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Sedentary behavior in obese pregnant women is associated with inflammatory markers and lipid profile but not with glucose metabolism

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ABSTRACT

Background: Sedentary behavior is an independent risk factor for the metabolic syndrome, but the role of sedentary behavior in the development of gestational diabetes is unclear.
Objectives: This study tested the hypothesis that less sedentary behavior is related to better insulin sensitivity, lipid and cytokine profile in obese pregnant women.
Methods: A longitudinal observational study with 46 overweight and obese pregnant women was conducted. Sedentary behavior was measured objectively using accelerometers at 15, 24 and 32 weeks of gestation, and at those time points fasting blood was taken as well. A 100 g oral glucose tolerance test was performed at 24 and 32 weeks. Levels of glucose, insulin, total cholesterol, HDL, LDL, triglycerides were measured, as well as cytokines. The relationship between sedentary behavior and metabolic outcomes was assessed using linear regression analysis.
Results: Women spent almost 60% of their time sitting throughout pregnancy. In cross-sectional analyses, an association of sedentary time at 24 weeks was found with increased total cholesterol and HDL. More sedentary time was associated with lower IL-6 at 24 weeks and with higher IL-10, TNF-α and leptin levels at 32 weeks of pregnancy. Changes in sedentary time were not associated with changes in any of the metabolic outcomes.
Conclusions: In conclusion, time spent sedentary in pregnancy was associated with lipid and cytokine profile. Whether decreasing sedentary time beneficially influences lipid profile and influences cytokine profiles of overweight and obese women needs to be assessed in future intervention studies.

1. Introduction

Physical activity before and in early pregnancy is associated with a lower risk of developing gestational diabetes (GDM) [1]. Physical activity increases both insulin-mediated and non-insulin mediated glucose disposal. Physical activity is also known for improving glucose homeostasis through its direct or indirect impact on insulin sensitivity via several other mechanisms such as lipid metabolism [2]. Previously, we reported an association of moderate-to-vigorous physical activity (MVPA) with first phase insulin response and insulin sensitivity in pregnancy [3], which might be mediated by interleukin (IL)-6 [4]. However, during pregnancy most women decrease their daily physical activities and participate less in exercise and sports [5].

Evidence is accumulating that, independent of physical activity, sedentary behavior is related to increased mortality and morbidity [6,7]. Sedentary behavior is defined as being engaged in activities at the level of resting energy expenditure which includes activities such as sitting, lying down, computer activities and watching television [8]. Sedentary behavior is an important independent risk factor for the development of insulin resistant conditions, such as the metabolic syndrome [9,10] and type 2 diabetes [11]. The role of sedentary behavior for insulin resistance in pregnancy and the development of GDM is not well understood, since most previous studies focused on physical activity only.

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We hypothesized that obese and overweight women spending less hours in sedentary behavior have lower fasting glucose and insulin levels, higher insulin sensitivity, have a healthier lipid profile, and a less pro-inflammatory cytokine profile. Cytokines of interest were those that reflect inflammatory status (CRP, IL-6, IL-10, TNF-α, IL-1β) and/or are related to insulin sensitivity (IL-6, leptin, adiponectin) [4,12–17]. To test these hypotheses, we determined the cross-sectional and longitudinal relationships between objectively measured sedentary behavior and estimates of fasting blood glucose, fasting insulin, insulin sensitivity, first and second phase insulin response, lipids and cytokines.

2. Research design and methods

2.1. Study design

This longitudinal study was conducted between January 2007 and January 2011. Approval of the Medical Ethics Committee of VU University Medical Centre in Amsterdam (2007/133) was obtained.

