) Nutrition knowledge; (F) Living environment. All p-values refer to significant differences between the subgroups at each trimester and are not a sign of heterogeneity across trimesters.

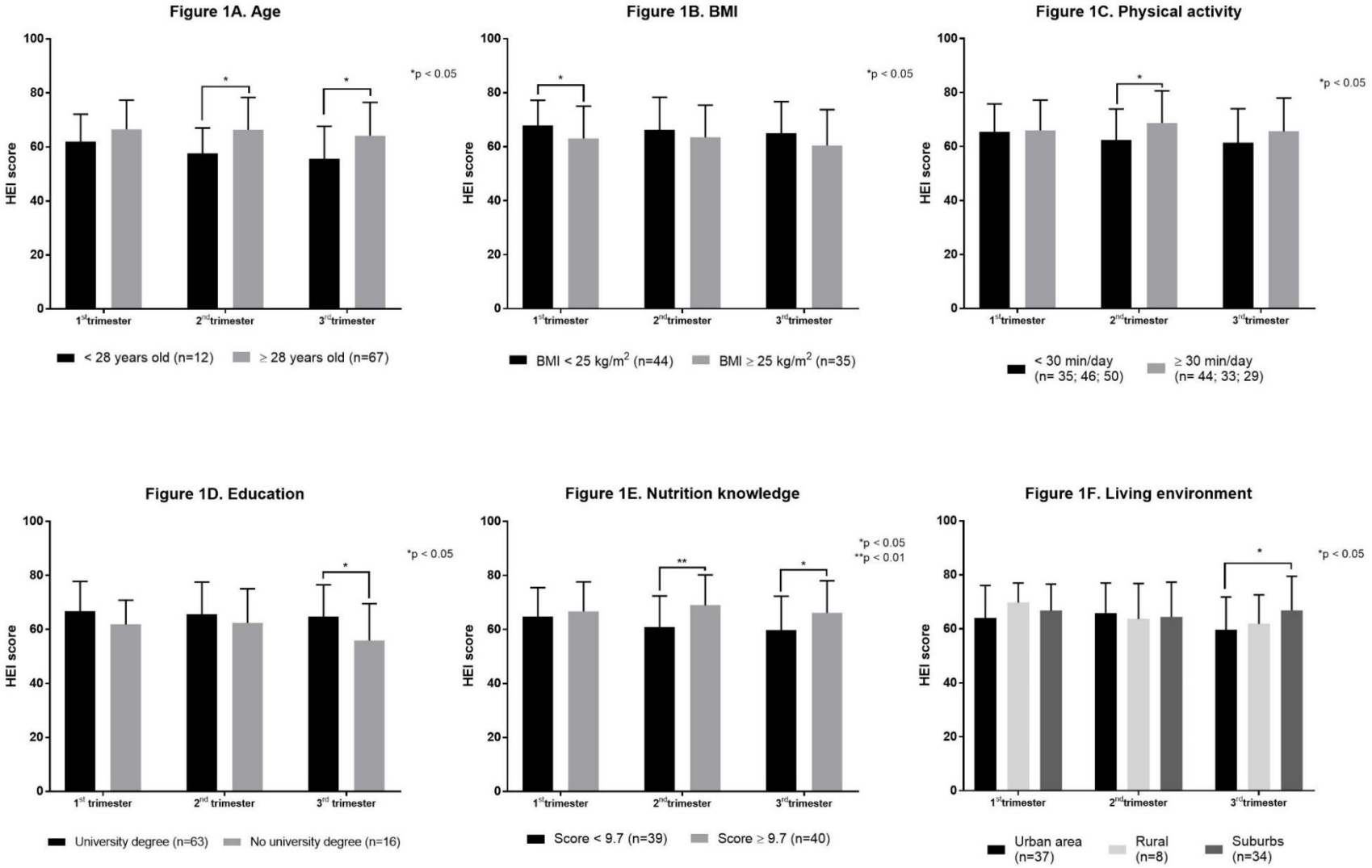

Figure 1. Trimester-specific diet quality according to maternal characteristics: (A) Age; (B) BMI; (C) Physical activity; (D) Education; (E) Nutrition knowledge; (F) Living environment

Supplementary material

Supplementary Table S1. Components of Canadian adaptation of Healthy Eating Index, range of scores and scoring criteria

Component	Maximum points	Scoring criteria (daily servings)*	
		Minimum score	Maximum score
Adequacy†	60		
Total vegetables and fruits	10	0	4 to 10 servings
Whole fruits	5	0	0.8 to 2.1 servings
Dark green and orange vegetables	5	0	0.8 to 2.1 servings
Total grain products	5	0	3 to 8 servings
Whole grains	5	0	1.5 to 4 servings
Milk and alternatives	10	0	2 to 4 servings
Meat and alternatives	10	0	1 to 3 servings
Unsaturated fats	10	0	30 to 45 grams/day§
Moderation‡	40		
Saturated fats	10	≥15% of total energy intake	≤7% of total energy intake
Sodium	10	twice the UL (4600 mg)	AI or less (≤ 1500 mg)
Other foods	20	≥40% of total energy intake	≤5% of total energy intake

Adapted from Garriguet D. (2009); UL, Upper Intake limit; AI, Adequate intake.

*According to age and sex, as specified in Canada's Food Guide

†For adequacy components, 0 points for minimum intake or less, 5, 10 or 20 for maximum intake or more, and proportional for amounts between minimum and maximum.

‡For moderation components, 10 or 20 points for minimum intake or less, 0 points for maximum intake or more, and proportional for amounts between minimum and maximum.

§Refers only to the amount of unsaturated fats added directly to food during cooking or through salad dressings and does not represents total dietary intake of unsaturated fats.

Supplementary Table S2. Frequency of nausea and vomiting among participants

	n (%)		
	1st trimester	**2nd trimester**	**3rd trimester**
Experienced nausea	70 (88.6)	26 (32.9)	16 (20.3)
> 2 times/day	37 (46.8)	3 (3.8)	0
1 time/day	10 (12.7)	1 (1.3)	5 (6.3)
3 to 6 times/week	10 (12.7)	6 (7.6)	1 (1.3)
1 to 2 times/week	2 (2.5)	6 (7.6)	2 (2.5)
Occasionally	10 (12.7)	4 (5.1)	4 (5.1)
Rarely	1 (1.3)	6 (7.6)	4 (5.1)
Experienced vomiting	25 (31.7)	15 (19.0)	2 (2.5)
> 2 times/day	2 (2.5)	1 (1.3)	0
1 time/day	4 (5.1)	0	0
3 to 6 times/week	1 (1.3)	1 (1.3)	0
1 to 2 times/week	2 (2.5)	4 (5.1)	0
Occasionally	10 (12.7)	3 (3.8)	1 (1.3)
Rarely	6 (7.6)	6 (7.6)	1 (1.3)

Supplementary Table S3. Food cravings and aversions among participants

		n (%)		
	Foods included in each category	**1st trimester**	**2nd trimester**	**3rd trimester**
Number of women who reported cravings		44 (55.7)	33 (41.8)	25 (31.7)
Sweet	Chocolate, sweets, ice cream, soft drinks, desserts	23 (29.1)	22 (27.8)	20 (25.3)
Fruit	Fruit, fruit juice	11 (13.9)	13 (16.5)	8 (10.1)
Dairy	Milk, yoghurt, cheese, cream	17 (21.5)	5 (6.3)	5 (6.3)
Proteins	Meat, poultry, fish, eggs	6 (7.6)	3 (3.8)	4 (5.1)
Carbohydrates	Cereal, bread, pasta, potatoes	13 (16.5)	4 (5.1)	2 (2.5)
Salty snacks	Crisps, hummus, nuts, olives, condiments	17 (21.5)	5 (6.3)	5 (6.3)
Pickles	Pickles	4 (5.1)	0	0
Fast food	Pizza, burgers, fries, sushi, poutine	14 (17.7)	5 (6.3)	4 (5.1)
Vegetables	Vegetables, salads, soups	8 (10.1)	5 (6.3)	2 (2.5)
Number of women who reported aversions		50 (63.3)	28 (35.4)	17 (21.5)
Sweet	Chocolate, sweets, ice cream, soft drinks, desserts	6 (7.6)	0	1 (1.3)
Fruit	Fruit, fruit juice	0	0	1 (1.3)
Dairy	Milk, yoghurt, cheese, cream	3 (3.8)	0	0
Proteins	Meat, poultry, fish, eggs	33 (41.8)	22 (27.8)	14 (17.7)
Carbohydrates	Cereal, bread, pasta, potatoes	2 (2.5)	0	0
Salty snacks	Crisps, hummus, nuts, olives, condiments	10 (12.7)	4 (5.1)	2 (2.5)
Coffee and alcohol	Coffee, beer, wine, liquor	9 (11.4)	4 (5.1)	3 (3.8)
Fast food	Pizza, burgers, fries, sushi, poutine	3 (3.8)	0	2 (2.5)
Vegetables	Vegetables, salads, soups	14 (17.7)	3 (3.8)	2 (2.5)

Supplementary Table S4. Proportions of vitamin- and mineral-supplement users among participants

	Proportion (%)		
	1st trimester	2nd trimester	3rd trimester
≥ 1 supplement (all types)	86.1	84.8	78.5
Number of supplements (all types) taken during pregnancy			
0	13.9	15.2	21.5
1	68.4	74.7	64.6
2	10.1	6.3	11.4
3 (Maximum)	7.6	3.8	2.5
Type of supplements most commonly taken			
Multivitamins	74.7	77.2	70.9
Folic acid supplement	16.5	7.6	5.1
Vitamin D supplement	7.6	5.1	3.8
Iron supplement	1.3	0	5.1
Omega-3 supplement (mostly EPA-DHA)	5.1	3.8	5.1

Chapitre 8 – Do pregnant women eat healthier than nonpregnant women of childbearing age?

Résumé

L'objectif était de comparer l'alimentation des femmes enceintes à celle de 1) femmes planifiant une grossesse et 2) en âge de procréer. Cinquante-cinq femmes enceintes ont été appariées pour l'âge et l'IMC avec 55 femmes planifiant devenir enceinte et 55 femmes en âge de procréer. Trois rappels de 24 heures ont été complétés, à partir desquels le *Canadian Healty Eating Index* (C-HEI) a été calculé. Les femmes enceintes avaient un score C-HEI plus élevé (66.8 ± 10.7) comparativement aux deux groupes de femmes non enceintes (60.3 ± 14.1 et 61.4 ± 12.8), ce qui s'expliquait entre autres par des apports plus élevés en fruits, légumes et produits céréaliers. Les apports énergétiques étaient plus élevés chez les femmes enceintes vs. celles qui planifiaient une grossesse. Bref, les femmes enceintes avaient une meilleure qualité alimentaire, mais celle-ci pourrait être améliorée dans les trois groupes. Ainsi, les saines habitudes alimentaires devraient être encouragées chez toutes les femmes en âge de procréer.

Title page

Title: Do pregnant women eat healthier than nonpregnant women of childbearing age?

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Keywords: pregnancy, preconception, prenatal nutrition, diet quality, healthy eating index

Abstract

We aimed to compare the dietary quality and intake of pregnant women, women planning to conceive and women of childbearing age. Fifty-five pregnant women were matched for age and pre-pregnancy body mass index with 55 women planning to conceive and 55 women of childbearing age. Three Web-based 24-h recalls were completed, from which the Canadian Healthy Eating Index was calculated. Pregnant women had greater overall diet quality scores (66.8 ± 10.7, 60.3 ± 14.1 and 61.4 ± 12.8, in pregnant vs. planning to conceive and childbearing age women, p = .009), explained by a higher intake in fruits, vegetables and grain products and lower intake of foods that are high in fat, sugar or salt. Energy intake was significantly higher in pregnant versus planning to conceive women only (2283 ± 518 vs. 2062 ± 430 kcal, p = .03). Diet quality was greater among pregnant women, but diet quality scores were low in all groups, indicating that healthier dietary behaviours should be encouraged for all childbearing age women.

Introduction

Accumulating evidence now shows that diet before conception, as well as during pregnancy, will affect maternal and neonatal outcomes (Lee 2015; Jarman et al. 2018; Raghavan et al. 2019). Preconception diet may impact health outcomes by influencing pre-pregnancy body mass index (BMI) or by inducing nutrient deficiencies (Stephenson et al. 2018). Moreover, various studies have found no difference in preconception and pregnancy dietary patterns, suggesting that dietary intake during pregnancy is similar to that prior to conception (Cuco et al. 2006b; Crozier et al. 2009; King 2016). However, other studies have observed an increase in fruit and vegetable intake (Pinto et al. 2009; Alves-Santos et al. 2016; Skreden et al. 2017) and a decrease in intake of fast-food, meat, eggs, dairy products and grain products (Pinto et al. 2009) from preconception to pregnancy. Similar findings were reported in a recent systematic review (Hillier and Olander 2017), with the authors mentioning the studies' heterogeneity and the need for additional research.

Furthermore, pregnancy intention could influence health-related behaviours (Hellerstedt et al. 1998). In fact, women planning a pregnancy are more likely to adopt healthier preconception behaviours, such as taking a folic acid supplement and ceasing alcohol consumption (Hellerstedt et al. 1998; Naimi et al. 2003; Rosenberg et al. 2003). Still, few studies have assessed the differences in dietary variables between women planning a pregnancy or not. One study reported no difference between women planning to conceive or not, in fruit and vegetable intake and physical activity levels (Chuang et al. 2010), thus contrasting with the suggested healthier behaviours associated with pregnancy intention. It should be noted that the study did not assess its participants' diet quality.

We and others (Talai Rad et al. 2011; Vioque et al. 2013; Abeysekera et al. 2016; Jebeile et al. 2016; Savard et al. 2018b) have shown that, contrary to national guidelines (Otten et al. 2006a), energy intake does increase throughout pregnancy (Savard et al. 2018b). In the latter study, most women exceeded their estimated energy requirements (EERs) in their first trimester, although national guidelines state that energy intake in early pregnancy should remain similar to preconception (Otten et al. 2006a). Few authors have investigated the differences in energy intake prior versus during pregnancy but, in general, they observed increased energy intake from preconception to pregnancy (Kopp-Hoolihan et al. 1999; Cuco et al. 2006a, 2006b; Ådén et al. 2007; Pinto et al. 2009). However, those studies were heterogenous in terms of design and dietary assessment tools, and only one assessed statistical significance (Pinto et al. 2009), making it difficult to link early pregnancy with increased energy intakes.

In an ideal research setting, a woman's diet would be assessed prospectively, before and during pregnancy. However, since the moment of conception is rarely known and impossible to control, prospective designs raise some recruitment and follow-up challenges. Investigators can, alternatively, enrol pregnant women early in pregnancy and retrospectively evaluate their preconception diet, using a food frequency questionnaire (FFQ). However, FFQs are subject to memory bias and may not be sensitive to short-term changes (Naska et al. 2017). Another option is to compare diets between pregnant and non-pregnant women. In this case, although women are not compared to themselves, challenges related to retrospective bias, recruitment and follow-up are attenuated. Moreover, the latter option allows investigators to match pregnant women for important characteristics and include multiple comparators.

Evaluating dietary changes from preconception to pregnancy is challenging. Few research groups have compared, altogether, preconception and pregnancy diet quality, energy and nutrient intakes. This study therefore aimed to compare diet quality and dietary intake between (1) pregnant women, (2) women planning to conceive and (3) women of childbearing age, using a matched pairs design.

Methods

Study population

Pregnant women

From April 2016 to May 2017, 86 pregnant women were recruited as part of the *Apports Nutritionnels durant la GrossessE* (ANGE) study that took place in Quebec City, Canada. The study design and population were previously described (Savard et al. 2018b). Pregnant women were followed prospectively during on-site visits and completed Web questionnaires (described below). Exclusion criteria were twin pregnancy, severe medical condition (i.e. type 1 or type 2 diabetes, renal disease, inflammatory and autoimmune disorders), gestational age (confirmed by ultrasound) greater than 11 weeks of pregnancy at enrolment and being younger than 18 years. The study was approved by the CHU de Québec—Université Laval Research Centre's Ethics Committee (Reference number: 2016–2866) and participants gave their informed written consent during an on-site visit. Seven (7) participants were lost at follow-up due to miscarriage (n = 3) or lack of time (n = 4). The final ANGE cohort consisted in 79 pregnant women followed throughout pregnancy (Savard et al. 2018b), with only first trimester data considered in the present analyses.

Non-pregnant women planning to conceive

As part of an ongoing study (*Apports Nutritionnels durant la GrossessE – Cohorte contrôle,* ANGE-Ctrl*),* non-pregnant women planning to conceive were recruited in Quebec City, Canada. The aim of the ANGE-Ctrl study is to assess women's diet in preconception. Participants were recruited through social media and e-mails sent to members of Laval University and the CHU of Québec. Exclusion criteria was: previous diagnosis of a severe medical condition (i.e. type 1 or type 2 diabetes, renal disease, inflammatory and autoimmune disorders) and being younger than 18 years. Participants are only required to complete Web-based questionnaires (described below), therefore all collected data for this study are self-reported. Since June 2017, 180 women were recruited and completed the mandatory Web questionnaires related to the study. The ANGE-Ctrl study was approved by the CHU de Québec—Université Laval Research Centre's Ethics Committee as part of the ANGE study (Reference number: 2016–2866) and participants sent their informed written consent via e-mail. Twenty (20) women were excluded due to pregnancy (*n* = 15), lack of time (*n* = 3), limited computer access (*n* = 1) or unspecified reasons (*n* = 1). The actual ANGE-Ctrl cohort thus consisted in 160 non-pregnant women of childbearing age who were planning to conceive.

Non-pregnant women of childbearing age

The present study also included non-pregnant women of childbearing age living in Quebec City and recruited as part of a larger study that took place throughout the province, the *PRÉDicteurs Individuels, Sociaux et Environnementaux* (PREDISE) study (Carbonneau et al. 2019). The PREDISE study aimed to identify healthy eating determinants in a probability sample of French-Canadian adults, recruited in 5 different regions of the province of Quebec. Recruitment took place between August 2015 and April 2017 and was conducted by a research and survey firm, using random digit dialling. Participants were recruited to represent the French-speaking adult population in terms of sex and age. Participants had to have access to Internet and exclusion criteria were pregnancy, lactation and intestinal malabsorption. The PREDISE study received approval from the Research Ethics Committee at Laval University (reference number: 2014-271), *Centre Hospitalier Universitaire de Sherbrooke* (reference number: MP-31-2015-997), Montreal Clinical Research Institute (reference number: 2015-02) and at the *Université du Québec à Trois-Rivières* (reference number: 15-2009-07.13). All participants gave their written informed consent during an on-site visit. One thousand and forty-five (1045) men (*n* = 516) and women (*n* = 529) were included in the final sample of the PREDISE study, but only women of childbearing age living in Quebec City were considered for the present analyses (*n* = 92).

Assessment of dietary intake and diet quality

All participants completed the same Web-based 24 h dietary recall on three randomly generated, non-consecutive days, using the R24W (*Rappel de 24 h Web*) application over a 14- to 21-day period. Pregnant women completed their 3 dietary recalls between gestational weeks 8 and 14. ANGE and ANGE-Ctrl participants completed recalls on 2 weekdays and 1 weekend day. PREDISE participants completed their recalls on three different days, but not necessarily on 2 weekdays and 1 weekend day. The R24W application was developed and validated in a general adult population (Jacques et al. 2016; Lafreniere et al. 2018). Our research team later validated the application in pregnant women (Savard et al. 2018a). The Web recall asks respondents to report all food and drink consumed over a 24 h period and to select, for example, portion size and added condiments. The R24W database is linked to the 2015 Canadian Nutrient File (Health Canada 2015), ensuring the automatic collection of nutrient values of all reported foods. The obtained average nutrient intake was compared to dietary reference intake levels (DRIs) by analysing the proportions of women with an intake below the estimated average requirements (EARs) and above the upper intake limit (UL). These analyses were done a first time using average intake levels from food sources only, and a second time after adding intake levels from supplements (see below for supplement use assessment). Only synthetic forms of folic acid (fortified foods and supplements), niacin and magnesium were compared to their respective UL, as it only applies to intake from synthetic forms.