2.2. Subjects

Participants were overweight (Body Mass Index (BMI) $\geqslant$ 25) and obese (BMI $\geqslant$ 30) pregnant women, who are at increased risk for gestational diabetes mellitus (GDM). These pregnant women were selected based on their pre-pregnancy BMI. Other additional inclusion criteria were gestational age <15 weeks, age $\geqslant$18, no diabetes mellitus or history of GDM, and adequate knowledge of Dutch language. Pregnant women were excluded from the study if they were diagnosed with GDM at baseline, were using medication that affects insulin secretion or insulin sensitivity, or if they had any chronic medical conditions or psychiatric problems. All women provided written informed consent. The study sample consisted of 46 women for whom data were available from accelerometers and fasting blood samples collected at three time points.

2.3. Sedentary behavior and physical activity measurement

Sedentary behavior was measured by an accelerometer (Actigraph GT3X+, GT1M or Actitrainer) worn for four days by the pregnant women on the right hip at all times except at night during sleep and during water-based activities. The accelerometers collected data in 1-min epochs and the unit of data was counts per minute. For valid data, the accelerometer had to be worn at least 8 h per day, which was calculated after periods of consecutive zero counts $\geqslant$30 min were removed. Participants had to wear the accelerometer for a minimum of 3 days to be included in the analyses.

Sedentary time was calculated in minutes per day, using the Freedson cut-off point of <100 counts/min [18]. Sedentary behavior was calculated as a percentage of total wear time, by dividing the time spent sedentary by the total wear time of that day. Sedentary time as percentage of total wear time was averaged over the days the accelerometer was worn.

In addition time spent in moderate-to-vigorous physical activity (MVPA) [>1952 counts/min] was calculated. For MVPA, the average hours per week were calculated by adding up the total time in MVPA in hours, dividing this by the number of days the accelerometer was worn and then multiplying by seven.

2.4. Blood samples

Venous blood samples were collected at 15, 24 and 32 weeks of gestation after 10 h of overnight fasting. An oral glucose tolerance test (OGTT) was conducted at 24 and 32 weeks of gestation. For the OGTT, after the collection of blood for fasting tests, women were given a glucose drink (100 g glucose in 500 ml of water) and blood samples were collected at 30, 60, 90, 120 and 180 min. Women were not allowed to eat during the test. Women with a threshold plasma glucose concentration above 5.3 mmol/l (fasting), or 10.0 mmol/l (60 min), or 8.6 mmol/l (120 min) or 7.8 mmol/l (180 min) were diagnosed as GDM [19].

Glucose (mmol/l), insulin (pmol/l), total cholesterol (mmol/l), HDL-cholesterol (HDL-C; mmol/l), LDL-cholesterol (LDL-C; mmol/l) and triglycerides (mmol/l) were measured as described below.

2.5. Biochemical analyses

Plasma glucose was measured by a Glucose/HK kit (Glucoquant; Roche/Hitachi Modular P analyzer; Roche Diagnostics GmbH, Mannheim, Germany) and insulin by immunometric assay (Luminescence, Advia Centaur, Siemens Medical Solutions Diagnostics). Total cholesterol, triglycerides, and HDL-C were measured with commercial enzymatic kits on Roche/Hitachi modular P analyzers (Roche Diagnostics GmbH, Mannheim, Germany), whereas LDL-C was calculated using the Friedewald formula [20]. Insulin sensitivity was estimated with the HOMA index [21]. Using Stumvoll equations: $1194 + 4.724 * \text{Ins0} - 117.0 * \text{Glu60} + 1.414 * \text{Ins60}$ and $295 + 0.349 * \text{Ins60} - 25.72 * \text{Glu60} + 1.107 * \text{Ins0}$, first phase insulin response and second phase insulin response was estimated respectively [22].

Protein levels of cytokines (CRP, IL-6, IL-10, TNF-α, IL-1β, leptin, and adiponectin) in the serum samples were quantified by multiplex assay according to manufacturer's instructions (eBioscience, San Diego, CA, USA).