Diet quality was evaluated using the Canadian Healthy-Eating index 2007 (C-HEI), adapted from Kennedy et al. (Kennedy et al. 1995) and calculated by the R24W application. The C-HEI recommendations are expressed as numbers of servings, as specified in Canada's 2007 Food Guide (Health Canada 2007; Garriguet 2009). For each of the 11 C-HEI components (see Supporting Information Table S1), respondents receive either no points when failing to meet the recommendation; the maximum score when the recommendation is met perfectly; or a proportional score when their behaviour falls between the two extremes (Garriguet 2009). A maximum of 100 points can be scored, corresponding to a diet that perfectly adheres to Canada's 2007 Food Guide. An individual's score can be classified into three categories: good quality (over 80 points); requiring improvement (50 to 80 points); and poor quality (fewer than 50 points) (Garriguet 2009). Since its validation in the general population, the C-HEI has been used among pregnant women (Tsigga et al. 2011; Moran et al. 2013; Shin et al. 2014).

Assessment of supplement use and sociodemographic variables

Through the R24W application, all participants were asked if they were taking a supplement. They specified the type of supplement (multivitamin or single nutrient) taken, but no dosage information was collected. An additional questionnaire was completed by ANGE and ANGE-Ctrl participants only and was designed to collect detailed information on supplement use, such as the supplement's drug identification number, its dosage and the frequency of reported dosage. Information on all reported supplements was gathered via the Health Canada Licenced Natural Health Product Database (Politique gouvernementale de prévention en santé 2016) and company websites. Research assistants contacted participants whose answers were incomplete to obtain the missing information. Finally, all participants (from all 3 groups) completed a web-based questionnaire on economic and sociodemographic characteristics.

Physical activity level

All participants completed the validated French version of either the Pregnancy Physical Activity Questionnaire (PPAQ) or the International Physical Activity Questionnaire (IPAQ), from which total minutes of moderate- and high-intensity activities were calculated (Craig et al. 2003; Chasan-Taber et al. 2004; Chandonnet et al. 2012). Based on the DRIs' classification (Otten et al. 2006a), participants were either categorised as sedentary, low-active, active or very active. Each physical activity level (PAL) was translated into a coefficient for the calculation of EERs (see below; Otten et al. 2006a).

Estimation of energy and protein requirements

Pre-pregnancy or actual weight was self-reported by participants in ANGE and ANGE-Ctrl and was measured in PREDISE participants. Height was measured for ANGE and PREDISE participants, but self-reported by ANGE-Ctrl participants. Height and pre-pregnancy or actual weight were used to calculate pre-pregnancy or actual BMI. EERs were calculated for each participant using age, weight (actual or pre-pregnancy), height and PAL coefficient (Otten et al. 2006a). Estimated protein requirements (EPRs) were calculated as either 0.8 g/kg of actual weight (non-pregnant women) or 1.1 g/kg of pre-pregnancy weight (pregnant women) (Otten et al. 2006a). Women's reported energy intake (rEI) was compared to their basal metabolic rate (BMR), estimated with the Mifflin St-Jeor equation (Frankenfield et al. 2005). Participants were classified as under- (rEI:BMR < 1.35), adequate

(1.35 ≤ rEI:BMR ≤ 2.5) or over-reporters (rEI:BMR > 2.5) (Goldberg and Black 1998). Energy intake was compared to EERs and percentages of energy coming from protein, carbohydrate and fat intake were compared with acceptable macronutrient distribution ranges (AMDR) (Otten et al. 2006a). Protein intake (in grams/day) was also compared to EPRs.

Statistical analyses

Fifty-five pregnant women from the ANGE cohort were matched for age (±5 years) and pre-pregnancy BMI (±1 kg/m^2) with women from the ANGE-Ctrl (n = 55) and PREDISE (n = 55) cohorts. This number (n = 55) represents the number of participants that could be matched according to our age and BMI criteria. For all analyses, each matched pregnant woman was compared to her two matched "controls". Descriptive analyses were used to characterise the study groups. Analyses of variance (ANOVA) with Tukey's honest significant difference (HSD) post hoc tests were performed to assess overall and between-groups differences in C-HEI scores and in energy and nutrient intakes. Our sample size of n = 165 provided 71% power to detect a 5.4% difference in diet quality scores between groups, at p = .05, representing a greater than two-thirds likelihood of rejecting false null hypotheses. All ANOVAs considered the matching of participants and were adjusted for educational level and parity, as these two characteristics differed between groups (see Table 1). For categorical variables and frequencies, overall chi-squared tests were used to assess differences between groups, and additional chi-squared tests were performed to identify specific significant differences within each subcategory of one variable (e.g. education levels). Bonferroni corrections were applied to account for multiple comparisons. All statistical analyses were performed in JMP 14 (SAS Institute Inc., Cary, NC, USA).

Results

Participants' characteristics are presented in Table 1. The selected ANGE sample (n = 55) did not differ from the entire ANGE cohort (n = 79) for baseline characteristics (data not shown). The three matched groups were similar for age, BMI, PAL, ethnicity and annual household income. Women were, on average, 32-year-old, of normal weight, Caucasian, with a college education or more (in Québec, college refers to a degree after high school and before university) and an annual household income of C$80,000 or more. Compared to pregnant women and women planning to conceive, a higher proportion of childbearing age women had two children or more, and fewer of them had a university degree. Supplement use was higher in women planning to conceive (72.7%) than in women of

childbearing age (18.2%), but both groups' supplement use was lower compared to that of pregnant women (92.8%). Folic acid supplement use was lower in women of childbearing age (1.8%) compared to the other 2 groups (18.2% and 23.6% in pregnant women and women planning to conceive, respectively).

Total C-HEI scores and subscores are presented in Table 2. Total C-HEI scores were higher in pregnant women than in women who are planning to conceive and of childbearing age. In comparison with women planning to conceive, pregnant women had higher scores for the "Total vegetables and fruits" and "Whole fruits" categories, and the "Total grain products" subscore was higher in pregnant women than in the two other groups. Pregnant women also had a higher "other foods" subscore than women of childbearing age, indicating a lower proportion of energy intake from the "other foods" category among pregnant women. Differences in C-HEI scores remained significant after adjustment for energy intakes. Overall, women planning to conceive had diet quality scores similar to those of women of childbearing age.

Table 3 shows energy and macronutrient intake among the 3 groups. Comparisons with DRIs are presented in Supporting Information Table S2. Women planning to conceive reported lower energy intake than pregnant and childbearing age women. Proportions of under- (rEI:BMR < 1.35) and over-reporters (rEI:BMR > 2.5) did not differ between groups (16%, 25% and 24% of under-reporters and 0%, 2% and 4% of over-reporters in the ANGE, ANGE-Ctrl and PREDISE groups, respectively, $p > .05$). Carbohydrate intake and monounsaturated fatty acid intake as percentages of energy intake were higher in pregnant women than in other groups. Pregnant women also reported higher carbohydrate and dietary fibre intake (in grams) compared to women planning to conceive.

Micronutrient intake levels from food alone are presented in Table 4 and compared to DRIs in Supporting Information Table S3. Pregnant women reported higher folate and folic acid intake compared to the other two groups. When compared to women planning to conceive, pregnant women had a higher intake of iron, vitamin C, thiamine, selenium and copper. However, more pregnant women were below the EAR for vitamin C (compared to women planning to conceive only), iron, folate and vitamin B_6 in comparison with the other two groups. More pregnant women also exceeded the UL for sodium compared to women planning to conceive (Supporting Information Table S3). After addition of intake levels from supplements (pregnant and planning to conceive women only), pregnant women had a significantly higher intake in all micronutrients, except for vitamin D, magnesium, phosphorus and

sodium (Table 5). Consequently, more planning to conceive women were below the EAR for vitamin D and vitamin C, compared to pregnant women. However, more pregnant women were above the UL for iron and folic acid (Supporting Information Table S4).

Discussion

This study assessed dietary differences among pregnant women, women planning to conceive and women of childbearing age, by matching them for age and BMI. To our knowledge, this is the first study to assess differences in diet quality, dietary intake and adequacy to recommendations between preconception and early pregnancy, by using a matched pairs design and by including two preconception groups. Our results suggest that pregnant women have better diet quality compared to women of childbearing age and women who are planning to conceive, which could be explained by a higher intake of fruits, vegetables and grain products. In general, planning to conceive and childbearing age women had similar diets, with the exception of lower energy intake in women planning to conceive compared to the other groups. Pregnant women had a higher intake in 7 micronutrients (iron, folate, folic acid, vitamin C, thiamine, selenium and copper) compared to women planning to conceive, and this number increased to 16 after adding the intake from supplements.

Compared to the non-pregnant groups, pregnant women had a greater overall diet quality, explained by a higher intake of fruits, vegetables and grain products and lower intake of “other foods”. Similarly, a systematic review of longitudinal studies by Hillier and Olander (Hillier and Olander 2017) found an increase in fruit and vegetable intake and a decrease in fast-food consumption, from preconception to pregnancy. However, that review excluded cross-sectional studies comparing preconception and pregnancy diets. The existing cross-sectional studies found that preconception and pregnancy diets were relatively similar (Hure et al. 2009; Cuervo et al. 2014; Gresham et al. 2016), though none used a matched pairs design. The fact that these studies used unmatched groups might explain the discrepancy with our results. Indeed, our matched pairs design may explain why we observed significant differences in diet quality between pregnant and non-pregnant women while other cross-sectional studies did not, since we limited between-group differences and probably gained precision. This remains a hypothetical explanation since our study is the first to use this design to assess differences in preconception versus pregnancy diet. Moreover, only one of the three cross-sectional study mentioned assessed age and BMI differences between pregnant and non-pregnant women and found a difference in mean age (Cuervo et al. 2014). Therefore, it is not possible to conclude that the

lack of significant dietary differences in those cross-sectional studies is due to factors related to age and BMI.

Our results and those of Hillier and Olander (Hillier and Olander 2017) are in line with the suggestion that pregnant women may be more aware of their diet and more motivated to adopt healthier behaviours (Szwajcer et al. 2012; Lindqvist et al. 2017). Nonetheless, it is still possible that the lower quality diet observed in childbearing age women is due to their lower educational level, even though we adjusted our results for this variable (Estaquio et al. 2008; Hu et al. 2013). Furthermore, although pregnant women had a greater diet quality, the mean C-HEI score of each group fell into the category "diet that requires improvement", i.e. between 50 and 80 out of 100 (Garriguet 2009). Other authors also found that overall diet quality could be improved in all women of childbearing age, independently of pregnancy status (Hure et al. 2009; Cuervo et al. 2014; Alves-Santos et al. 2016; Skreden et al. 2017), thus suggesting that pregnant and non-pregnant women could benefit from dietary counselling encouraging the adoption of healthy dietary behaviours.

In addition to greater diet quality, pregnant women reported a higher energy intake than women planning to conceive. Similarly, four out of five longitudinal studies that assessed energy intake from preconception to pregnancy found an increase in energy intake (Kopp-Hoolihan et al. 1999; Cuco et al. 2006a; Cuco et al. 2006b; Ådén et al. 2007). Only one cross-sectional study assessed energy intake and found that pregnant women ate an additional 395 kcal compared to their counterparts who were trying to become pregnant (unreported statistical significance) (Hure et al. 2009). In our study, energy intake was 221 kcal higher in pregnant compared to planning to conceive women, which could be explained by pregnant women's higher intake in fruits, vegetables and grain products. This could also explain the higher carbohydrates and fibres intake reported by pregnant women, since fruits, vegetables and grain products constitute sources of these nutrients. Moreover, proportions of under- and over-reporters were similar between groups and were comparable to those observed among women in preconception and pregnancy (Mullaney et al. 2015; Moran et al. 2018; Shiraishi et al. 2018). Therefore, women's misreporting status cannot explain the differences in energy intakes. Furthermore, the different C-HEI scores but a similar energy intake between pregnant women and women from the PREDISE study could be explained by the higher intake of "other foods" among the PREDISE group. Indeed, foods in the "other foods" category are generally of higher energy density (Health Canada 1997), therefore, a high intake increases total energy intakes, but lowers the C-HEI total score

(Garriguet 2009). We could thus hypothesise that during pregnancy, diet quality is increased in a conscious manner while a higher energy intake is rather unconscious and resulting from consuming more "healthy" foods such as fruits and vegetables.

In general, pregnant women reported higher micronutrient dietary intakes, specifically iron, folate, folic acid, vitamin C, thiamine, selenium and copper. This aligns with pregnant women's greater diet quality score and higher energy intakes, since diet quality scores correlate with nutrient intake (Kennedy et al. 1995). A higher intake of some micronutrients in pregnant women could, on the one hand, reflect their higher energy intake and, on the other hand, indicate a greater diet quality. Two retrospective studies examined micronutrient intake levels from preconception to pregnancy and found increases in some micronutrients (Ådén et al. 2007; Pinto et al. 2009). Similarly, one cross-sectional study observed higher intake levels of various micronutrients (e.g. vitamin C, vitamin A and folate) among pregnant women compared to women trying to conceive (unreported statistical significance). In our study, even though micronutrient intake from foods was higher in pregnant women, a higher proportion of pregnant women failed to meet the DRIs, due to the greater requirements during pregnancy (Otten et al. 2006b). In this regard, after adding intake levels from supplements, pregnant women had a higher intake for almost all micronutrients and fewer of them failed to meet the DRIs, when compared to women planning to conceive.

We found that the diet of women planning to conceive was fairly similar to that of women of childbearing age. Literature regarding the influence of pregnancy intention on women's diet is very limited, as most studies focussed on general health behaviours, and not specific dietary variables (Hellerstedt et al. 1998; Naimi et al. 2003; Rosenberg et al. 2003). Nevertheless, one study assessed fruit and vegetable intake levels in women intending or not to become pregnant (Chuang et al. 2010) and found no difference. Although these findings are similar to ours, women of childbearing age in our study were not questioned on their pregnancy intention. Hence, some of them may have been trying to become pregnant at the time of the study, which could have attenuated dietary differences between our non-pregnant groups. Still, more women planning to conceive reported taking multivitamins and folic acid supplements, compared to women of childbearing age, which is in accordance with other studies (Hellerstedt et al. 1998; Rosenberg et al. 2003; Green-Raleigh et al. 2005). Women planning to conceive may be more aware of prenatal guidelines that recommend daily folic acid supplementation during preconception (Health Canada 2009) even though more than 25% of them did not take any

supplement. Differences in supplement use could also be explained by the lower educational level of women in the childbearing age group, as it was reported that folic acid supplement use was greater among more educated women (Toivonen et al. 2018). Furthermore, since more childbearing age women already had two children or more, it is possible that women from this group did not want more children, hence, explaining why fewer of them were taking folic acid supplements. Similarly, one study found that multiparous non-pregnant women were less likely to take folic acid supplements (Kurzawinska et al. 2018). Considering the importance of sufficient micronutrient intake during pregnancy (Barua et al. 2014; De-Regil et al. 2016; Rogne et al. 2017), it would be relevant to assess the knowledge of women of childbearing age regarding the nutritional guidelines for women planning to conceive.

One of the strengths of our study is the use of a Web-based 24 h recall validated in a pregnant and a general adult population providing detailed dietary information (Lafreniere et al. 2018; Savard et al. 2018a). The diets of all groups were assessed with the same tool and on the same number of occasions, which is also a strength. Similarly, our supplement use questionnaire allowed the assessment of total micronutrient intake in comparison with DRIs. However, those analyses were not performed in childbearing age women, since no detailed information on supplements was collected. Furthermore, the use of web-based questionnaires meant that participants had to own a computer and/or a smartphone to take part in our study, thus limiting the generalizability of our results. Nevertheless, our sample is still similar to the Canadian population, since 98% of Canadians have access to the Internet, and 87% have an Internet subscription (Canadian Radio-television and Telecommunications Commission 2018). Another strength is the matched pairs design, considering participants' age and BMI, variables known to influence diet in pregnancy (Stravik et al. 2019), and allowing us to match each pregnant woman with two non-pregnant women from two distinct cohorts. However, our approach may still be biased because of the individual variance associated with dietary intake and could also be less precise than a prospective or retrospective design where women are compared to themselves. Our main study limitation is our small sample size, yet we observed significant differences that are in accordance with larger cohort studies. Nevertheless, the validity of some differences should be interpreted with caution, as we performed multiple comparisons in fairly small samples. Self-reported weights and heights could have affected our matching process, since the real BMI of ANGE-Ctrl participants, for example, was probably higher than the one we used for matching. Similarly, all of our nutritional data was self-reported, which represents a limitation, although self-

reported questionnaires are widely used in research settings. It should be noted that following the new Canadian dietary guidelines (Health Canada 2019), the C-HEI is outdated and some of its components, such as grain products, are arguably not strong indicators of a greater diet quality, hence the argument that the C-HEI is not a good marker of diet quality (Lucas and Willett 2019). However, it was shown that the C-HEI strongly correlates with other diet quality indexes like the Alternate Healthy Eating Index (AHEI), which predicts cardiovascular disease risk (Brassard and Lamarche 2019). Finally, our sample became more homogenous, following the matching process, i.e. most women were Caucasian and of higher socioeconomic status, thus limiting the generalizability of our results.

Conclusion

Pregnant women reported dietary intakes of greater quality than those of women planning to conceive and non-pregnant women of childbearing age that were similar in age and BMI. Pregnant women may become more aware of the importance of a healthy diet upon learning that they are pregnant, leading to conscious increases in intake of nutrient-rich foods, such as fruits, vegetables and grain products, explaining their higher energy intakes. Although we found no differences between the diets of women of childbearing age and women planning to conceive, the greater use of multivitamins and folic acid supplements observed in the latter group suggests better adherence to nutritional recommendations when women are planning a pregnancy. Nevertheless, our results do not show a link between pregnancy intention and healthier dietary behaviours. Future studies should investigate knowledge of nutritional guidelines in women of childbearing age who are planning to conceive. Finally, despite pregnant women's greater diet quality, overall diet quality scores were relatively low in all groups, regardless of pregnancy status, suggesting that dietary counselling tailored for women of childbearing age could be beneficial for all women.