2.6. Covariates

Information on age, pre-pregnancy body weight and height, ethnicity (White European/non-white (mostly from Morocco and Surinam), level of education (low = 10 years of education or less, middle = 11–14 years of education, high = 15 years of education or more), history of type-II diabetes in first line relatives as well as employment status were recorded. Maternal body weight was measured at 15, 24 and 32 weeks using calibrated electronic scales, with participants wearing only indoor clothing and no shoes. Prepregnancy weight was self-reported. At the first measurement, maternal body height was measured with bare feet and a (wall-mounted) height scale. Body Mass Index (BMI, kg/m^2) was calculated based on self-reported prepregnancy weight, and measured weight at 15, 24 and 32 weeks.

2.7. Statistical analysis

Values of continuous variables are expressed as mean with standard deviation for normally distributed variables, and as median and interquartile range (IQR) for skewed variables. In the figures, box-plots with whiskers indicating the 10–90th percentiles are presented. To test for differences in sedentary behavior, cytokines and insulin parameters over time, paired Wilcoxon Rank tests were used. Changes in sedentary time and in metabolic outcomes were calculated as the value at 24 or 32 weeks minus the value at 15 weeks.

To test for differences in metabolic outcomes between tertiles of percentage of sedentary time, *T*-tests (normally distributed data) or Kruskal-Wallis tests (skewed data) were used. The cross-sectional relationship between the percentage of wearing time spent in sedentary habits at all three time points and metabolic outcomes at the same time points were assessed using linear regression analysis. For these models, a natural log-transformation was performed on cytokine data. Results of regression analyses are presented as beta-values and 95% confidence interval (CI).

Table 1
Descriptive characteristics of participants, and per tertile of % sedentary time at 15 weeks of gestation.

Characteristics	Participants N = 46	1st tertile N = 14	2nd tertile N = 14	3rd tertile N = 14
Age, year, mean (SD)	31.9 (4.1)	30.8 (3.1)	32.6 (4.1)	30.9 (4.2)
Parity, N (%)				
Primiparous	15/45 (33%)	5/14 (36%)	2/13 (15%)	6/14 (43%)
Multiparous	30/45 (67%)	9/14 (64%)	11/13 (85%)	8/14 (57%)
Educational level, N (%)				
High	12/44 (27%)	8/14 (57%)	4/13 (31%)	2/13 (15%)
Middle	17/44 (39%)	3/14 (21%)	7/13 (54%)	6/13 (46%)
Low	15/44 (34%)	3/14 (21%)	2/13 (15%)	5/13 (39%)
Ethnicity, N (%)				
White European	22/45 (49%)	6/14 (43%)	8/13 (62%)	5/14 (36%)
None-white	23/45 (51%)	8/14 (57%)	5/13 (39%)	9/14 (64%)
Working at this moment, N (%)				
Yes	33/45 (73%)	9/14 (64%)	10/13 (77%)	11/14 (79%)
No	12/45 (27%)	5/14 (36%)	3/13 (23%)	3/14 (21%)
Type-II Diabetes in 1st grade relative, N (%)				
Yes	16/45 (36%)	5/14 (36%)	6/13 (46%)	4/14 (29%)
No	26/45 (58%)	8/14 (57%)	6/13 (46%)	10/14 (71%)
Don't know	3/45 (7%)	1/14 (7%)	1/13 (8%)	0/14 (0%)
Weight pre-pregnancy, kg, mean (SD)	92.6 (17.8)	89.2 (12.5)	94.6 (20.4)	95.6 (17.1)
BMI pre-pregnancy, kg/m^2, mean (SD)	33.4 (5.7)	32.7 (4.6)	33.5 (5.8)	34.7 (7.2)
BMI category pre-pregnancy, N (%)				
Overweight (<30)	10/46 (22%)	4/14 (29%)	3.14 (21%)	2/14 (14%)
Obese- I (30–35)	24/46 (52)	7.14 (50%)	7/14 (50%)	8/14 (57%)
Obese- II (⩾35)	12/46 (26%)	3/14 (21%)	4/14 (21%)	4/14 (29%)

Table 2
Sedentary behavior, moderate to vigorous physical activity (MVPA), metabolic outcomes and cytokines at three time points in pregnancy (n = 46).