Declarations

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Tables

Table 1. Participants' characteristics

Variables	Mean ± SD or n (%)			Overall *p*-value
	Pregnant women (n=55)	**Women planning to conceive** (n=55)	**Women of childbearing age** (n=55)	
Age (years)	32.4 ± 4.0	32.0 ± 3.9	32.4 ± 5.0	0.8914
Parity (n)				< 0.0001
0	17 (30.9)[a]	29 (52.7)[a]	17 (30.9)[a]	
1	30 (54.5)[a]	19 (36.4)[a,b]	11 (20.0)[b]	
≥ 2	8 (14.5)[a]	7 (12.7)[a]	27 (49.1)[b]	
BMI (kg/m^2)	24.3 ± 4.7	24.4 ± 4.6	24.4 ± 4.7	0.5109
Underweight	2 (3.6)	1 (1.8)	2 (3.6)	
Normal weight	33 (60.0)	32 (58.2)	32 (58.2)	
Overweight	13 (23.6)	15 (27.3)	15 (27.3)	
Obese	7 (12.7)	7 (12.7)	6 (10.9)	
Physical activity level				0.3256
Sedentary	32 (58.2)	33 (60.0)	30 (54.5)	
Low active	8 (14.5)	9 (16.4)	15 (27.3)	
Active	15 (27.3)	12 (21.8)	8 (14.5)	
Very active	0 (0.0)	1 (1.8)	2 (3.6)	
Ethnicity				0.5237
Caucasian	54 (98.2)	51 (92.7)	52 (94.5)	
Hispanic	1 (1.8)	3 (5.5)	1 (1.8)	
African	0 (0.0)	0 (0.0)	1 (1.8)	
Asian	0 (0.0)	1 (1.8)	0 (0.0)	
Native American	0 (0.0)	0 (0.0)	1 (1.8)	
Education				< 0.0001
High school	3 (5.5)[a]	0 (0.0)[a]	14 (25.5)[b]	
College	7 (12.7)	11 (20.0)	12 (21.8)	
University	45 (81.8)[a]	44 (80.0)[a]	29 (52.7)[b]	
Household income				0.8311
< 60 000 $	11 (20.0)	11 (20.0)	14 (25.5)	
60 000 – 79 999 $	11 (20.0)	7 (12.7)	7 (12.7)	
80 000 – 99 999 $	7 (12.7)	6 (10.9)	9 (16.4)	
≥ 100 000 $	25 (45.5)	28 (50.9)	22 (40.0)	
Income missing	1 (1.8)	3 (5.5)	3 (5.5)	
Supplement use				< 0.0001
None	4 (7.2)[a]	15 (27.3)[b]	45 (81.8)[c]	
Multivitamin	46 (83.6)[a]	24 (43.6)[b]	5 (9.1)[c]	
Folic acid	10 (18.2)[a]	13 (23.6)[a]	1 (1.8)[b]	

p-values refer to ANOVAs or Chi-squared test between the 3 groups. Tukey's HSD post-hoc tests were performed to identify specific differences between groups (continuous variables) and Bonferroni correction was used to account for multiple comparisons (categorical variables). Same letter indicates no significant difference; Bold indicates overall statistically significant difference.

Table 2. Comparison of the Canadian Healthy Eating Index total score and subscores between groups

	Mean ± SD			
	Pregnant women (n=55)	**Women planning to conceive** (n=55)	**Women of childbearing age** (n=55)	**Overall *p*-value**
Total	66.8 ± 10.7[a]	60.3 ± 14.1[b]	61.4 ± 12.8[b]	0.0090
Adequacy †	47.7 ± 7.8[a]	43.4 ± 9.6[b]	44.4 ± 8.9[a,b]	0.0208
Total vegetables and fruits	8.4 ± 1.9[a]	6.9 ± 2.6[b]	7.2 ± 2.5[a,b]	0.0033
Whole fruits	4.3 ± 1.5[a]	3.4 ± 1.6[b]	3.6 ± 1.7[a,b]	0.0088
Dark green and orange vegetables	3.6 ± 1.6	3.5 ± 1.5	3.2 ± 1.7	0.1365
Total grain products	4.5 ± 0.7[a]	3.9 ± 1.2[b]	3.7 ± 1.1[b]	0.0008
Whole grains	2.7 ± 1.8	2.4 ± 1.8	2.1 ± 1.7	0.2058
Milk and alternatives	8.8 ± 2.1	8.2 ± 2.5	8.2 ± 2.4	0.4105
Meat and alternatives	8.8 ± 1.9	8.5 ± 2.3	8.7 ± 1.8	0.6858
Unsaturated fats	6.5 ± 3.1	6.6 ± 3.1	7.7 ± 3.0	0.1050
Moderation ‡	19.2 ± 6.9	16.9 ± 7.5	17.0 ± 8.4	0.1188
Saturated fats	4.2 ± 2.8	3.5 ± 3.0	4.5 ± 3.2	0.3563
Sodium	4.4 ± 2.6	5.1 ± 2.8	5.0 ± 3.0	0.0912
Other foods	10.6 ± 4.7[a]	8.3 ± 5.8[a,b]	7.4 ± 6.0[b]	0.0093

†For adequacy components, 0 points for minimum intake or less, 5, 10 or 20 for maximum intake or more, and proportional for amounts between minimum and maximum; ‡ For moderation components, 10 or 20 points for minimum intake or less, 0 points for maximum intake or more, and proportional for amounts between minimum and maximum; p-values refer to ANOVAs between the 3 groups. Tukey's HSD post-hoc tests were performed to identify specific differences between groups. Same letter indicates no significant difference; Bold indicates overall statistically significant difference.

Table 3. Comparison of energy and macronutrient intake between groups

	Mean ± SD			
	Pregnant women (n=55)	**Women planning to conceive** (n=55)	**Women of childbearing age** (n=55)	**Overall *p*-value**
Energy (kcal/day)	2283 ± 518[a]	2062 ± 430[b]	2236 ± 628[a]	0.0147
Fat (E%)	34.8 ± 4.1	37.0 ± 4.2	36.4 ± 4.9	0.0642
Carbohydrates (E%)	49.6 ± 4.8[a]	44.5 ± 6.0[b]	43.9 ± 6.0[b]	< 0.0001
Proteins (E%)	17.1 ± 2.4	17.4 ± 3.3	16.6 ± 3.9	0.3059
SFA (E%)	12.7 ± 2.3	13.3 ± 3.0	12.2 ± 2.8	0.3291
MUFA (E%)	12.0 ± 2.1[a]	13.6 ± 2.3[b]	13.3 ± 2.6[b]	0.0010
PUFA (E%)	7.3 ± 2.0	7.8 ± 2.1	7.9 ± 2.3	0.6885
Fat (g/day)	88.4 ± 22.4	86.0 ± 20.3	91.4 ± 30.5	0.1271
Carbohydrates (g/day)	283.3 ± 73.2[a]	229.8 ± 58.2[b]	252.3 ± 75.0[a,b]	0.0003
Proteins (g/day)	97.0 ± 21.9	89.2 ± 21.4	90.7 ± 27.8	0.1166
Cholesterol (mg/day)	297 ± 103	277 ± 122	278 ± 123	0.1580
SFA (g/day)	32.1 ± 8.8	30.3 ± 9.0	30.6 ± 12.0	0.3575
MUFA (g/day)	30.6 ± 8.7	31.2 ± 8.5	33.3 ± 11.9	0.0798
PUFA (g/day)	18.4 ± 6.7	17.8 ± 5.6	19.9 ± 8.5	0.1312
Fibres (g/day)	23.8 ± 7.7[a]	21.0 ± 6.2[b]	20.6 ± 7.0[a,b]	0.0367

p-values refer to ANOVAs between the 3 groups. Tukey's HSD post-hoc tests were performed to identify specific differences between groups. Same letter indicates no significant difference; Bold indicates overall statistically significant difference. SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids; E%: as percentage of total energy intakes.

Table 4. Comparison of micronutrient intake from food alone between groups

	Mean ± SD			Overall p-value
	Pregnant women (n=55)	**Women planning to conceive** (n=55)	**Women of childbearing age** (n=55)	
Vitamin D (IU/day)	244.1 ± 117.1	242.1 ± 146.0	189.9 ± 108.0	0.2823
Iron (mg/day)	15.8 ± 5.2[a]	13.2 ± 3.9[b]	14.1 ± 4.2[a,b]	0.0070
Folate (µg DFE/day)	508.9 ± 132.9[a]	441.0 ± 128.7[b]	415.1 ± 114.5[b]	0.0027
Folic acid (µg/day)	152.7 ± 61.5[a]	111.4 ± 65.4[b]	102.5 ± 47.2[b]	0.0002
Vitamin B_6 (mg/day)	1.9 ± 0.5	1.7 ± 0.5	1.8 ± 0.6	0.1942
Magnesium (mg/day)	392.4 ± 114.5	383.5 ± 104.4	383.5 ± 123.8	0.8197
Vitamin A (µg RAE/day)	870.1 ± 296.9	839.8 ± 351.5	769.1 ± 311.2	0.6384
Zinc (mg/day)	12.5 ± 3.5	11.3 ± 3.3	11.8 ± 4.0	0.1679
Calcium (mg/day)	1304.5 ± 410.5	1173.6 ± 406.3	1102.4 ± 397.6	0.0781
Vitamin C (mg/day)	154.1 ± 70.6[a]	102.1 ± 49.9[b]	124.3 ± 65.9[a,b]	0.0006
Thiamin (mg/day)	1.9 ± 0.6[a]	1.5 ± 0.4[b]	1.7 ± 0.5[a,b]	0.0012
Vitamin B_{12} (µg/day)	4.9 ± 1.7	4.8 ± 2.0	4.7 ± 2.6	0.9944
Riboflavin (mg/day)	2.4 ± 0.7	2.1 ± 0.6	2.2 ± 0.7	0.1432
Niacin (mg NE/day)	46.3 ± 11.1	43.0 ± 10.0	44.1 ± 13.0	0.1587
Pantothenic acid (mg/day)	6.5 ± 1.9	6.2 ± 1.7	6.3 ± 2.1	0.4939
Phosphorus (mg/day)	1635.0 ± 421.8	1503.7 ± 391.6	1481.6 ± 413.0	0.1052
Sodium (mg/day)	3395.5 ± 827.9	3109.3 ± 912.5	3185.0 ± 1035.2	0.0863
Manganese (mg/day)	4.2 ± 1.7	3.7 ± 1.3	3.8 ± 1.3	0.0717
Selenium (µg/day)	136.7 ± 34.8[a]	120.0 ± 31.9[b]	118.5 ± 34.2[a,b]	0.0069
Copper (mg/day)	1.6 ± 0.6[a]	1.3 ± 0.3[b]	1.4 ± 0.4[a,b]	0.0048

p-values refer to ANOVAs between the 3 groups. Tukey's HSD post-hoc tests were performed to identify specific differences between groups. Same letter indicates no significant difference; Bold indicates overall statistically significant difference. DFE: dietary folate equivalent; RAE: retinol activity equivalents; NE: niacin equivalent.

Table 5. Comparison of total micronutrient intake (food and supplements) between pregnant women and women planning to conceive

	Mean ± SD		*p*-value
	Pregnant women (n=55)	**Women planning to conceive** (n=55)	
Vitamin D (IU/day)	704.1 ± 635.6	493.7 ± 355.7	0.0661
Iron (mg/day)	40.3 ± 12.7	24.0 ± 14.4	< 0.0001
Folate (µg DFE/day)	1787.1 ± 1075.0	1090.6 ± 757.2	< 0.0001
Folic acid (µg/day)	1430.9 ± 1056.3	761.0 ± 753.9	< 0.0001
Vitamin B_6 (mg/day)	5.8 ± 3.8	3.3 ± 2.9	< 0.0001
Magnesium (mg/day)	435.1 ± 117.7	404.4 ± 105.3	0.1532
Vitamin A (µg RAE/day)	1301.8 ± 368.2	1068.1 ± 410.3	0.0086
Zinc (mg/day)	20.6 ± 6.0	14.5 ± 5.3	< 0.0001
Calcium (mg/day)	1540.4 ± 383.8	1288.4 ± 417.9	0.0002
Vitamin C (mg/day)	237.1 ± 78.5	151.4 ± 100.8	< 0.0001
Thiamin (mg/day)	3.5 ± 1.2	2.5 ± 2.3	0.0012
Vitamin B_{12} (µg/day)	10.9 ± 6.6	7.8 ± 9.2	0.0283
Riboflavin (mg/day)	4.1 ± 1.3	3.1 ± 2.3	0.0008
Niacin (mg NE/day)	62.0 ± 14.0	50.4 ± 12.4	< 0.0001
Pantothenic acid (mg/day)	11.6 ± 3.1	9.0 ± 3.6	< 0.0001
Phosphorus (mg/day)	1637.2 ± 421.6	1503.7 ± 391.6	0.0526
Sodium (mg/day)	3395.5 ± 827.9	3109.3 ± 912.5	0.2753
Manganese (mg/day)	5.4 ± 2.0	4.5 ± 1.7	0.0233
Selenium (µg/day)	155.7 ± 39.0	132.9 ± 32.2	0.0006
Copper (mg/day)	2.7 ± 0.9	1.7 ± 0.7	< 0.0001

p-values refer to one-way ANOVAs used to assess differences between the 2 groups; Bold indicates statistically significant differences. DFE: dietary folate equivalent; RAE: retinol activity equivalents; NE: niacin equivalent.

Supplementary material

Supplementary Table S1. Components of Canadian adaptation of Healthy Eating Index, range of scores and scoring criteria

Component	Maximum points	Scoring criteria (daily servings)*	
		Minimum score	Maximum score
Adequacy†	60		
Total vegetables and fruits	10	0	4 to 10 servings
Whole fruits	5	0	0.8 to 2.1 servings
Dark green and orange vegetables	5	0	0.8 to 2.1 servings
Total grain products	5	0	3 to 8 servings
Whole grains	5	0	1.5 to 4 servings
Milk and alternatives	10	0	2 to 4 servings
Meat and alternatives	10	0	1 to 3 servings
Unsaturated fats	10	0	30 to 45 grams/day§
Moderation‡	40		
Saturated fats	10	≥15% of total energy intake	≤7% of total energy intake
Sodium	10	twice the UL (4600 mg)	AI or less (≤ 1500 mg)
Other foods	20	≥40% of total energy intake	≤5% of total energy intake

Adapted from Garriguet D. (2009); UL, Upper Intake limit; AI, Adequate intake.

*According to age and sex, as specified in Canada's Food Guide

†For adequacy components, 0 points for minimum intake or less, 5, 10 or 20 for maximum intake or more, and proportional for amounts between minimum and maximum.

‡For moderation components, 10 or 20 points for minimum intake or less, 0 points for maximum intake or more, and proportional for amounts between minimum and maximum.

§Refers only to the amount of unsaturated fats added directly to food during cooking or through salad dressings and does not represents total dietary intake of unsaturated fats.

Supplementary Table S2. Proportion of women below and above recommendations for energy and macronutrients between groups

	Pregnant women (n=55)			Women planning to conceive (n=55)			Women of childbearing age (n=55)			
	EER, EPR, AMDR or AI	% Below	% Above	**EER, EPR, AMDR or AI**	% Below	% Above	**EER, EPR, AMDR or AI**	% Below	% Above	**Overall *p*-value**
Energy (kcal/day)	2059 ± 210	31	69	2052 ± 256	51	49	2059 ± 257	38	62	0.0955
Proteins (g/kg/day)	68.2 ± 8.8	5	95	49.3 ± 6.6	2	98	49.4 ± 6.7	0	100	0.1664
Fibre (g/day)	32.0 ± 7.3	96	4	28.9 ± 6.0	90	9	31.3 ± 8.8	95	5	0.4747
Fat (E%)	20-35	0	49	20-35	0	67	20-35	0	64	0.1199
Carbohydrates (E%)	45-65	18[a]	0	45-65	47[b]	0	45-65	58[b]	0	< 0.0001
Proteins (E%)	10-35	0	0	10-35	0	0	10-35	4	0	0.1321

Overall *p*-values refer to Chi-squared tests across the 3 groups. The Bonferroni correction was used to account for multiple comparisons. Same letter indicates no significant difference; Bold indicates overall statistically significant difference, $p<0.05$. EER: estimated energy requirement, calculated with the following formula: 354 x (6.91 x age) + physical activity coefficient x [(9.36 x weight) + (726 x height)], EPR: estimated protein requirement, calculated as 1.1 g/kg of pre-pregnancy weight for pregnant women and 0.8 g/kg of weight for non pregnant women, AMDR: acceptable macronutrient distribution range, AI: adequate intake (AI of fiber was calculated as 14 g per 1000 kcal of total energy intakes).

Supplementary Table S3. Proportion of women below and above recommendations for micronutrients (from food alone) between groups

	Pregnant women (n=55)				Women planning to conceive (n=55)				Women of childbearing age (n=55)		Overall *p*-value (%Below EAR)	Overall *p*-value (%Above UL)
	EAR	**UL**	% Below EAR	% Above UL	**EAR**	**UL**	% Below EAR	% Above UL	% Below EAR	% Above UL		
Vitamin D (IU/day)	400	4000	93	0	400	4000	86	0	96	0	0.1124	-
Iron (mg/day)	22	45	86[a]	0	8.1	45	4[b]	0	6[b]	0	< 0.0001	-
Folate (µg DFE/day)	520	-	56[a]	-	320	-	13[b]	-	18[b]	-	< 0.0001	-
Folic acid (µg/day)	-	1000	-	0	-	1000	-	0	-	0	-	-
Vitamin B_6 (mg/day)	1.6	100	35[a]	0	1.1	100	4[b]	0	11[b]	0	< 0.0001	-
Magnesium (mg/day)	290-300	350	16	-	255-265	350	6	-	16	-	0.1403	-
Vitamin A (µg RAE/day)	550	3000	16	0	500	3000	13	0	16	0	0.8281	-
Zinc (mg/day)	9.5	40	15[a]	0	6.8	40	4[a]	0	4[a]	0	0.0393	-
Calcium (mg/day)	800	2500	13	0	800	2500	13	1.8	27	0	0.0687	0.3656
Vitamin C (mg/day)	70	2000	7[a]	0	60	2000	26[b]	0	11[a,b]	0	0.0166	-
Thiamin (mg/day)	1.2	-	6	-	0.9	-	4	-	2	-	0.5952	-
Vitamin B_{12} (µg/day)	2.2	-	4	-	2.0	-	7	-	11	-	0.3401	-
Riboflavin (mg/day)	1.2	-	2	-	0.9	-	0	-	0	-	0.3656	-
Niacin (mg NE/day)	14	35	0	-	11	35	0	-	0	-	-	-
Phosphorus (mg/day)	580	3500	0	0	580	4000	0	0	0	0	-	-
Sodium (mg/day)	-	2300	-	96[a]	-	2300	-	78[b]	-	84[a,b]	-	0.0185
Manganese (mg/day)	-	11	-	2	-	11	-	0	-	0	-	0.3656
Selenium (µg/day)	49	400	0	0	45	400	0	0	0	0	-	-
Copper (mg/day)	0.8	10	2	0	0.7	10	0	0	4	0	0.3611	-

Overall *p*-values refer to Chi-squared tests across the 3 groups. The Bonferroni correction was used to account for multiple comparisons. Same letter indicates no significant difference; Bold indicates overall statistically significant difference, $p<0.05$. EAR and UL are the same for the 2 cohorts of non pregnant women. When no EAR or UL was established for a nutrient, or when the UL refers only to intakes from supplements, the "-" is used instead of a 0. EAR: estimated average requirement; UL: upper intake limit; DFE: dietary folate equivalent; RAE: retinol activity equivalents; NE: niacin equivalent.