	15 weeks		24 weeks		32 weeks	
Activity behavior	Mean	SD	Mean	SD	Mean	SD
Sedentary time (h/wk)	51.2	9.8	52.5	11.1	48.7[c]	8.5
% Sedentary time	59.0	7.9	58.9	8.8	59.1	8.0
MVPA (h/wk)	3.6	1.9	3.5	2.3	2.9	1.6
% MVPA	4.2	2.4	4.0	2.8	3.5	1.9
Glucose and insulin	Mean	SD	Mean	SD	Mean	SD
Fasting glucose (mmol/l)	4.8	0.5	4.9	0.7	4.9	0.5
Fasting insulin (pmol/l)	76.7	33.5	85.6	31.3	102.9[b,c]	40.4
Insulin sensitivity (HOMA Index)	16.6	7.6	18.8	8.4	22.4[b,c]	9.1
First-phase insulin response (pmol/l)	–	–	1940.3	441.8	2451.1[c]	782.7
Second-phase insulin response (pmol/l)	–	–	417.3	96.6	516.8[c]	196.4
Lipids	Mean	SD	Mean	SD	Mean	SD
Total cholesterol (mmol/l)	5.1	0.9	5.6[a]	1.0	6.0[b,c]	1.0
HDL (mmol/l)	1.8	0.4	1.8	0.3	1.7[c]	0.3
LDL (mmol/l)	2.7	0.8	3.0[a]	0.9	3.3[b,c]	0.9
Triglycerides (mmol/l)	1.6	0.5	1.8[a]	0.5	2.3[b,c]	0.6
Cytokines	Median	IQrange	Median	IQrange	Median	IQrange
CRP (ng/ml)	10.1	5.7; 16.5	9.1	5.4; 14.3	7.1[c]	3.1; 15.6
IL-6 (pg/ml)	0.1	0.1; 2.7	0.1	0.1; 6.6	0.1[b]	0.1; 7.8
IL-10 (pg/ml)	11.7	6.7; 25.2	16.3	10.8; 32.9	15.2[b]	7.4; 40.3
TNF-α (pg/ml)	60.1	46.7; 97.9	91.3[a]	66.3; 134.7	90.5[b]	45.4; 122.3
IL-1β (pg/ml)	49.2	0.1; 85.0	69.5[a]	0.1; 104.4	62.0[b]	0.1; 109.0
Adiponectin (ng/ml)	7.1	4.3; 10.6	6.1[a]	3.7; 8.3	5.8[b]	3.9; 8.3
Leptin (pg/ml)	82.4	58.6; 101.3	80.6	59.1; 110.1	79.7	59.1; 111.7

[a] Represents a significant change from first trimester to second trimester (p-value < 0.05).
[b] Represents a significant change from first trimester to third trimester (p-value < 0.05).
[c] Represents a significant change from second trimester to third trimester (p-value < 0.05).

Longitudinal changes were determined by calculating changes in sedentary time and cytokines (not transformed) from 15 to 24 and 32 weeks of gestation. The longitudinal association of changes in sedentary time with changes in cytokine levels was assessed.

All analyses (cross-sectional and longitudinal) were controlled for age, BMI, and time spent in MVPA, because in previous studies these factors were found to be relevant confounders [23,24].

All analyses were performed using SPPS20 and associations were considered statistically significant when $p < 0.05$.

3. Results

The characteristics of the study population are described in Table 1. Approximately 49% of the women were Caucasian, and they were 31.9 ± 4.1 years of age. Their pre-pregnancy BMI was