Supplementary Table S4. Proportion of women below and above recommendations for micronutrients (including food sources and supplements) between pregnant women and women planning to conceive

	Pregnant women (n=55)				**Women planning to conceive** (n=55)					
	EAR	**UL**	% Below EAR	% Above UL	**EAR**	**UL**	% Below EAR	% Above UL	***p*-value** (%Below EAR)	***p*-value** (%Above UL)
Vitamin D (IU/day)	400	4000	20	2	400	4000	46	0	0.0044	0.3151
Iron (mg/day)	22	45	11	38	8.1	45	4	7	0.1419	0.0001
Folate (µg DFE/day)	520	-	6	-	320	-	2	-	0.3083	-
Folic acid (µg/day)	-	1000	-	95	-	1000	-	55	-	< 0.0001
Vitamin B_6 (mg/day)	1.6	100	7	0	1.1	100	4	0	0.4011	-
Magnesium (mg/day)	290-300	350	7	0	255-265	350	4	0	0.4011	-
Vitamin A (µg RAE/day)	550	3000	2	0	500	3000	6	0	0.3083	-
Zinc (mg/day)	9.5	40	4	0	6.8	40	2	0	0.5583	-
Calcium (mg/day)	800	2500	2	0	800	2500	9	2	0.0931	0.3151
Vitamin C (mg/day)	70	2000	2	0	60	2000	13	0	0.0276	-
Thiamin (mg/day)	1.2	-	2	-	0.9	-	0	-	0.3151	-
Vitamin B_{12} (µg/day)	2.2	-	2	-	2.0	-	4	-	0.5583	-
Riboflavin (mg/day)	1.2	-	2	-	0.9	-	0	-	0.3151	-
Niacin (mg NE/day)	14	35	0	0	11	35	0	0	-	-
Phosphorus (mg/day)	580	3500	0	0	580	4000	0	0	-	-
Sodium (mg/day)	-	2300	-	96	-	2300	-	78	-	0.0042
Manganese (mg/day)	-	11	-	2	-	11	-	0	-	0.3151
Selenium (µg/day)	49	400	0	0	45	400	0	0	-	-
Copper (mg/day)	0.8	10	2	0	0.7	10	0	0	0.3151	-

p-values refer to Chi-squared tests between the 2 groups. Bold indicates overall statistically significant difference, $p<0.05$. When no EAR or UL was established for a nutrient, the "-" is used instead of a 0. EAR: estimated average requirement; UL: upper intake limit; DFE: dietary folate equivalent; RAE: retinol activity equivalents; NE: niacin equivalent.

Chapitre 9 - Positive attitudes toward weight gain in late pregnancy are associated with healthy eating behaviours

Résumé

Cette étude a examiné les associations entre les attitudes face au gain de poids (GP) et 1) le GP total et 2) les comportements alimentaires au troisième trimestre de grossesse. Les 79 femmes enceintes recrutées ont complété, au troisième trimestre, les versions françaises de la *Pregnancy Weight Gain Attitude Scale*, du *Three-Factor Eating Questionnaire* et de l'*Intuitive Eating Scale-2*. La majorité des femmes excédaient les recommandations de GP de l'Institute of Medicine, mais il n'y avait aucune association entre le GP et les attitudes envers le GP. Des corrélations ont toutefois été observées entre des attitudes négatives face au GP et des comportements alimentaires défavorables, tels que la restriction alimentaire. Ainsi, les femmes ayant une attitude positive à l'égard de la prise de poids semblent avoir des comportements alimentaires plus sains. Une image corporelle plus positive pendant la grossesse pourrait influencer la santé des femmes enceintes, notamment via les comportements alimentaires.

Title page

Title: Positive attitudes toward weight gain in late pregnancy are associated with healthy eating behaviours.

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Keywords: body image; pregnancy; gestational weight gain; eating behaviours; intuitive eating

Abstract

Purpose: This cross-sectional study examined the associations between 3rd trimester attitudes toward weight gain and (1) pre-pregnancy BMI, (2) gestational weight gain (GWG) and (3) eating behaviours assessed in the 3rd trimester.

Methods: Seventy-nine (79) pregnant women completed the French version of the Pregnancy Weight Gain Attitude Scale (PWGAS), the Three-Factor Eating Questionnaire (TFEQ) and the Intuitive Eating Scale-2 (IES-2) in their 3rd trimester. Total GWG was calculated as the difference between the weight recorded before delivery and self-reported pre-pregnancy weight.

Results: Most (55.6%) women gained weight above the Institute of Medicine's (IOM) recommendations, but there was no association between PWGAS scores and total or 3rd trimester GWG. Women with obesity had lower PWGAS total scores compared to women with overweight (3.48 ± 0.6 vs. 3.99 ± 0.3, $p = 0.005$), indicating more negative attitudes in women with obesity vs. overweight. Higher total PWGAS scores were positively correlated with intuitive eating scores ($r = 0.28$, $p < 0.05$), and inversely associated with unfavourable eating behaviours such as dietary restraint ($r = -0.42$, $p < 0.01$).

Conclusion: Women with positive attitudes toward weight gain reported healthier eating behaviours in late pregnancy, which remains to be confirmed in prospective studies. Interventions addressing body image issues during pregnancy may positively influence pregnant women's health, including eating behaviours.

Introduction

During pregnancy, women must cope with substantial physical changes, like gestational weight gain (GWG) that can affect their body image [1], i.e., their internal representation of their appearance, influenced by attitudes, perceptions and behaviours [2]. Although GWG is essential to ensure a healthy pregnancy, the important weight changes that occur during that particular period of time can lead to or amplify already existing negative attitudes toward one's body [3]. In fact, negative body image concerns are highly prevalent in pregnant women [4], which is disturbing considering that such issues can lead to adverse consequences like altered self-esteem, eating disorders, and depressive symptoms [5, 6].

Moreover, studies have shown that higher GWG and pre-pregnancy BMI were associated with negative body image attitudes [4, 7, 8]. For instance, Shloim et al. observed that women with a higher pre-pregnancy BMI have a stronger desire for a smaller body after pregnancy, which represents a negative attitude [8]. Another study showed that greater body dissatisfaction during pregnancy is associated with excessive GWG [4]. Similarly, negative attitudes, such as an increased concern for weight gain, have been associated with excessive GWG [9].

Body image and attitudes toward weight gain could influence eating behaviours, although this has been poorly studied during pregnancy. In the general population, a positive body image was associated with healthier eating behaviours, including intuitive eating, an approach in which what and how much to eat is based on internal signals [10,11,12]. In pregnancy, studies showed that lower body satisfaction predicted disordered eating behaviours [13, 14], whereas in non-pregnant women, intuitive eating was associated with greater body satisfaction [15, 16]. In one study among postpartum women, body satisfaction was found to be associated with a more intuitive diet and less disordered eating attitudes [11]. Moreover, our team previously observed that women with adequate GWG, i.e., within the recommended guidelines [17], had higher intuitive eating scores compared to women with excessive GWG [18], but those results were not examined in association with women's attitudes toward weight gain.

Considering the health implications of body image concerns, such as excessive GWG, and its prevalence among women of higher pre-pregnancy BMI, it appears crucial to further investigate pregnant women's attitudes toward weight gain and their association with eating behaviours. Therefore, this cross-sectional study aimed to examine associations between 3rd trimester attitudes toward weight gain and (1) pre-pregnancy BMI, (2) GWG and (3) eating behaviours assessed in the 3rd trimester. Those variables were evaluated in the third trimester, because it is

at that time that the body is the most different vs. pre-pregnancy. We recognise that attitudes toward weight gain is not interchangeable with body image. Nevertheless, in this study, we considered attitudes toward weight gain to be one of the many aspects of body image, i.e., positive attitudes are associated with a positive body image. We hypothesize that positive attitudes toward weight gain are associated with a normal pre-pregnancy BMI, adequate GWG and healthier eating behaviours.

Materials and methods

Participants

Seventy-nine (79) pregnant women were recruited at the *CHU de Québec – Université Laval* (Québec City, Canada) to participate in the ANGE project (*Apports Nutritionnels Durant la GrossessE*). The study protocol has been previously described [19]. Briefly, the ANGE study used a prospective design to assess diet during pregnancy and examine its associations with, among other variables, nutritional guidelines, eating behaviours and gestational weight gain. Women were excluded if they were younger than 18 years or if they had a severe pre-existing medical condition. The ANGE project was approved by the *CHU de Québec – Université Laval* Research Center's Ethical Committee (Reference number: 2016–2866) and participants gave their informed written consent upon their first on-site visit.

Attitudes toward weight gain

The French version of the Pregnancy Weight Gain Attitude Scale (PWGAS) [20] was used to assess women's attitudes toward weight gain [21]. That version comprises 16 (out of the original 18) items divided into five subscales: (1) fear about weight gain (e.g., "I worry that I may get fat during this pregnancy"), (2) absence of weight gain preoccupation (e.g., "I would gain 40 lb if it meant my baby would be healthier"), (3) positive attitudes about weight gain, (e.g., "I like being able to gain weight for a change"), (4) feeling overwhelmed by weight gain (e.g., "I am embarrassed at how big I have gotten during this pregnancy") and (5) control over weight gain (e.g., "I tried to keep my weight down so I didn't look pregnant earlier on") [21]. The total and five subscale scores are summed and range from 1 (negative) to 5 (positive). The PWGAS scores were inversely correlated with the body shape questionnaire, which assesses body dissatisfaction [21]. The PWGAS was completed by our participants once during the 3rd trimester (range 31.6–36.9 weeks), since the French version of the PWGAS was only validated in that trimester and because body image attitudes may variate throughout pregnancy [3].

Gestational weight gain and pre-pregnancy BMI

Medical records were reviewed to extract body weight values during pregnancy. Those values and the self-reported pre-pregnancy weights were then computed into a weight gain curve, allowing us to derive body weights for each gestational week as well as 3rd trimester GWG. The difference between the last body weight value (≥ 37th week) in medical records and the self-reported pre-pregnancy weight was used to determine total GWG. Participants were classified as having total and 3rd trimester GWG either below, within or above the Institute of Medicine's (IOM) guidelines [17]. Pre-pregnancy BMI was calculated with self-reported weight and measured height.

Eating behaviours

The Three-Factor Eating Questionnaire (TFEQ) contains 51 questions and measures three dietary behaviours: (1) dietary restraint (e.g., "I often stop eating when I am not really full as a conscious means of limiting the amount that I eat"), comprising the rigid and flexible restraint subscales, (2) disinhibition (e.g., "Sometimes things just taste so good that I keep on eating even when I am no longer hungry") comprising the habitual, emotional and situational disinhibition subscales, and (3) susceptibility to hunger (e.g., "I am usually so hungry that I eat more than three times a day"), comprising the internal and external locus subscales [22]. Although it was not developed for that particular population, the TFEQ has been used in pregnant women before [23,24,25]. Participants of the present study completed the TFEQ in each trimester, but only data from the 3rd trimester (range 31.6–34.3 weeks) was used.

Intuitive eating was assessed using the Intuitive Eating Scale-2 (IES-2), a-23-item scale that measures a total intuitive score and four sub-scores: (1) Eating for physical rather than emotional reasons (e.g., "I find other ways to cope with stress and anxiety than by eating"); (2) Unconditional permission to eat (e.g., "I have forbidden foods that I don't allow myself to eat" (reverse-scored)); (3) Reliance on hunger and satiety cues (e.g., "I trust my body to tell me when to stop eating"); and (4) body-food choice congruence (e.g., "I mostly eat foods that give my body energy and stamina") [12]. Participants rate items on a five-point Likert scale ranging from "strongly disagree" to "strongly agree". Total and sub-scores were calculated, with higher scores representing a more intuitive way of eating. Participants completed the IES-2 in each trimester, but only data from the 3rd trimester (range 31.6–34.3 weeks) was used. This questionnaire was validated in French [26].

Statistical analyses

Descriptive analyses were conducted to characterize the population. Nonparametric Wilcoxon Mann–Whitney tests were used to compare PWGAS scores between BMI categories and adherence to GWG guidelines. The Tukey–Kramer adjustment was used to account for multiple comparisons. Spearman correlations were performed to examine associations between PWGAS scores and pre-pregnancy BMI (continuous), 3rd trimester and total GWG (continuous) as well as eating behaviours (IES-2 and TFEQ scores). Since PWGAS scores differed according to pre-pregnancy BMI categories (see Table 2), we adjusted all correlations between PWGAS, GWG, IES-2 and TFEQ scores for pre-pregnancy BMI. Differences were considered statistically significant at $p < 0.05$. Statistical analyses were performed using JMP version 14 (SAS Institute Inc, NC, USA).

Results

The participants' characteristics are presented in Table 1. Most women had a pre-pregnancy BMI within the normal category, were highly educated and had an annual household income of at least 80,000 CAD. Women gained on average 15.2 kg during their pregnancy and the majority gained weight above recommendations in the 3rd trimester (46.0%) and for the whole pregnancy (55.6%).

Body image, pre-pregnancy BMI, and gestational weight gain

Pre-pregnancy BMI was not associated with total PWGAS score ($r = -0.20$; $p = 0.07$). Table 2 presents the differences between the PWGAS scores and pre-pregnancy BMI categories. Compared to women with overweight, women with obesity had lower means for total scores ($p = 0.005$) and "fear about weight gain" sub-score ($p = 0.03$). We also found that women with obesity had lower scores for "control over weight gain" than women of normal weight and with overweight ($p = 0.001$). No significant associations were observed between total PWGAS score and 3rd trimester GWG ($r = 0.14$; $p = 0.26$) or total GWG ($r = 0.19$; $p = 0.15$). No differences were observed in PWGAS scores between women that were below, within or above recommendations of 3rd trimester GWG (mean: 3.62 ± 0.4; 3.91 ± 0.5; 3.79 ± 0.5, respectively, $p = 0.13$) and total GWG (mean: 3.68 ± 0.4; 3.75 ± 0.5; 3.82 ± 0.5, respectively, $p = 0.54$).

Attitudes toward weight gain and eating behaviours

A lower total PWGAS score, demonstrating negative attitudes toward weight gain, was significantly associated with higher dietary restraint (Table 3; $r = -0.42$, $p < 0.01$). The sub-score "fear about weight gain" was also negatively associated with dietary restraint ($r = -0.54$, $p < 0.01$) and

susceptibility to hunger ($r = -0.25$, $p < 0.05$). Similarly, "feeling overwhelmed by weight gain" was negatively correlated with dietary restraint ($r = -0.31$, $p < 0.01$) and susceptibility to hunger ($r = -0.28$, $p < 0.05$).

A higher total PWGAS score was significantly associated with a higher total intuitive eating score ($r = 0.28$; $p < 0.05$) and the "unconditional permission to eat" sub-score ($r = 0.51$; $p < 0.01$). We also found significant correlations between PWGAS sub-scores "fear about weight gain", "feeling overwhelmed by weight gain" and "control over weight gain" and total intuitive eating score.

Discussion

To our knowledge, the associations between pregnant women's attitudes toward weight gain and eating behaviours in late pregnancy have not been studied. Contrary to what was expected, there was no significant association between attitudes toward weight gain and pre-pregnancy BMI or GWG as continuous variables. Nevertheless, we found that women with obesity had a greater fear of gaining weight compared to women with overweight and exerted more control over their weight gain, in comparison to women with normal weight and with overweight. Overall, positive attitudes toward weight gain during pregnancy were associated with healthier eating behaviours and greater intuitive eating behaviours. Our results suggest that women with less positive attitudes, specifically those fearful and overwhelmed by weight gain, reported more restrictive eating behaviours and were more susceptible to hunger.

First, we did not find that attitudes toward weight gain were associated with pre-pregnancy BMI, but we observed differences in PWGAS scores between pre-pregnancy BMI categories, which is concordant with the literature [4, 8]. In previous studies, pregnant women with a higher pre-pregnancy BMI were more likely to be dissatisfied with their bodies, in comparison with women of lower pre-pregnancy BMI [4, 8]. Nevertheless, it seems that the relation between pre-pregnancy BMI and body satisfaction is complex. In fact, our results suggest that the association between attitudes toward weight gain and pre-pregnancy BMI is not linear, as women with overweight had higher PWGAS scores than women with obesity and normal weight. Since women with normal weight are required to gain more weight, their body may change more drastically. Thus, their attitudes toward weight gain in late pregnancy may be more negative than in pre-pregnancy, given the extent to which their body changes. Fox and Yamaguchi obtained similar results, as they reported that women with overweight had a positive change in body image throughout pregnancy, whereas women with normal weight had a negative change [27]. A possible explanation as to why women with overweight had higher PWGAS scores compared to women with obesity could be that

the latter group has a history of feeling judged on the basis of their weight [28]. That feeling might be amplified in pregnancy, since women are frequently weighted by their physician. The non-linear association between weight gain attitudes and pre-pregnancy BMI should be further investigated, especially in a prospective design. Indeed, our cross-sectional design makes it impossible to assess whether pregnant women's attitudes became more negative as pregnancy progressed. Future studies should also investigate prenatal body image issues in relation to postpartum weight retention and postnatal eating behaviours.

Second, our results did not confirm an association between pregnant women's attitudes toward weight gain and their GWG. Some studies have demonstrated that a negative body image was associated with higher GWG [29, 30]. In those studies, women who reported an increased body dissatisfaction were more likely to gain weight excessively [7, 29, 30]. In our study, attitudes toward weight gain were measured once in late pregnancy, thus, we are not able to assess weight gain attitudes as a predictor of GWG. Therefore, future studies should examine, first, how attitudes in early pregnancy may impact GWG while considering eating behaviours, and, second, how early pregnancy GWG might influence women's attitudes and eating behaviours. The findings of Hill et al. highlighted the complex and contradictory nature of the association between body image and GWG [29]. In fact, they found that, at different times during pregnancy, self-rated unattractiveness was associated with both lower and higher GWG [29]. The authors suggested that although feeling unattractive represented a negative attitude, it might drive women to be more cognizant of their weight, thus limiting GWG. This matter should be further investigated, to better understand how to discuss such concerns with pregnant women. Moreover, the discrepancy between our results and those of other studies may be explained by the fact that the questionnaire we used (1) only assessed one aspect of body image (attitudes) and (2) was only assessed once, in late pregnancy. As previously mentioned, our results must be confirmed in larger, prospective studies, since GWG occurs prior to the 3rd trimester, thus, any body image issue may also exert influence in early pregnancy.

Third, we showed that attitudes toward weight gain were associated with eating behaviours. Women with positive attitudes toward weight gain had healthier behaviours like lower levels of dietary restraint. Similarly, one study showed that women dissatisfied with their bodies were more likely to adopt harmful attitudes and behaviours such as the use of restrictive diets [31]. Thus, we could hypothesize that a woman with negative attitudes toward weight gain might adopt unfavourable eating behaviours, such as dietary restraint, to exert greater control over her weight gain. This might be even more prevalent in women with obesity, as have shown previous results of

the ANGE study [32]. However, dietary restraint is not a desirable solution to limit weight gain, because it does not necessarily lead to a reduction in food intake. On the contrary, dietary restraint may lead to deprivation, which could lead to binge eating [33].

Finally, we found that women with positive attitudes toward weight gain had higher intuitive eating scores, especially for the sub-score “unconditional permission to eat”. This would align with our results regarding associations between positive attitudes and lower scores of restrictive eating. To our knowledge, no study examined the association between attitudes toward weight gain and intuitive eating during pregnancy, thus making it impossible to compare our results. Nevertheless, a recent review showed that intuitive eating could help improve body satisfaction by influencing the complex associations between food and eating behaviours [34]. Considering the negative impacts that poor body image and negative attitudes toward weight gain may have, the promotion of intuitive eating during pregnancy may be a promising approach to improve body image among pregnant women. Similarly, interventions that favour body image during pregnancy might help women adopt healthier prenatal eating behaviours.

The originality of this study is based on its assessment of attitudes toward weight gain based on several parameters: BMI, GWG, and eating behaviours, including intuitive eating. However, some limitations must be recognized. Pre-pregnancy weight was self-reported which may have biased pre-pregnancy BMI and GWG estimations. Our small sample size and its lack of representativeness may have reduced our statistical power. Our analyses should be conducted in women of lower income and education level. Finally, the PWGAS was completed in the 3rd trimester as it was only validated in that trimester [21]. Therefore, we were unable to assess the evolution of attitudes toward weight gain. Future studies could opt for another type of questionnaire to assess the evolution of attitudes toward weight gain, such as the body attitudes questionnaire [35].

In conclusion, we showed that women with better attitudes toward weight gain in late pregnancy reported healthier eating behaviours, such as being less dietary restrained and more intuitive. The associations between weight gain attitudes and eating behaviours are consistent with the literature but these results must be confirmed in larger, prospective cohorts. A lot of pregnant women are currently dissatisfied with their body image [4], which could result in adverse psychological outcomes, both during and after pregnancy [36, 37]. Innovative care is needed to help women achieve a satisfying body image and healthy eating behaviours. This study reinforces the need to design and evaluate interventions for pregnant women to maintain or improve their body image during and after pregnancy.

Declarations

Contributions: All authors made substantial contributions to the conception and design of the manuscript, and all critically revised a first draft of the manuscript for important intellectual content. All authors participated in the interpretation of data. All authors gave their approval of the manuscript's final version to be published and, therefore, take public responsibility for the content of the manuscript.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the CHU de Québec – Université Laval research center's ethical committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: All participants gave their informed written consent upon their first on-site visit.

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Tables

Table 1. Study population characteristics (n=79)

Variables	Mean ± SD or n (%)	Range
Age (years)	32.1 ± 3.7	23.7 – 40.3
BMI pre-pregnancy (kg/m²)	25.7 ± 5.8	17.9 – 48.2
Underweight	2 (2.5)	
Normal weight	43 (54.4)	
Overweight	19 (24.1)	
Obese	15 (19.0)	
Ethnicity		
Caucasian	77 (97.5)	
Middle Eastern	1 (1.25)	
Venezuelan	1 (1.25)	
Education		
High school	4 (5.1)	
College	13 (16.5)	
University	62 (78.5)	
Household Annual income (CA $)[a]		
< 60,000	15 (19.2)	
60,000 – 79,999	13 (16.7)	
80,000 – 99,999	17 (21.8)	
≥ 100,000	33 (42.3)	
Total gestational weight gain (kg)[b]	15.2 ± 4.9	3.6 – 35.6
Below recommendations	6 (9.5)	
Within recommendations	22 (34.9)	
Above recommendations	35 (55.6)	
3rd trimester gestational weight gain (kg/week)[b]	0.45 ± 0.24	0.01 – 1.36
Below recommendations	15 (23.8)	
Within recommendations	19 (30.2)	
Above recommendations	29 (46.0)	
3rd trimester: PWGAS total score	3.8 ± 0.5	2.1 – 4.6
Fear about weight gain	3.7 ± 0.7	2.0 – 5.0
Absence of weight gain preoccupation	4.1 ± 1.0	1.0 – 5.0
Positive attitudes about weight gain	3.2 ± 0.7	1.0 – 4.5
Feeling overwhelmed by weight gain	4.3 ± 0.6	2.7 – 5.0
Control over weight gain	3.8 ± 0.7	1.3 – 5.0
3rd trimester: TFEQ score[c]		
Dietary restraint	6.8 ± 4.3	0.0 – 16.0
Disinhibition	5.0 ± 3.0	1.0 – 14.0
Susceptibility to hunger	4.9 ± 3.1	0.0 – 12.0
3rd trimester: IES-2 total score	3.7 ± 0.6	2.3 – 4.7
Unconditional permission to eat	3.4 ± 0.8	1.2 – 5.0
Eating for physiological rather than emotional reasons	3.7 ± 0.8	2.0 – 5.0
Reliance on internal hunger and satiety cues	3.6 ± 0.8	1.0 – 5.0
Body food choice congruence	4.0 ± 0.6	2.3 – 5.0

[a] For n=78; [b] For n=63; [c] For n=73. BMI, body mass index; PWGAS, Pregnancy weight gain attitude scale; IES-2, Intuitive eating scale 2; TFEQ, Three factor eating questionnaire.

Table 2. Attitudes toward weight gain according to pre-pregnancy BMI categories

PWGAS	BMI categories (kg/m²)			*p*-value
	< 25 kg/m²	25-30 kg/m²	≥30 kg/m²	
Total score	3.76 ± 0.5[ab]	3.99 ± 0.3[a]	3.48 ± 0.6[b]	0.005
Fear about weight gain	3.73 ± 0.7[ab]	4.03 ± 0.5[a]	3.42 ± 0.8[b]	0.025
Absence of weight gain preoccupation	4.02 ± 1.0	4.34 ± 0.5	3.80 ± 1.2	0.524
Positive attitudes about weight gain	3.03 ± 0.7	3.47 ± 0.4	3.18 ± 0.8	0.063
Feeling overwhelmed by weight gain	4.35 ± 0.5	4.53 ± 0.5	4.10 ± 0.7	0.138
Control over weight gain	4.02 ± 0.7[a]	3.86 ± 0.5[a]	3.13 ± 0.9[b]	0.001

Data are presented as mean ± SD. Same letter indicates no significant difference. Bold indicates an overall statistically significant difference. BMI: Body mass index; PWGAS: Pregnancy weight gain attitude scale

Table 3. Spearman's correlations between attitudes toward weight gain eating behaviours and intuitive eating in the 3rd trimester

	PWGAS					
	Total score	Fear about weight gain	Absence of weight gain preoccupation	Positive attitudes about weight gain	Feeling overwhelmed by weight gain	Control over weight gain
TFEQ[a]						
Dietary restraint	-0.42**	-0.54**	-0.21†	-0.19	-0.31**	-0.12
Rigid restraint	-0.31**	-0.37**	-0.13	-0.18	-0.24*	-0.05
Flexible restraint	-0.33**	-0.50**	-0.24*	-0.20 †	-0.25*	-0.01
Disinhibition	-0.06	-0.17	0.23	0.00	-0.10	-0.09
Habitual	-0.09	-0.13	0.19	-0.03	-0.13	-0.02
Emotional	-0.08	-0.16	0.09	-0.09	-0.07	-0.13
Situational	-0.04	-0.13	0.21	0.04	-0.12	-0.11
Susceptibility to hunger	-0.20†	-0.25*	0.03	-0.15	-0.28*	-0.01
Internal locus	-0.12	-0.20†	-0.04	-0.05	-0.19	0.06
External locus	-0.22†	-0.23†	0.03	-0.15	-0.32**	-0.12
IES-2[b]						
Total score	0.28*	0.29*	0.05	0.06	0.33**	0.30**
Unconditional permission to eat	0.51**	0.51**	0.17	0.33**	0.35**	0.36**
Eating for physiological rather than emotional reasons	0.15	0.23*	-0.05	-0.01	0.27*	0.14
Reliance on internal hunger and satiety cues	0.16	0.13	0.01	-0.04	0.26*	0.24*
Body food choice congruence	0.00	-0.04	0.04	-0.16	0.04	0.09

[a]For n=73; [b]For n=79; PWGAS: Pregnancy Weight Gain Attitude Scale; TFEQ: Three-Factor Eating Questionnaire; IES-2: Intuitive eating scale-2; *P*-values: †<0.10; * <0.05; **<0.01; All correlations are adjusted for pre-pregnancy BMI.

Chapitre 10 – Longitudinal changes in circulating concentrations of inflammatory markers throughout pregnancy: are there associations with diet and weight status?

Résumé

Cette étude visait à : 1) évaluer les concentrations de leptine, d'adiponectine, d'interleukine-6 (IL-6) et de protéine C-réactive (CRP) durant la grossesse et 2) examiner les associations entre ces concentrations, le score d'adhésion à la diète méditerranéenne (MDS) et l'indice inflammatoire alimentaire (IIA). Les concentrations de leptine, d'adiponectine et d'IL-6 ont été mesurées par ELISA, et la CRP par immunonéphélométrie, chez 79 femmes enceintes. Trois rappels de 24h Web ont été complétés à chaque trimestre et utilisés pour calculer les scores alimentaires. Les concentrations de CRP étaient stables au cours des trimestres, tandis que les concentrations de leptine et d'IL-6 ont augmenté et les concentrations d'adiponectine ont diminué (p <0,001). La seule association significative a été observée au deuxième trimestre entre les concentrations de leptine et le MDS (r=-0,26, p <0,05). La progression de la grossesse elle-même supplante possiblement les associations potentielles entre l'alimentation et l'inflammation.

Title page

Title: Longitudinal changes in circulating concentrations of inflammatory markers throughout pregnancy: are there associations with diet and weight status?

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Keywords: pregnancy, preconception, prenatal nutrition, diet quality, healthy eating index

Abstract

The natural inflammation occurring during pregnancy can, under certain conditions, be associated with adverse pregnancy outcomes. This study aimed to (1) quantify changes in circulating concentrations of leptin, adiponectin, interleukin-6 (IL-6) and C-reactive protein (CRP) across trimesters of pregnancy, according to pre-pregnancy body mass index (ppBMI); and (2) examine the trimester-specific associations between the inflammatory markers' concentrations, a Mediterranean diet score (MDS) and the dietary inflammatory index (DII). We measured leptin, adiponectin and IL-6 by ELISA and CRP by high-sensitivity immunonephelometry, in blood samples from 79 pregnant women (age: 32.1 ± 3.7 years; ppBMI: 25.7 ± 5.8 kg/m^2). Three Web-based 24-h recalls were completed at each trimester and used to compute the MDS and the DII. CRP concentrations remained stable across trimesters, whereas concentrations of leptin and IL-6 increased, and adiponectin concentrations decreased (p <0.001). Changes in leptin and adiponectin concentrations also differed according to ppBMI categories (p <0.05). As for the dietary scores, the only significant association was observed in the second trimester between leptin concentrations and the MDS (r=−0.26, p <0.05). In conclusion, ppBMI and the progression of pregnancy itself probably supplant the potential associations between diet and the inflammation occurring during that period.

Introduction

Pregnancy is associated with a naturally induced low-grade inflammatory state that ensures metabolic adaptation and success of specific physiological processes such as implantation (Romero et al. 2007). That inflammation is important and inevitable, but it must remain under control. Indeed, an amplified and soaring inflammatory state can alter the body's homeostatic control systems. In that case, inflammation has been associated with the development of various pregnancy complications (Lekva et al. 2016; Poston et al. 2011; Villar et al. 2006; Walker 2011). Markers such as the C-reactive protein (CRP), a pro-inflammatory protein, and adipokines such as interleukin-6 (IL-6) and leptin, a satiety signaling hormone secreted by white adipose tissue and the placenta, are all indicative of a low-grade pro-inflammatory state. On the contrary, circulating concentrations of adiponectin, an adipokine associated with glucose level regulation, are inversely associated with inflammation. The evolution of those markers throughout pregnancy has been somewhat documented in the past (Andersson-Hall et al. 2020; Highman et al. 1998; Lepsch et al. 2016; Stokkeland et al. 2019). Still, how this evolution varies according to pre-pregnancy body mass index (ppBMI) has not been investigated yet. Considering that ppBMI and adipose tissue are associated with inflammation, it is possible that the progression of inflammatory markers during pregnancy differs according to ppBMI category (Kac et al. 2011; Ramsay et al. 2002). Moreover, women with lower ppBMI are required to gain more weight during pregnancy (National Research Council 2009b). Is this greater weight gain associated with a larger increase in concentrations of inflammatory markers? Inversely, are women of higher ppBMI predisposed to an altered metabolic profile that could translate into a greater increment in inflammation? These questions remain unanswered.

It is also of interest to investigate specific dietary patterns that may have the potential to attenuate an elevated pro-inflammatory state in pregnancy. In fact, in non-pregnant adults, adherence to dietary patterns such as the Mediterranean diet was found to be inversely associated with concentrations of inflammatory markers (Chrysohoou et al. 2004; Esmaillzadeh et al. 2006; Galland 2010; Panagiotakos et al. 2009; Salas-Salvado et al. 2008). Similarly, a higher adherence to an anti-inflammatory diet, assessed with the dietary inflammatory index (DII), was correlated with lower circulating CRP concentrations and various cytokines (Shin et al. 2019; Shivappa et al. 2017). Similar associations were identified in pregnant women (Sen et al. 2016; Shin et al. 2017; Spadafranca et al. 2018). However, most studies among pregnant women did not analyze trimester-specific associations between diet and inflammatory markers. This is problematic since diet and concentrations of inflammatory markers have been reported to change during pregnancy

(McGowan and McAuliffe 2013; Mor et al. 2011; Moran et al. 2013). It is also important to document trimester-specific associations between diet and inflammation because associations can differ from 1 trimester to another and thus influence the nature, timing and intensity of future nutritional interventions during pregnancy.

Therefore, this study aimed to 1) quantify changes in circulating concentrations of leptin, adiponectin, IL-6 and CRP across trimesters of pregnancy, according to ppBMI; and 2) examine the trimester-specific associations between the inflammatory markers' concentrations, a Mediterranean diet score (MDS) and the DII. We tested the hypothesis that circulating leptin, IL-6 and CRP concentrations increase, whereas circulating adiponectin concentrations decrease across trimesters, and that those fluctuations vary according to ppBMI categories. We also hypothesized that, at each trimester, circulating leptin, IL-6 and CRP concentrations are positively associated with DII and inversely with MDS while associations in opposite directions are found with circulating adiponectin concentrations.

Materials and methods

Participants

The data used in the present study is part of the ANGE (*Apports Nutritionnels durant la GrossessE*) project, a prospective cohort of 86 French-Canadian pregnant women followed from their first to their third trimester of pregnancy. Participants were recruited through e-mail lists and social media ads, from April 2016 to May 2017. The primary aim of that study was the validation of a Web-based 24-h dietary recall (Savard et al. 2018*a*). The ANGE study took place in 2016–2017 in Québec City, Canada, and consisted of trimester-specific, on-site visits as well as self-administered Web questionnaires (described below). Exclusion criteria were multiple pregnancies, previous diagnosis of a severe medical condition (i.e., type 1 or type 2 diabetes, renal or liver disease, inflammatory and autoimmune disorders) and age <18 years. The ANGE study was conducted according to the Declaration of Helsinki guidelines and was approved by the CHU de Québec-Université Laval Research Centre's Ethics Committee (Reference number: 2016-2866). All participants gave their informed written consent.

Measurement of inflammatory markers

Fasting blood samples were drawn at each trimester (9.9–14.7, 20.7–25.3 and 31.6–34.6 gestational weeks) and centrifuged for serum. All serum samples were stored at −80° C for future

analyses. Circulating concentrations of leptin (MilliporeSigma, Billerica, MA, USA.), adiponectin (B-Bridge International Inc., Santa Clara, CA, USA) and IL-6 (R&D Systems Inc., Minneapolis, MN, USA) were measured by commercial ELISA kits, according to the manufacturers' instructions. Circulating concentrations of CRP were measured by high sensitivity immunonephelometry at Québec's Heart and Lung Institute's clinical laboratory (Siemens Medical Solutions USA Inc., Malvern, PA, USA). Since no known specific value or threshold of inflammatory markers' concentration is associated with an acute inflammatory state in pregnancy, values of circulating leptin (n = 1), adiponectin (n = 3), IL-6 (n = 6) and CRP (n = 5) with more than 2 standard deviations compared with the mean were considered as extreme and were excluded from analysis.

Assessment of dietary intakes

Dietary intakes were assessed by self-administered Web-based 24-hour dietary recalls, through the R24W (*Rappel de 24 h Web*) platform. Three dietary recalls were completed in each trimester (8.4–14.0, 19.3–28.3 and 31.9–37.7 gestational weeks). The R24W has been described elsewhere (Jacques et al. 2016; Lafreniere et al. 2018) and validated among pregnant women (Savard et al. 2018a). Briefly, the participants receive an automatically generated e-mail on 3 random days, alerting them they have to report all foods and drinks consumed the day before. The database includes food items that are linked to the 2015 Canadian Nutrient File (Health Canada 2015), therefore enabling automatic extraction of nutritional information. The participants' trimester-specific dietary intakes were published elsewhere (Savard et al. 2018*b*).

Mediterranean diet score

The MDS was calculated on the basis of the Mediterranean pyramid as previously described (Goulet et al. 2003; Willett et al. 1995). Briefly, the Mediterranean diet is characterized by higher intakes of plant-based foods, moderate intakes of fish, poultry and dairy products and lower intakes of red meat and processed foods (Willett et al. 1995). Thus, the food groups included in the MDS are (1) whole grain products, (2) vegetables, (3) fruits, (4) legumes, nuts and seeds, (5) olive oil, olives and margarine made from olive oil, (6) milk and dairy products, (7) fish and seafood, (8) poultry, (9) eggs, (10) sweets and (11) red and processed meats. Mean numbers of daily or weekly servings for each food group were directly obtained from the dietary recalls and compared with the MDS criteria to compute the total MDS and its subscores. (Information regarding the MDS's scoring criteria is presented in a supplementary file; Table S1.[1]) The subscores for whole grains,

[1] Supplementary data are available with the article at https://doi-org.acces.bibl.ulaval.ca/10.1139/apnm-2021-0395

vegetables, fruits, legumes, olive oil and fish are positively correlated with the total score, i.e., a greater consumption of those foods leads to a higher MDS. The subscores for poultry, eggs, sweets and red meats are inversely correlated with the total score. Finally, intakes of milk and dairy have more of an inverse U shape association with the subscore, i.e., the lowest score (0) is attributed to both a lower (<1/day) and higher (>4/day) intake of dairy products.

Dietary inflammatory index

Nutritional data from the 3 dietary recalls were used to compute the DII at each trimester. The DII is a literature-derived, population-based index developed to assess the inflammatory potential properties of a population's diet (Shivappa et al. 2014). The revised version of the DII includes 45 food parameters but as shown in various other studies, it is possible to calculate the DII with less than 45 food parameters (Pieczyńska et al. 2020; Sen et al. 2016; Shin et al. 2017; Yang et al. 2020). In the present study, dietary data was available for the following 29 nutrients: energy, fat, alcohol, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, n-3 fatty acids, n-6 fatty acids, trans fatty acids, cholesterol, carbohydrate, protein, dietary fiber, caffein, vitamins A, B_1, B_2, B_6, B_{12}, C and D, β-carotene, α-tocopherol, folate, iron, magnesium, niacin, selenium and zinc. The development and calculation of the DII is described elsewhere (Shivappa et al. 2014). In brief, each nutrient's intake has to be converted to a Z-score using its corresponding global daily mean and standard deviation provided by the DII database. The resulting Z-scores are converted into a percentile score (between 0 and 1) and then into a centered proportion (between −1 and 1). Finally, all food parameters' centered proportions are multiplied by their respective overall inflammatory effect score, which are then summed to obtain each participant's total DII (Shivappa et al. 2014). Although the DII was not developed for pregnant populations, it has been used in numerous cohorts of pregnant women (McCullough et al. 2017; Moore et al. 2018; Pieczyńska et al. 2020; Sen et al. 2016; Shin et al. 2017; Shivappa et al. 2019; Yang et al. 2020).

Other Variables

Self-reported pre-pregnancy weight and measured height were used to calculate ppBMI. Because only 2 women were underweight, ppBMI was categorized as follows: <25 (normal weight), 25–29.9 (overweight) and ≥30 kg/m^2 (obesity). Total gestational weight gain (GWG) was calculated as the difference between the last weight measured before delivery (≥37th week), retrieved from the participants' medical records (data available for 63 women), and the self-reported pre-pregnancy weight. Finally, information on education level, annual household income and ethnicity was

collected through a self-administered Web-based questionnaire, and weeks of gestation were confirmed by ultrasound in the first trimester.