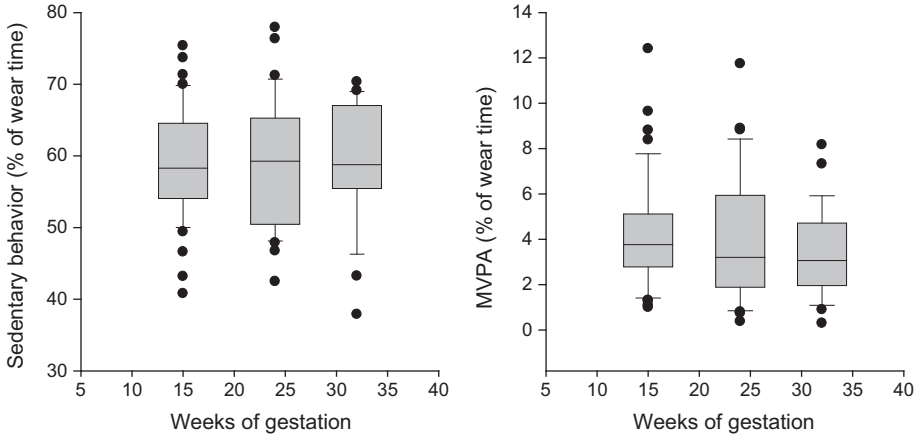

Fig. 1. Time spent sedentary and on MVPA (Box-Whiskers plots) as percentage of wear time at three different periods in pregnancy.

33.4 ± 5.7 kg/m^2. None of the women reported smoking during pregnancy. Nine women developed GDM.

Sedentary activity measures of these women were available at 15, 24, 32 weeks of gestation (Table 2). Throughout pregnancy, the percentage of time spent sedentary remained relatively stable ($p > 0.05$) (Fig. 1). The number of hours per week spent on MVPA tended to decrease without reaching statistical significance (Fig. 1).

Fasting glucose remained stable throughout the pregnancy ($p > 0.05$), whereas fasting insulin and insulin resistance (HOMA) increased ($p < 0.001$; Table 2) between 24 and 32 weeks. This was paralleled by an increase in first phase and second phase insulin response ($p = 0.001$ and $p = 0.01$, respectively). In the lipid profile, total cholesterol, triglycerides and LDL levels increased throughout pregnancy (all $p < 0.001$). HDL levels decreased from 24 to 32 weeks ($p < 0.05$).