Statistical Analyses

Means, standard deviations and proportions were used to characterize the study sample. Mixed models for repeated measures were used to examine circulating concentrations of leptin, adiponectin, IL-6 and CRP across trimesters, with ppBMI included as a fixed effect. When the change in concentrations across trimesters was significant, the test slice analysis was used. This analysis performs the repeated measures mixed model for each ppBMI category to identify in which category the change in concentrations was significant. Pearson correlations were used to examine associations between ppBMI, GWG and circulating concentrations of inflammatory markers as well as associations between dietary scores and concentrations of inflammatory markers. Multivariate linear regression analyses were used to identify factors associated with inflammation, in models that included trimesters of pregnancy, ppBMI, weight gain and MDS as independent variables. Inflammatory markers were included in the models as dependent variables either as individual circulating concentration or globally, by using Z-scores. The global inflammatory Z-score corresponded to the averaged Z-scores [(X – mean)/standard deviation] that were computed independently for each inflammatory marker. The residuals of all statistical analyses were normally distributed; therefore, we did not normalize any of our data. Statistical analyses were performed with JMP Pro version 15 (SAS Institute Inc., Cary, NC, USA) and differences were considered statistically significant at $p \leq 0.05$.

Results

Of the 86 pregnant women initially recruited, 7 were lost to follow-up due to miscarriage (n = 3) or a lack of time to devote to the project (n=4). The remaining 79 pregnant women were predominantly French-Canadian, multiparous, aged (mean ± SD) 32.1 ± 3.7 years, had an average ± SD ppBMI of 25.7 ± 5.8 kg/m^2, a university degree and a household income ≥80 000 CAD (Table 1). Mean total MDS, and DII did not vary across trimesters, but the subscore for milk and dairy products, included in the MDS, significantly decreased with time (p=0.02). (Data regarding the MDS and DII are presented in Tables S2 and S3.[1]) That decrease was associated with an increase in milk and dairy servings reported across trimesters (2.5 ± 1.1, 2.7 ± 1.4 and 3.0 ± 1.4 servings per day in

[1] Supplementary data are available with the article at https://doi-org.acces.bibl.ulaval.ca/10.1139/apnm-2021-0395

the first, second and third trimesters; p = 0.002). The DII and MDS were inversely correlated in the second and third trimesters (r =−0.27 and −0.29; p <0.05).

Circulating leptin and IL-6 concentrations increased across trimesters whereas circulating adiponectin and CRP concentrations decreased and remained stable, respectively (Fig. 1). It can also be noted in Fig. 1 that absolute changes in circulating leptin and adiponectin concentrations across trimesters varied according to ppBMI categories (p trimester*ppBMI < 0.05). Circulating leptin increased significantly in women with a ppBMI ≥30 kg/m^2 (test slice p-value <0.0001), but not in women of lower ppBMI. Regarding adiponectin, circulating concentrations decreased significantly in all ppBMI categories (test slice p-values <0.01). The increase in circulating concentrations of IL-6 was only significant among women with a ppBMI <25 kg/m^2 (test slice p-value <0.001).

In all trimesters, circulating leptin, IL-6 and CRP concentrations were positively associated with ppBMI (Table 2). Circulating adiponectin concentrations were inversely correlated with ppBMI in the first and second trimesters only. Total GWG was positively correlated with circulating concentrations of leptin in the second and third trimesters, and inversely correlated with circulating concentrations of IL-6 and CRP in the second trimester (Table 2). No associations were observed between total GWG and circulating concentrations of adiponectin.

In the first trimester, the MDS was inversely associated with circulating leptin concentrations, but that association was non-significant after adjustment for ppBMI (Table 3). In the second trimester, the MDS was inversely correlated with circulating leptin concentrations, but only after adjustment for ppBMI. The DII was not correlated with any of the inflammatory markers; therefore, it was not included in the regression models (see below).

Finally, in 5 distinct regression models, ppBMI was significantly associated with all markers' circulating concentrations and overall inflammation status (Fig. 2). Pregnancy itself, as represented by advancing trimesters, was also significantly associated with overall inflammation status and circulating concentrations of inflammatory markers, with the exception of CRP. The MDS and the weight gain were only associated with circulating leptin concentrations.

Discussion

This study assessed the changes in circulating leptin, adiponectin, IL-6 and CRP concentrations across trimesters of pregnancy, according to ppBMI. We observed a significant increase in

circulating leptin and IL-6 and a significant decrease in circulating adiponectin concentrations across trimesters, which is in line with the progression of an inflammatory state during pregnancy. However, circulating CRP concentrations remained stable. Changes in circulating leptin and adiponectin concentrations across trimesters varied according to ppBMI, which is in accordance with our initial hypotheses. Furthermore, we believe this study is the first to examine trimester-specific associations between circulating concentrations of leptin, adiponectin, IL-6 and CRP and inflammation-related dietary scores. Overall, there was almost no association between the dietary scores and the concentrations of inflammatory markers. The regression analyses performed suggest that inflammation is strongly associated with ppBMI and maybe the pregnancy itself, which may supplant potential associations between inflammation and dietary variables.

First, the observed changes in circulating leptin concentrations are in accordance with the current literature (Masuzaki et al. 1997; Perez-Perez et al. 2018). Further analyses in our sample showed that leptin concentrations only increased significantly among women with obesity. Misra and Trudeau obtained contrasting results and found that the rate at which leptin concentrations increased was greater in women with a normal weight vs. overweight or obesity (Misra and Trudeau 2011). They hypothesized that the lower rate in leptin increase in women with obesity could be explained by a lower weight gain. Still, in the present study, a lower weight gain in women with obesity did not translate into a lower rate in leptin increase. It is possible that in a physiological context such as pregnancy, in which energy and nutrient intakes need to be increased and transferred to the fetus, leptin production is regulated by other mechanisms than those predicted by ppBMI and GWG (Brunton and Russell 2010; Hauguel-de Mouzon et al. 2006). Moreover, any given circulating leptin concentration is hard to interpret without knowing the extent of leptin resistance, which occurs during pregnancy and also varies with obesity (Augustine et al. 2008). Furthermore, other factors like placental leptin production, efficacy of leptin production by the adipose tissue as well as pre-pregnancy levels of adipose tissue may differ between ppBMI categories, which might partly explain our results (Franco-Sena et al. 2015; Tessier et al. 2013). Additional studies are necessary to better understand the complex physiology between circulating leptin concentrations and GWG across ppBMI categories.

Second, we found that circulating adiponectin concentrations decreased across trimesters, similarly to what was reported in previous studies (Catalano et al. 2006; Lekva et al. 2017). The decrease in adiponectin was significant in all ppBMI categories, which differs from the results of Andersson-Hall et al., who found that pregnant women of lower ppBMI had a more pronounced decrease in circulating adiponectin concentrations (Andersson-Hall et al. 2020). It could be

hypothesized that since an increase in fat mass leads to the downregulation of adiponectin, the decrease in circulating adiponectin concentrations may be more pronounced in women of lower ppBMI, as they are required to gain more weight (Mazaki-Tovi et al. 2005; National Research Council 2009b). In the present study, the decrease in adiponectin also appears to be more pronounced, although not significantly, among women with a ppBMI <25 kg/m^2 (Fig. 2). However, we found no associations between total GWG and circulating adiponectin concentrations. Similarly to what we observed with leptin concentrations and GWG, it is possible that the new adipose tissue gained during pregnancy becomes less and less functional as pregnancy progresses. This dysfunction could be reflected in an altered production or downregulation of adiponectin (Simjak et al. 2018; Svensson et al. 2016). These hypotheses should however be confirmed in future studies. It is also important to note that total GWG comprises several components other than the gain in adipose tissue, namely the development of the placenta, an increase in total body water, fat-free mass, blood, amniotic fluid, etc. (National Research Council 2009a). These tissues are not all implicated in the regulation of adiponectin. Nevertheless, the associations between GWG, ppBMI and circulating adiponectin concentrations should be further investigated.

Third, circulating IL-6 concentrations increased across trimesters, but only in women with a ppBMI <25 kg/m^2, whereas circulating CRP concentrations remained stable for all ppBMI categories. The patterns of circulating IL-6 concentrations in pregnancy are still unclear, as both increases and decreases have been reported (Holtan et al. 2015; Stokkeland et al. 2019; Vassiliadis et al. 1998). Those conflicting results might be due to differences in sample size and measurement methods as well as by the fact that, in the present study, women who developed pregnancy complications such as gestational diabetes (n = 10) and hypertension (n = 8) were not excluded. Such complications are generally diagnosed later in pregnancy and are associated with a greater inflammatory state, which could explain the increase in circulating IL-6 concentrations we observed (Lekva et al. 2016; Villar et al. 2006; Walker 2011). In fact, Stokkeland et al., who observed a decrease in IL-6 concentrations, excluded women with previous or current disease from their analyses (Stokkeland et al. 2019). Still, in the present study, the overall increase in circulating IL-6 concentrations remained significant even after the exclusion of women who developed gestational diabetes and/or hypertension (data not shown). The evolution of CRP concentrations throughout pregnancy also remains unclear in the current literature. Belo et al. observed, similarly to the present study, a stability in CRP concentrations, in their prospective cohort of 23 Portuguese pregnant women (Belo et al. 2005). Furthermore, in the present study, advancing trimesters of pregnancy were significantly associated with all inflammatory markers' concentrations, except for CRP, which is in line with the

stability of that marker across trimesters. This stability may however be explained by ours and Belo et al.'s smaller samples. Indeed, other studies with greater samples observed an increase in circulating CRP concentrations, from the 10th to the 24th week of pregnancy (Stokkeland et al. 2019) as well as from the first to the third trimester (Larsson et al. 2008; Skarżyńska et al. 2018). Other important factors like physical activity, anxiety and depression were reported to be associated with inflammation in non-pregnant cohorts, and it is possible that it might have affected our sample's circulating CRP and IL-6 concentrations (Naude et al. 2018; Ostrowski et al. 1998; Wedell-Neergaard et al. 2019; Werneck et al. 2020). Future studies should consider those factors in the assessment of inflammation during pregnancy.

Fourth, contrary to our hypothesis, dietary scores were very poorly associated with inflammatory markers. As such, the only significant association observed in our multivariable regression analyses was between the MDS and circulating leptin concentrations. The literature is limited regarding the potential effect of the Mediterranean diet on circulating leptin concentrations, but some studies observed lower leptin concentrations among pregnant women with lower intakes or lower blood levels of saturated fatty acids and with higher intakes of fibers (Lepsch et al. 2016; Vähämiko et al. 2013). Although those studies did not assess their participants' adherence to the Mediterranean diet, the latter is associated with lower intakes of foods that are high in saturated fatty acids and with higher intakes of foods rich in fibers. Finally, a recent Brazilian study by Alves-Santos et al. found that a greater adherence to a 'Western' dietary pattern, characterized by higher intakes of fast food, snacks and processed meats, for example, was associated with higher circulating leptin concentrations in 173 pregnant women (Alves-Santos et al. 2018). Their results are comparable to ours, since the 'Western' dietary pattern that they identified could be considered as the Mediterranean diet's opposite.

Fifth, the DII was not associated with any of the 4 inflammatory markers. Our results are in contrast with previous studies among pregnant women (Moore et al. 2018; Sen et al. 2016; Shivappa et al. 2017) and with the fact that a pro-inflammatory diet should be associated with higher concentrations of inflammatory markers. Still, other studies found few or no association between the DII and concentrations of CRP and IL-6 among pregnant women (McCullough et al. 2017; Pieczyńska et al. 2020). Pregnancy-induced inflammation most certainly differs from the systemic inflammation of non-pregnant populations. Therefore, the associations between the DII and inflammatory markers observed in the general population may not always be replicated in pregnancy. Furthermore, according to the regression analyses of the present study, pregnancy-induced inflammation appears to be mostly associated with ppBMI and the progression of pregnancy itself.

Overall, our results regarding associations between diet and inflammation are inconsistent, which is in line with the observations of a recent systematic review (Yeh et al. 2021). Most of the 17 studies included in that review showed associations between pro-inflammatory markers and dietary patterns like the pro-/anti-inflammatory diet and the Mediterranean diet. However, the 3 studies with a more rigorous methodology that were reviewed, including 1 cross-sectional and 2 intervention studies, found no significant associations.

Finally, the present study has various strengths, namely the assessment of trimester-specific dietary intakes and the measurement of 4 distinct inflammatory markers. The use of a validated Web-based 24-h recall provided detailed information on our sample's dietary intakes. It is also worth mentioning that the DII may have some limitations regarding pregnancy, since the DII's global database is not based on intakes of pregnant populations. Moreover, no information was found regarding the inclusion of supplemental intakes in the calculation of the DII. Most of our sample were taking prenatal supplements (Savard et al. 2018b), thus, those additional nutrient intakes may have altered some of our analyses. We did not collect dietary data prior to pregnancy, thus we were not able to, for example, explore the associations between pre-pregnancy diet and inflammatory status in the first trimester. In a similar way, our study does not include fetal and neonatal data, which would have been interesting to study in association with concentrations of inflammatory markers. Furthermore, our small sample size certainly impacted the statistical power of some of our analyses. Still, posteriori analyses revealed that our sample size of n = 79 provided 65% power to detect a correlation of $r = -0.26$ at $p < 0.05$ between the MDS and circulating leptin concentrations in the second trimester. As previously mentioned, the present study used data from an existing cohort whose primary objective was not to study associations between diet and inflammation. Our study sample was fairly homogenous in terms of ethnicity and socioeconomic status, which limits the generalizability of our findings.

In conclusion, the gradual increase in circulating leptin and decrease in adiponectin concentrations are in line with the physiological inflammation settling in during pregnancy, but other studies are necessary to understand how ppBMI influences their evolution. Further prospective studies are also needed to better understand the fluctuations of IL-6 and CRP in pregnancy. Very few associations were observed between diet and inflammation, and the impact of ppBMI and pregnancy itself appeared to surpass the effect that diet can have on inflammatory markers during that period. Our results should however be confirmed in larger samples with the consideration of other factors that can influence inflammation (physical activity level, stress, etc.). Still, diet remains an important factor to consider in the prenatal period, as a greater diet quality is associated with a

healthier pre-pregnancy weight status, which can positively influence maternal and neonatal outcomes. It is also possible that prenatal anti-inflammatory dietary patterns, through pathways other than inflammation, are beneficial for various health outcomes.

Declarations

Competing interests statement: André Tchernof received research funding from Johnson & Johnson, Medtronic and Bodynov for studies unrelated to this manuscript, in addition to consulting fees from Novo Nordisk and Bausch Health. All the remaining authors declare they have no competing interests.

Contributors' statement: A.-S.M., A.V., A.T., S.L. and C.-S. designed research; A.-S.M., C.S., and A.-S.P. conducted research; C.S, A.-S.P., M.G. and N.L. analyzed data; and C.S. wrote the first draft of the manuscript. A.-S.M. had primary responsibility for final content. All authors made substantial contributions to the conception and design of the manuscript, and all critically revised a first draft of the manuscript for important intellectual content. Finally, all authors read and approved the final manuscript.

Data availability statement: The datasets generated and/or analyzed during the present study are available from the corresponding author upon reasonable request.

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Tables

Table 1. Baseline characteristics of pregnant women in the ANGE cohort (n=79)

Age, years	32.1 ± 3.7
Gestational age at enrollment, weeks	9.3 ± 0.7
Parity[a]	
0	28 (35.4)
≥1	51 (64.6)
Pre-pregnancy body mass index, kg/m^2	25.7 ± 5.8
Underweight	2 (2.5)
Normal weight	43 (54.4)
Overweight	19 (24.1)
Obesity	15 (19.0)
Total gestational weight gain, kg[b]	15.2 ± 4.9
Ethnicity	
Caucasian	77 (97.5)
Hispanic	1 (1.3)
Arab	1 (1.3)
Education	
High school	4 (5.0)
College[c]	13 (16.5)
University	62 (78.5)
Annual household income	
< 60,000 CAD	15 (19.0)
60,000-79,999 CAD	13 (16.5)
80,000-99,999 CAD	17 (21.5)
≥ 100,000 CAD	33 (41.8)
Income not disclosed	1 (1.2)

Note: Values are mean ± SD or n (%).

[a]Refers to the number of children previously born, excluding the current pregnancy.

[b]For n=63, the other 16 participants' medical records had no documented body weight value ≥37 weeks.

[c]In Québec, college refers to a degree obtained after high school and before university.

Table 2. Correlations between pre-pregnancy BMI or total GWG and trimester-specific circulating concentrations of leptin, adiponectin, interleukin-6 and C-reactive protein

	First trimester	Second trimester	Third trimester
		Pre-pregnancy BMI	
Leptin, n=78	**0,75*** **	**0,75*** **	**0,74*** **
Adiponectin, n=76	**-0,33** **	**-0,35** **	-0,18
IL-6, n=73	**0,48*** **	**0,28***	**0.31** **
CRP, n=74	**0,30** **	**0,56*** **	**0,41** **
		Total GWG	
Leptin, n=63	0.20	**0.45** **	**0.30***
Adiponectin, n=61	0.01	0.11	-0.01
IL-6, n=57	-0.11	**-0.27***	0.09
CRP, n=59	-0.14	**-0.30***	0.01

Note: Values are presented as Pearson correlation coefficients (*r*). For the total GWG correlations, all coefficients are adjusted for ppBMI. CRP, C-reactive protein; GWG, gestational weight gain; IL-6, interleukin-6; ppBMI, pre-pregnancy body mass index. * p <0.05, ** p <0.01, *** p <0.0001.

Table 3. Correlations between trimester-specific circulating concentrations of leptin, adiponectin, IL-6 and CRP and dietary scores

	Leptin, n=78		Adiponectin, n=76		IL-6, n=73		CRP, n=74	
	r	r_{adj}	r	r_{adj}	r	r_{adj}	r	r_{adj}
First trimester								
MDS	**-0.26***	-0.09	0.10	0.02	-0.05	0.04	-0.10	0.06
DII	0.01	0.21	-0.02	-0.04	-0.22	-0.20	-0.02	0.06
Second trimester								
MDS	-0.19	**-0.26***	-0.12	-0.16	-0.10	-0.09	-0.05	-0.004
DII	-0.01	-0.07	0.05	0.08	-0.05	-0.06	0.17	0.15
Third trimester								
MDS	-0.12	-0.20	-0.12	-0.11	0.22	0.21	0.03	0.02
DII	0.07	0.10	0.10	0.11	-0.03	-0.03	0.06	0.05

Note: Values are presented as Pearson correlation coefficients, raw (*r*) or adjusted for ppBMI (r_{adj}). Correlation analyses were performed between circulating concentrations and dietary scores measured in the same trimesters (e.g., first trimester leptin concentrations with first trimester MDS). Mean scores were calculated using the mean intakes from the 9 dietary recalls from the 3 trimesters. CRP, C-reactive protein; DII, dietary inflammatory index; IL-6, interleukin-6; MDS, Mediterranean diet score; ppBMI, pre-pregnancy body mass index. * p <0.05.

Figures

Figure 1. Circulating concentrations of leptin, adiponectin, IL-6 and CRP across trimesters, according to ppBMI categories. Legend. *p*-values refer to the mixed models for repeated measures used to examine the evolution of trimester-specific circulating concentrations of (A) leptin (n=78), (B) adiponectin (n=76), (C) IL-6 (n=73) and (D) CRP (n=74) according to ppBMI. CRP, C-reactive protein; IL-6, interleukin-6; ppBMI, pre-pregnancy body mass index.

Figure 2. Standardized regression coefficients of independent predictors of circulating concentrations of (A) leptin, (B) adiponectin, (C) IL-6, (D) CRP and (E) overall inflammation status. Legend. Trimester-specific circulating concentrations of (A) leptin (n = 78), (B) adiponectin (n = 76), (C) IL-6 (n = 73), (D) CRP (n = 74) and (E) overall inflammation status (n = 66) were entered as dependent variables. Trimester, ppBMI, weight gain (kg) and MDS were entered as independent variables. The overall inflammation status corresponds to the averaged Z-scores [(X – mean) / standard deviation] computed independently for each inflammatory marker. Confidence intervals not crossing the zero line indicate statistical significance (p <0.05). CI, confidence interval; CRP, C-reactive protein; IL-6, interleukin-6; MDS, Mediterranean diet score; ppBMI, pre pregnancy body mass index.

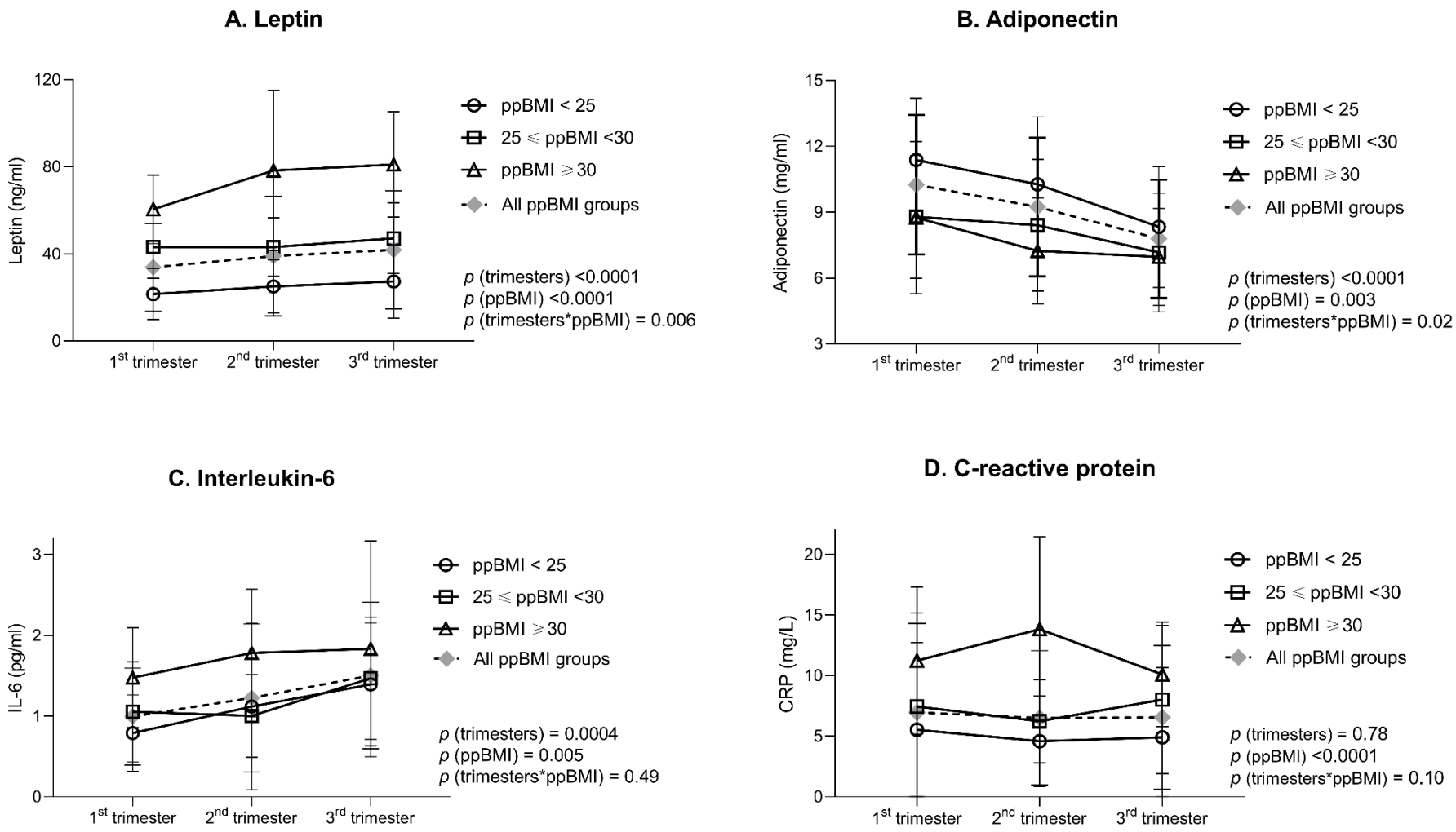

Figure 1. Circulating concentrations of leptin, adiponectin, IL-6 and CRP across trimesters, according to ppBMI categories

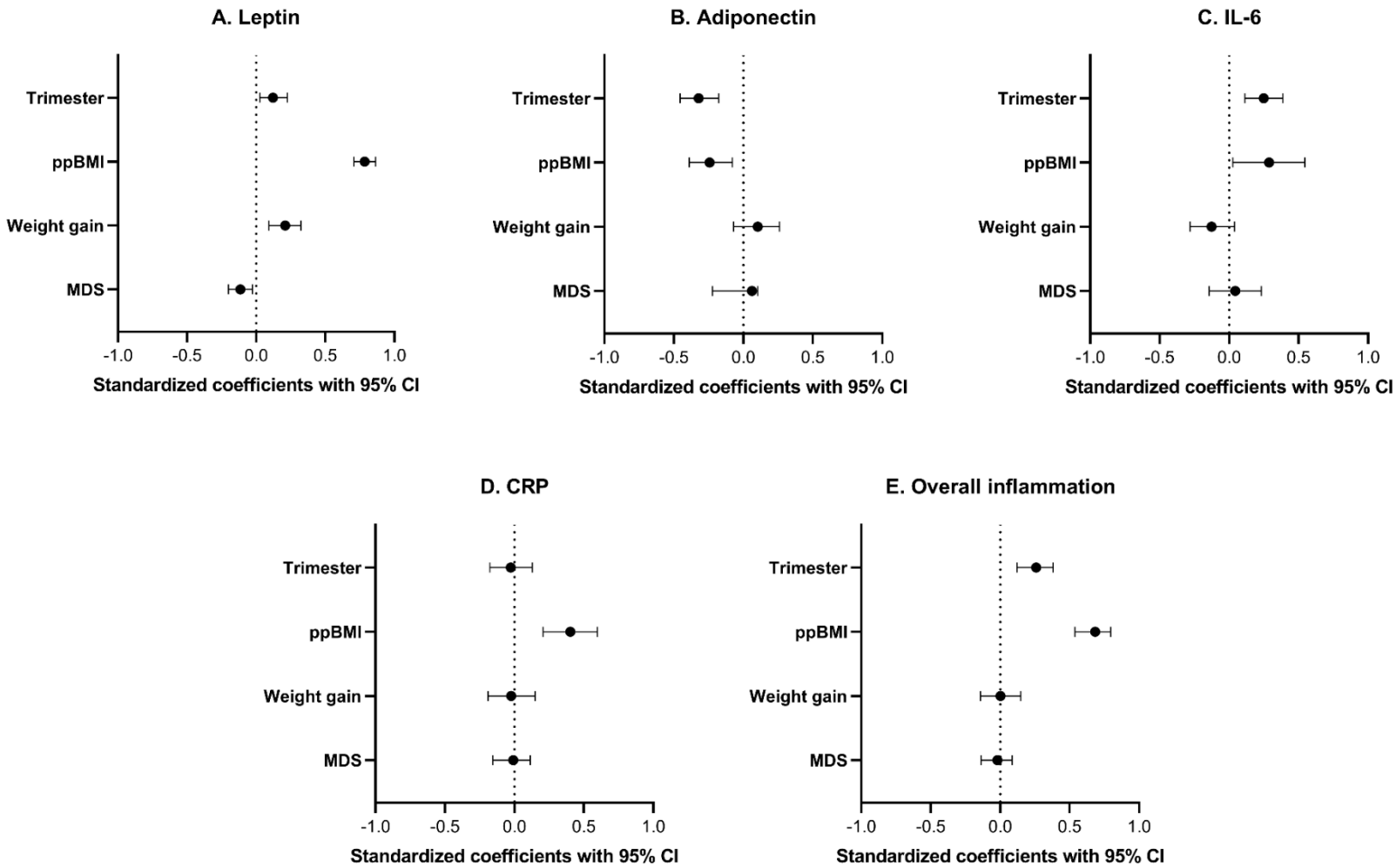

Figure 2. Standardized regression coefficients of independent predictors of circulating concentrations of leptin, adiponectin, IL-6, CRP and overall inflammation status

Supplementary material

Table S1. Scoring criteria for the Mediterranean diet score

Components	Score (Number of servings per day or week)				
	0	**1**	**2**	**3**	**4**
Whole grain products[1]	<1/day	1-2/day	3-4/day	5-6/day	≥7/day
Vegetables[2]	<1/day	1/day	2/day	3/day	≥4/day
Fruits[3]	<1/day	1/day	2/day	3/day	≥4/day
Legumes, nuts and seed[4]	<0.5/day	0.5/day	1/day	2/day	>2/day
Olive oil, olives and olive oil margarine[5]	<1/day	1/day	2/day	3/day	≥4/day
Milk and dairy[6]	<1 or > 4/day	4/day	-	1/day	2-3/day
Fish and seafood (not breaded)	0	<1/week	1/week	2/week	≥3/week
Poultry (not breaded)	0	<1/week	1 or ≥4/week	2/week	3/week
Eggs	≥7/week	-	5-6/week	-	0-4/week
Sweets[7]	≥7/week	5-6/week	3-4/week	1-2/week	<1/week
Red meat/processed meat[8]	≥7/week	5-6/week	3-4/week	1-2/week	<1/week

[1]For grain products, a serving was equivalent to 1 slice of whole wheat bread, 125 ml of whole wheat pasta, rice or couscous or 30 g of cereal. A maximum of 1 point was attributed to intakes of refined grain products (e.g., white bread).
[2]For vegetables, a serving was equivalent to 125 ml or one medium vegetable. A maximum of 1 point was attributed to vegetable juice intake.
[3]For fruits, a serving was equivalent to half a cup or one medium fruit. A maximum of 1 point was attributed for fruit juice intake.
[4]For legumes, nuts and seeds, a serving was equivalent to 125 ml of legumes, 60 ml of nuts/seeds or 100 g of tofu.
[5]For olive oil, 1 point was attributed for each using (regardless of quantity) of this oil. A maximum of 1 point was attributed for the consumption of canola/olive oil margarine.
[6]For milk and dairy products, a serving was equivalent to 250 ml of milk or enriched soy beverages, 50 g of cheese or 175 g of yogurt.
[7]For sweets, a serving was equivalent to 1/12 of cake, 1/6 of pie or 1 regular chocolate bar, for example.
[8]For red meat/processed meat, poultry, or fish, a serving may vary from 50 to 100 g.

Table S2. Mean Mediterranean diet scores across trimesters

	First trimester	Second trimester	Third trimester	*p*-value
Total score (/44)	18.4 ± 4.3	18.1 ± 5.1	17.8 ± 4.6	0.56
Whole grain products (/4)	1.9 ± 0.9	2.1 ± 1.2	2.2 ± 1.3	0.34
Vegetables (/4)	2.4 ± 1.2	2.2 ± 1.1	2.2 ± 1.2	0.40
Fruits (/4)	1.9 ± 1.2	1.8 ± 1.3	1.7 ± 1.1	0.62
Legumes, nuts and seeds (/4)	0.5 ± 0.7	0.5 ± 0.8	0.6 ± 0.8	0.47
Olive oil, olives and olive oil margarine (/4)	0.1 ± 0.2	0.1 ± 0.3	0.04 ± 0.19	0.78
Milk and dairy (/4)	2.6 ± 1.4	2.1 ± 1.6	1.9 ± 1.6	**0.02**
Fish and seafood (not breaded) (/4)	1.4 ± 1.7	1.6 ± 1.7	1.3 ± 1.7	0.33
Poultry (not breaded) (/4)	1.9 ± 1.1	1.7 ± 1.2	1.6 ± 1.4	0.17
Eggs (/4)	3.3 ± 1.5	3.5 ± 1.2	3.5 ± 1.2	0.59
Sweets (/4)	1.1 ± 1.4	1.5 ± 1.7	1.3 ± 1.5	0.21
Red meat/processed meat (/4)	1.3 ± 1.4	1.1 ± 1.4	1.4 ± 1.4	0.31

Values are mean ± SD, n=79. *p*-values refer to repeated measures analyses of variance performed to compare mean scores across trimesters.

Table S3. Trimester-specific mean and median values of the dietary inflammatory index

	1st trimester	2nd trimester	3rd trimester	*p*-value
DII				
Mean ± SD	-1.23 ± 1.10	-1.12 ± 1.13	-0.98 ± 1.16	0.16
Median (IQR)	-1.16 (-2.12, -0.45)	-1.24 (-1.86, -0.45)	-0.97 (-1.76, 0.002)	

Values are mean ± SD or median (interquartile range), n=79. *p*-values refer to repeated measures analyses of variance performed to compare mean DII across trimesters. DII, dietary inflammatory index.

Conclusion

L'importance de la nutrition au cours des différentes périodes de la grossesse est indéniable. Cependant, la prévalence considérable de certaines conditions liées aux variables alimentaires, comme une anémie ferriprive et un gain de poids gestationnel inadéquat [73, 74, 116], suggère que les habitudes alimentaires des femmes enceintes ne sont pas optimales. Ainsi, l'objectif général de ce projet de doctorat visait à caractériser prospectivement les apports alimentaires durant la grossesse, en comparaison avec les recommandations, et à identifier les variables associées à la qualité alimentaire dans un échantillon de femmes enceintes québécoises. Les articles originaux inclus dans cette thèse mettent en évidence les écarts existants entre les apports nutritionnels de ces femmes et les recommandations en vigueur. De plus, les résultats de cette thèse contribueront à l'avancement des connaissances en ce qui concerne les associations entre l'alimentation et certaines variables sociodémographiques comportementales et métaboliques durant la grossesse. Les pages qui suivent constituent la conclusion générale de cette thèse, qui inclut un résumé puis une discussion des principaux résultats présentés aux chapitres 4 à 10, ainsi que plusieurs perspectives à envisager.

D'abord, la revue systématique présentée au chapitre 4 soutient notre hypothèse suggérant que les preuves scientifiques rapportent une augmentation de la dépense énergétique au cours de la grossesse, mais que la valeur de cette augmentation est variable et généralement inférieure aux recommandations touchant l'apport énergétique durant la grossesse (environ 150-200 kcal de moins). Les résultats de notre revue ne nous permettent toutefois pas de conclure que les recommandations actuelles sont trop élevées ou bien de statuer sur la quantité d'énergie supplémentaire qui est nécessaire au maintien du métabolisme de base de la mère et au développement de nouveaux tissus. En fait, comme discuté au chapitre 4, les apports énergétiques des femmes enceintes ne devraient pas être égaux à leur dépense énergétique, puisqu'un bilan énergétique positif est nécessaire au gain de poids gestationnel. Ainsi, la comparaison des apports énergétiques recommandés aux mesures de dépense énergétique constitue une méthode d'estimation qui est sujette à l'erreur. Néanmoins, il demeure pertinent de s'intéresser aux données qui montrent une faible augmentation ou une stabilité de la dépense énergétique totale ou au repos, puisque cela est en contradiction avec la notion d'augmentation de la demande métabolique en contexte gestationnel [48]. À cet effet, Pontzer et al. ont effectué une analyse secondaire de données sur la dépense énergétique totale au cours du cycle de la vie et ont observé, après un ajustement pour les masses grasse et maigre, une stabilité dans la dépense énergétique des

femmes adultes, et ce, même durant la période de la grossesse [301]. Ces observations vont de pair avec la stabilité des apports énergétiques que nous, et d'autres auteurs, avons observée au cours des trimestres de la grossesse [66]. De plus, nos résultats et ceux de Pontzer et al. pourraient être interprétés comme une adaptation possible du métabolisme de base des femmes enceintes; il est possible que celui-ci s'adapte, à la baisse, en prévision des nombreux changements métaboliques qui nécessiteront une grande quantité d'énergie plus tard durant la grossesse. En fait, une revue de la littérature publiée en 1994 suggérait déjà que, chez les femmes enceintes dont les réserves énergétiques étaient limitées (ex. femmes malnutries), des adaptations au niveau du métabolisme pourraient s'installer dans le but d'épargner de l'énergie et assurer la croissance du fœtus [302]. Néanmoins, ces hypothèses mériteraient d'être étudiées davantage, idéalement en association avec les apports énergétiques et le gain de poids. Ces analyses pourraient être envisagées par notre équipe de recherche, dans le cadre d'une future étude de cohorte.

Dans un même ordre d'idées, il convient de mentionner que la *National Academy of Sciences*, qui publie les ANREF, a récemment entrepris un processus de recensement des études en lien avec les besoins énergétiques des populations aux différents cycles de la vie, dont la grossesse [303]. Le comité d'experts responsable de ce projet devra, entre autres, publier un rapport qui inclura, si applicable, une mise à jour du BÉE. Il sera donc intéressant de voir si les recommandations énergétiques pour les femmes enceintes seront modifiées à la baisse et/ou ajustées selon le statut pondéral prégrossesse, considérant la prévalence élevée de gain de poids gestationnel excessif en Amérique du Nord. À ce sujet, et comme mentionné au chapitre 4, certains auteurs ont suggéré que les femmes enceintes présentant un surpoids ou une obésité prégrossesse auraient besoin de moins de calories supplémentaires, et même d'une restriction calorique, comparativement aux 340 et 452 kcal recommandées à toutes les femmes enceintes aux deuxième et troisième trimestres [304-306]. Ces suggestions devraient être interprétées avec prudence, car même si les femmes enceintes présentant un surpoids ou une obésité soient, proportionnellement, plus nombreuses à excéder les recommandations de gain de poids gestationnel, une restriction calorique visant un maintien ou une perte de poids durant la grossesse n'est pas conseillée et pourrait, comme cela a été mentionné au chapitre 1, être associée à un faible poids à la naissance [67, 72, 307]. Certes, comme le montrent les données présentées au chapitre 5, la presque totalité des femmes enceintes de la cohorte ANGE ont rapporté des apports énergétiques qui étaient inférieurs à leur BÉE, aux deuxième et troisième trimestres de grossesse. Ces résultats n'indiquent probablement pas une restriction consciente de l'apport énergétique de la part des femmes enceintes, mais ils suggèrent que les recommandations touchant l'apport énergétique durant la

grossesse sont peut-être trop élevées. Ainsi, et selon les résultats des chapitres 4 et 5 de cette thèse, la réflexion qu'a entreprise la *National Academy of Sciences* au sujet des besoins énergétiques des populations au cours des cycles de la vie est justifiée.

Ensuite, contrairement aux apports énergétiques inférieurs aux besoins observés aux deuxième et troisième trimestres, les résultats présentés au chapitre 5 montrent qu'au premier trimestre, la majorité des femmes rapportent des apports en énergie supérieurs à leurs besoins. Il est possible que cet excès énergétique était déjà présent en préconception, mais il se peut également que cela reflète une augmentation de la prise alimentaire, de la préconception au premier trimestre. À cet effet, certains auteurs ont suggéré que la faim des femmes pouvait augmenter dès les premières semaines de la grossesse pour induire une augmentation de la prise alimentaire, en prévision de la future demande métabolique associée à la grossesse [308-310]. Il a aussi été suggéré que l'augmentation des concentrations de progestérone, dès le début de la grossesse, pouvait entraîner une plus grande sensation de faim chez les femmes enceintes [311]. Ces hypothèses n'ont pas encore été confirmées au sein de cohortes prospectives, mais des études longitudinales ont tout de même observé une augmentation des apports énergétiques, de la préconception à la première moitié de la grossesse, comme cela a été discuté au chapitre 8 [57, 209, 312]. Puis, parallèlement à ces observations, nous avons rapporté qu'un sous-échantillon de femmes enceintes de la cohorte ANGE avait des apports énergétiques plus élevés, au premier trimestre, que ceux d'un groupe de femmes non enceintes, mais planifiant le devenir. Ces résultats suggèrent une prise alimentaire plus importante durant le premier trimestre, en comparaison avec la préconception, mais ils ne confirment pas l'hypothèse que le début de la grossesse serait associé avec une plus grande sensation de faim. En fait, l'évolution de cette sensation, de la préconception à la grossesse, a été très peu étudiée. Crozier et al. ont tout de même rapporté que, parmi les femmes enceintes de leur échantillon qui mentionnaient manger davantage au premier trimestre vs. avant leur grossesse, la majorité d'entre elles justifiaient cette augmentation par une sensation de faim plus importante [221]. D'autres auteurs ont quant à eux questionné des femmes enceintes de moins de 28 semaines de grossesse par rapport à leur faim perçue, comparativement à lorsqu'elles n'étaient pas enceintes, et 62% d'entre elles rapportaient effectivement avoir plus faim durant la grossesse [313]. Ces résultats sont intéressants, mais il convient de mentionner que ces sensations perçues ne sont pas une mesure objective de la faim. Il serait donc pertinent de caractériser l'évolution gestationnelle des hormones liées à la régulation des sensations de faim et de satiété, en plus d'examiner l'association de ces hormones avec les apports énergétiques et alimentaires. Les données du projet PAGG, dont j'étais responsable lors de mon doctorat, seront

entre autres analysées pour combler cette lacune dans la littérature scientifique actuelle. Ces analyses devraient nous permettre de mieux comprendre l'évolution et/ou la stabilité des apports alimentaires durant la grossesse.

Puis, malgré le fait que les participantes aient rapporté des apports énergétiques supérieurs à leurs besoins lors du premier trimestre, les apports alimentaires à eux seuls semblaient insuffisants pour atteindre les ANREF du fer, du folate et de la vitamine D, entre autres. À ce sujet, la prise de suppléments prénataux, en majorité des suppléments à nutriments multiples (multivitamine) apparaît comme efficace pour augmenter les apports en plusieurs micronutriments. En revanche, la prise de suppléments prénataux était associée, dans notre échantillon, à des apports totaux en fer et en acide folique qui dépassent l'AMT. Cette problématique avait déjà été soulevée dans la littérature [102, 135] et elle peut certainement sembler inquiétante. Il convient toutefois de rappeler que l'AMT ne constitue pas une limite associée à des effets toxiques, mais bien l'apport maximal pouvant être consommé quotidiennement sans effets indésirables [161]. L'AMT est généralement bien inférieur à l'apport qui est nécessaire pour produire des effets indésirables après une seule exposition [161]. De plus, il est important de mentionner que les AMT du fer et de l'acide folique sont les mêmes en grossesse qu'en préconception [79]. En revanche, durant la grossesse, les nutriments sont en partie transférés au fœtus; il est donc possible qu'un apport supérieur à l'AMT durant la grossesse n'a peut-être pas les mêmes implications que chez une femme non enceinte, puisqu'une certaine proportion de nutriments n'est pas utilisée par la mère. Néanmoins, cette hypothèse devrait être interprétée avec prudence, et les femmes enceintes devraient avoir des apports totaux en fer et en acide folique qui se situent sous l'AMT. D'ailleurs, depuis la publication de nos résultats, certaines compagnies ont revu à la baisse (de 1 à 0,6 mg) le contenu en acide folique de leurs comprimés, ce qui pourrait contribuer à diminuer la proportion de femmes ayant des apports excessifs en acide folique [107, 108]. Quant au contenu en fer des différents suppléments prénataux disponibles sur le marché, il ne semble pas avoir diminué et se situe encore entre 24 et 35 mg [105-108]. Il semble toutefois important de continuer de s'assurer que les apports en fer et en acide folique des femmes enceintes se situent à l'intérieur des recommandations, surtout considérant que les effets indésirables associés à des excessifs en ces deux nutriments n'ont été que très peu étudiés. Une analyse du statut en folate et en fer des femmes enceintes québécoises pourrait également être envisagée, comme cela a été fait pour la vitamine D au chapitre 6, afin d'identifier quelle dose de ces deux nutriments devrait contenir les suppléments prénataux. Des analyses visant à combiner l'évaluation des apports et du statut en folate sont d'ailleurs en cours au sein de notre laboratoire de recherche.

Dans un autre ordre d'idées, nos résultats ont permis de confirmer certaines des associations rapportées dans la littérature, par rapport à la qualité alimentaire et certaines variables sociodémographiques (âge, éducation, connaissances en nutrition), physiologiques (IMC prégrossesse) et comportementales (activité physique) [217, 231, 232]. De plus, les analyses présentées aux chapitres 7 et 8 suggèrent que les femmes enceintes ont une meilleure qualité alimentaire que les femmes non enceintes et en âge de procréer, mais que cette augmentation se stabilise au cours de la grossesse, contrairement à notre hypothèse de départ. Face à ces résultats, il peut être intéressant de se questionner quant aux habitudes alimentaires après la grossesse. En fait, selon des analyses effectuées au sein d'un sous-échantillon de la cohorte ANGE, la qualité alimentaire semble diminuer, via les apports en fruits et légumes, du troisième trimestre jusqu'aux troisième et sixième mois suivant l'accouchement [314]. Ces résultats, et ceux présentés aux chapitres 7 et 8, suggèrent que les femmes enceintes sont peut-être réellement plus motivées à mieux s'alimenter, comparativement aux femmes non enceintes, mais cette motivation semble s'estomper, du premier trimestre de la grossesse jusqu'à la période post-natale. Puisque nous n'avons pas questionné nos participantes quant à leur motivation par rapport à leurs habitudes alimentaires, il nous est impossible de confirmer cette hypothèse. Quelques études se sont tout de même intéressées aux facteurs qui influencent ou motivent les choix alimentaires des femmes enceintes. Une synthèse d'études qualitatives portant sur les conseils alimentaires et la gestion du poids en contexte de suivi prénatal a rapporté que les femmes enceintes semblent être motivées à faire des choix plus sains principalement et avant tout pour assurer la santé de leur bébé, ce qui a aussi été rapporté dans une cohorte de femmes enceintes canadiennes [315, 316]. Toutefois, cette même revue de la littérature mentionnait que malgré une plus grande motivation à adopter des comportements plus sains au début de la grossesse, les symptômes et inconforts (nausées, vomissements, maux de dos, fatigue) associés à la période prénatale rendaient plus complexe la pratique d'activité physique et la saine alimentation. De plus, certaines femmes considèrent la grossesse comme une pause temporaire où tous les aliments, peu importe leur qualité nutritive, sont permis [315]. Cette vision de la grossesse pourrait, à un certain niveau, être bénéfique pour les femmes enceintes aux prises avec des comportements alimentaires restrictifs, par exemple, mais elle pourrait aussi influencer négativement la qualité globale de l'alimentation. Ainsi, il apparaît comme primordial de mieux comprendre les facteurs qui motivent (ou empêchent) les femmes enceintes à faire de meilleurs choix alimentaires, afin de cibler et d'élaborer des interventions efficaces de promotion de la saine alimentation durant la grossesse.

Parallèlement à la motivation des femmes enceintes à adopter de saines habitudes de vie, il est également important que les professionnels de la santé s'intéressent à leurs préoccupations à l'égard du poids et de l'image corporelle, puisque celles-ci semblent être de plus en plus prévalentes. Ces préoccupations pourraient, comme le montrent les résultats présentés au chapitre 9, être associées à des comportements alimentaires défavorables durant la grossesse. À cet effet, l'attitude, le soutien et les conseils provenant des professionnels de la santé en contexte prénatal pourraient avoir un impact sur les attitudes des femmes enceintes vis-à-vis leur gain de poids gestationnel [317]. Malheureusement, selon un sondage effectué auprès de 321 professionnels de la santé de la province de Québec, la majorité d'entre eux ne se considèrent pas complètement à l'aise pour questionner et accompagner les femmes enceintes par rapport à leurs préoccupations quant au gain de poids gestationnel [318]. Les professionnels sondés ont mentionné que le manque de temps lors des rencontres de suivi et le caractère plus prioritaire d'autres sujets à discuter avec les femmes constituaient les principales raisons pour lesquelles ils questionnent très rarement les femmes par rapport à leurs préoccupations corporelles [318]. Il a été suggéré que la réticence de certains professionnels de la santé à aborder les préoccupations des femmes face aux changements corporels pouvait aussi s'expliquer par une crainte de blesser ou stigmatiser les femmes enceintes par rapport à leur poids [319, 320]. Ces constats sont désolants, et ils suggèrent que les professionnels de la santé ont besoin d'aide et d'éducation en lien avec les préoccupations corporelles des femmes enceintes, afin qu'ils se sentent suffisamment à l'aise pour questionner, soutenir et accompagner les femmes qui pourraient être plus préoccupées par rapport à leur gain de poids. L'organisme Équilibre offre d'ailleurs des formations pour les intervenants en périnatalité, via une boîte à outils intitulée *« Maman bien dans sa peau, bébé en santé* ». Cette boîte comprend des capsules vidéo ainsi que différents outils de réflexion et d'intervention qui visent à accompagner les intervenants afin qu'ils contribuent, via leur pratique, « *à favoriser le développement d'une image corporelle positive chez la femme enceinte* » [321].

Comme il a été mentionné dans les discussions des chapitres 5 à 10 de cette thèse, plusieurs facteurs psychosociaux n'ont pas été évalués dans le cadre de cette thèse, mais certains seraient susceptibles d'influencer la qualité alimentaire des femmes enceintes et/ou leur motivation à adopter de saines habitudes de vie. Les niveaux de stress et d'anxiété ainsi que les symptômes de dépression en sont un exemple. Le fait que ces variables n'aient pas été considérées dans la cohorte ANGE représente une limite importante, puisque les changements associés à la grossesse ne sont pas seulement d'ordre physiologique, mais aussi d'ordre psychologique et émotionnel. Les femmes doivent en effet se préparer à l'arrivée d'un enfant et à leur rôle de mère, tout en assimilant

les nombreuses recommandations à respecter pour assurer la santé de leur bébé [257]. La grossesse elle-même peut donc rendre certaines femmes enceintes plus vulnérables au stress et à l'anxiété et dans certains cas, à une dépression prénatale [322]. L'impact de la grossesse sur la santé mentale des femmes enceintes devrait certainement être pris en considération, puisque des plus hauts niveaux de stress et d'anxiété ainsi que des symptômes dépressifs ont été associés avec une qualité alimentaire moindre durant la grossesse [231, 316, 323-325]. Ainsi, et parallèlement aux préoccupations corporelles durant la grossesse, les professionnels de la santé gagneraient à questionner les femmes enceintes quant à leur bien-être psychologique. De plus, certains groupes de femmes pourraient être plus à risque de détresse psychologique, puisqu'un faible statut socioéconomique a été identifié comme un facteur de risque d'anxiété et de dépression prénatale [322]. Comme cela a été évoqué dans les discussions des chapitres 5 à 10, les femmes enceintes vulnérables au niveau socioéconomique n'étaient pas bien représentées dans la cohorte ANGE. En effet, le taux de diplomation universitaire, le revenu annuel ainsi que la proportion de femmes d'ethnicité caucasienne étaient beaucoup plus élevés au sein de la cohorte ANGE comparativement à ce qui est observé dans la population adulte québécoise [326-328]. Ces disparités entre notre échantillon et la population de femmes québécoises affectent grandement la généralisation de nos résultats. En fait, étant donné le statut socio-économique élevé de notre échantillon, et considérant les associations entre les variables sociodémographiques et économiques et la qualité alimentaire durant la grossesse, nos résultats pourraient sous-estimer la prévalence d'apports nutritionnels insuffisants et de qualité alimentaire sous-optimale. Il serait important que des études subséquentes s'intéressent à l'impact du statut socio-économique des femmes enceintes québécoises sur leur alimentation et leur motivation à adopter de saines habitudes alimentaires, tout en considérant les variables de santé mentale.

Contrairement à notre hypothèse initiale, nos analyses n'ont pas démontré d'associations entre la qualité alimentaire, mesurée par le score d'adhésion à la diète méditerranéenne et l'indice inflammatoire alimentaire, et les marqueurs de l'inflammation durant la grossesse. Nos résultats suggèrent quand même que la grossesse elle-même, ainsi que le statut pondéral prégrossesse, sont associés aux concentrations de certains marqueurs inflammatoires. Ces observations ne devraient toutefois pas être interprétées comme une absence de relation entre la qualité alimentaire et les variables de la santé durant la grossesse. D'une part, l'évaluation de ces associations n'était pas l'objectif de départ du projet ANGE. Ainsi, et comme cela a été mentionné dans la discussion du chapitre 10, la puissance de nos analyses statistiques n'était pas optimale, et cela pourrait expliquer, en partie, pourquoi nous n'avons observé qu'une association significative

après l'ajustement pour l'IMC prégrossesse. D'autre part, de nombreuses études ont montré que des habitudes alimentaires plus saines étaient associées à des variables de santé favorables, chez la mère comme chez le nouveau-né [329-332]. Il est très probable que la qualité de l'alimentation influence favorablement la santé de la femme enceinte en agissant sur d'autres facteurs, et pas seulement sur les marqueurs inflammatoires. De plus, des études futures pourraient effectuer des analyses similaires aux nôtres, mais seulement dans un échantillon de femmes à risque d'hypertension ou de diabète gestationnel, par exemple, puisqu'elles présentent généralement un état inflammatoire plus important que celui observé naturellement durant la grossesse [37-39].

Enfin, les associations entre l'IMC prégrossesse, l'alimentation et les variables de la santé prénatale ont été amplement discutées tout au long de cette thèse. Dans la littérature actuelle, et dans certaines recommandations provenant d'associations médicales à travers le monde, beaucoup d'accent est mis sur le statut pondéral des femmes et sur les risques associés à une obésité prégrossesse [16-18, 84]. D'une part, en ce qui a trait à la période de préconception, certaines recommandations suggèrent de conseiller les femmes présentant une obésité par rapport à leur alimentation et leur pratique d'activité physique [84]. Des associations obstétricales du Canada, des États-Unis et de l'Australie/Nouvelle-Zélande suggèrent même qu'une chirurgie bariatrique pourrait être envisageable et bénéfique, chez une femme qui présente une obésité prégrossesse et qui désire devenir enceinte [84]. Cette suggestion devrait toutefois être interprétée avec prudence, car le fait d'avoir subi une chirurgie bariatrique avant la grossesse semble être associé à un faible poids à la naissance, à un retard de croissance intra-utérin ainsi qu'à un plus grand risque d'accoucher d'un bébé petit pour l'âge gestationnel [333, 334]. D'autre part, en ce qui concerne la grossesse elle-même, différentes associations médicales recommandent une dose plus élevée d'acide folique via les suppléments pour les femmes présentant une obésité, en comparaison avec la dose recommandée pour les femmes avec un IMC plus faible [84]. Bien que nos résultats ne contredisent pas les associations existantes entre une obésité prégrossesse et certains risques prénataux, quelques-unes de nos observations suggèrent qu'un IMC plus élevé ne devrait pas automatiquement être associé à de mauvaises habitudes de vie ou à un statut nutritionnel inadéquat. En fait, comme le montrent nos résultats des chapitres 6 et 7, l'IMC prégrossesse est inversement associé au statut en 25(OH)D et à la qualité alimentaire, certes, mais ces associations semblent s'estomper avec la progression de la grossesse. Il est possible que les femmes, peu importe leur IMC, adoptent de meilleures habitudes alimentaires au cours de leur grossesse, en plus de respecter la recommandation de prendre une multivitamine à tous les jours. Cela pourrait expliquer pourquoi, aux deuxième et troisième trimestres, nous ne voyons plus

d'association entre l'IMC et le score C-HEI, et pourquoi la majorité des femmes avec un surpoids et une obésité présentent un statut suffisant en 25(OH)D. Ces hypothèses, ainsi que nos résultats, suggèrent que les femmes présentant un surpoids ou une obésité en préconception mériteraient une évaluation individualisée au début de leur grossesse pour déterminer si des changements alimentaires, une prise en charge spécialisée ou une supplémentation additionnelle en certains nutriments est nécessaire.

De plus, comme le montrent nos résultats du chapitre 9, les femmes présentant une obésité rapportent des attitudes plus négatives par rapport à leur gain de poids gestationnel. D'autres études avaient également observé des associations entre l'IMC prégrossesse et l'insatisfaction corporelle durant la grossesse [259, 262]. Comme cela a été mentionné plus tôt, la prise en considération de ces préoccupations représente un défi pour les professionnels de la santé, et cela semble être encore plus vrai auprès des femmes enceintes présentant une obésité. En fait, certains professionnels de la santé ont rapporté qu'un sentiment d'embarras et une prise de conscience, de leur part, de la stigmatisation liée au poids contribuaient à leur inconfort à discuter de questions de poids avec des femmes enceintes présentant un surpoids ou une obésité [335]. À cet effet, Johnson et al. ont suggéré, suivant leur analyse de données qualitatives, que d'opter pour des discussions sur la saine alimentation et la pratique d'activité physique serait moins stigmatisant, pour les femmes enceintes, que de seulement aborder la gestion du poids [319]. Ces suggestions vont de pair avec les nouvelles lignes directrices de pratique clinique en lien avec la prise en charge de l'obésité chez les adultes canadiens [336]. Bien sûr, puisque la littérature et nos données montrent que les femmes avec un IMC plus élevé sont plus nombreuses à excéder les recommandations de gain de poids, les professionnels de la santé devraient continuer de suivre le gain de poids de toutes les femmes enceintes. Néanmoins, il semble essentiel, pour la santé physique et psychologique des femmes, d'aborder le gain de poids avec bienveillance et en considérant les préoccupations par rapport à l'image corporelle [267].

En résumé, cette thèse fournit des données supplémentaires en lien avec l'adhésion aux recommandations nutritionnelles et l'évolution des habitudes alimentaires au cours des trimestres de la grossesse. Malgré l'impact reconnu de l'alimentation prénatale sur l'environnement *in utero*, le développement de l'enfant et la santé de la femme enceinte, l'objectif de ce doctorat n'était pas d'identifier ou d'élaborer le modèle alimentaire parfait visant à prévenir le développement de maladies. Néanmoins, cette thèse permet de brosser un portrait approximatif des apports et de la qualité alimentaires d'un échantillon de femmes enceintes québécoises avec un statut socioéconomique élevé. Les travaux inclus dans la présente thèse suggèrent que certains groupes

de femmes enceintes, notamment les femmes sans diplôme universitaire, moins actives physiquement, avec moins de connaissance en nutrition, et présentant un IMC prégrossesse plus élevé pourraient, suivant une évaluation individualisée, bénéficier de conseils alimentaires et/ou d'un accompagnement visant à promouvoir une image corporelle saine durant la grossesse. Ensuite, bien que cette thèse suggère que les femmes enceintes ont une alimentation de meilleure qualité comparativement aux femmes non enceintes, il serait pertinent, dans des études futures, de s'intéresser aux facteurs qui influencent la motivation des femmes enceintes à adopter de saines habitudes alimentaires. Puis, bien que la grossesse ait souvent été identifiée comme un moment idéal pour enseigner et promouvoir de saines habitudes de vie, il s'agit aussi d'une période caractérisée par plusieurs changements physiologiques, anatomiques et émotionnels, qui peuvent bouleverser la vie d'une femme. Ainsi, il importe de considérer ces facteurs dans l'élaboration et la transmission des messages et recommandations en lien avec l'alimentation durant la grossesse. Il serait pertinent que des recherches futures identifient quelles informations devraient être partagées aux femmes enceintes ou en préconception, par qui ces informations devraient être transmises, et de quelle façon elles devraient être communiquées. Finalement, cette thèse réitère l'importance de considérer l'alimentation en contexte prénatal comme un élément déterminant de la santé des générations futures.

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