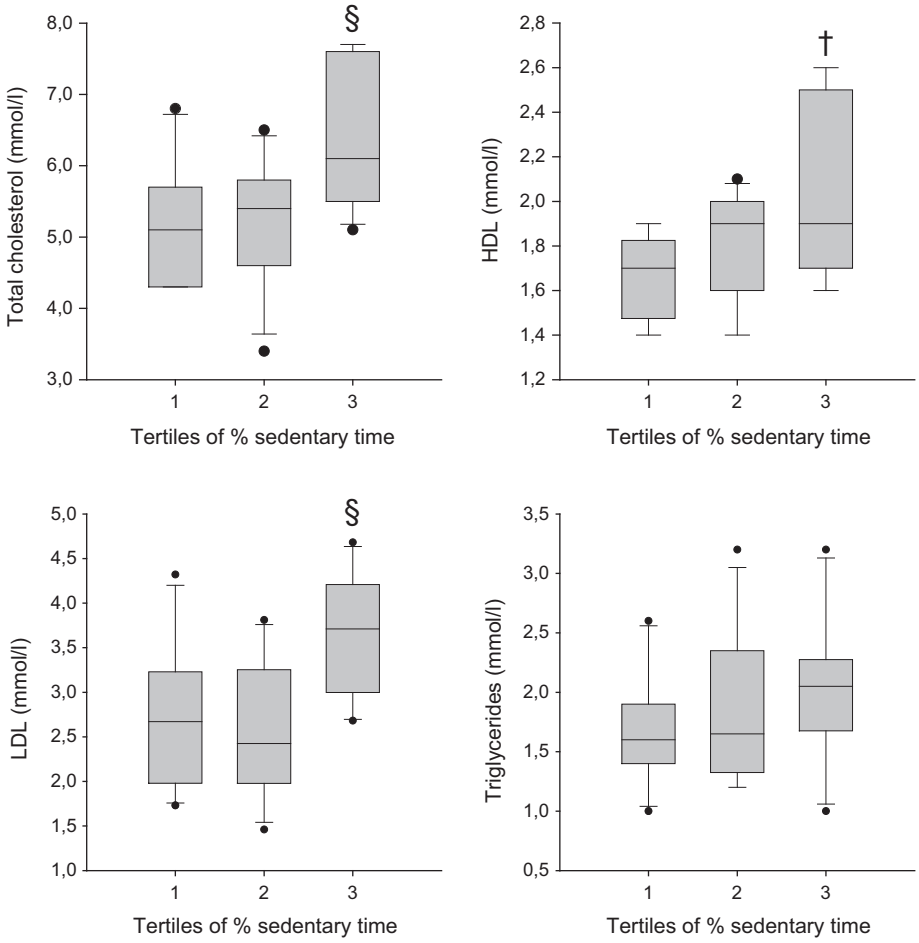

Fig. 2. Lipid levels per tertile of % sedentary time at 24 weeks of gestation (Box-Whisker plots). † indicates a significant ($p < 0.05$) difference with the first tertile, § with both the first and the second tertile (independent *T*-test).

Table 3
Cross-sectional associations between percentage of sedentary time, metabolic outcomes and cytokines at three time points in pregnancy.

	15 weeks		24 weeks		32 weeks	
	Beta[a]	95% CI	Beta[a]	95% CI	Beta[a]	95% CI
Glucose and insulin						
Fasting glucose (mmol/l)	0.01	−0.01, 0.03	−0.01	−0.04, 0.01	−0.01	−0.05, 0.03
Fasting insulin (pmol/l)	−0.18	−1.70, 1.34	−0.27	−1.85, 1.31	−1.64	−4.40, 1.12
Insulin sensitivity (HOMA Index)	−0.02	−0.36; 0.32	−0.11	−0.52, 0.30	−0.44	−1.09, 0.22
First-phase insulin response (pmol/l)	–	–	13.68	−7.74, 35.09	−40.72	−134.69, 62.26
Second-phase insulin response (pmol/l)	–	–	3.43	−1.24, 8.10	−4.88	−33.09, 23.33
Lipids						
Total cholesterol (mmol/l)	0.04	−0.003, 0.08	**0.06**	**0.02, 0.10**	0.03	−0.04, 0.10
HDL (mmol/l)	0.01	0.001, 0.03	**0.02**	**0.01, 0.03**	0.01	−0.02, 0.03
LDL (mmol/l)	0.02	−0.01, 0.06	0.04	−0.001, 0.08	0.03	−0.04, 0.10
Triglycerides (mmol/l)	0.001	−0.02, 0.03	0.01	−0.01, 0.04	−0.01	−0.05, 0.02
Cytokines[b]						
CRP (ng/ml)	−0.02	−0.05, 0.01	0.02	−0.02,0.05	0.03	−0.03, 0.09
IL-6 (pg/ml)	0.03	−0.07, 0.13	**−0.13**	**−0.24, −0.03**	0.12	−0.06, 0.29
IL-10 (pg/ml)	0.04	−0.04, 0.12	0.003	−0.08, 0.09	**0.15**	**0.03, 0.27**
TNF-α (pg/ml)	0.01	−0.01, 0.04	−0.01	−0.10, 0.08	**0.06**	**0.01, 0.12**
IL-1β (pg/ml)	0.02	−0.14, 0.17	−0.07	0.22, 0.07	0.17	−0.05, 0.38
Adiponectin (ng/ml)	0.02	−0.01; 0.05	0.00	−0.03, 0.03	−0.04	−0.09, 0.01
Leptin (pg/ml)	0.01	−0.01, 0.02	0.01	−0.001, 0.02	**0.03**	**0.003, 0.05**

Bold font indicates statistically significant associations.
[a] Analyses adjusted for maternal age, BMI and MVPA.
[b] For all cytokines, the natural log transformed values were used in the regression analyses.

The median and interquartile ranges for cytokines at the three time points in pregnancy are described in Table 2. At 32 weeks, levels of IL-6, IL-10, TNF-α and IL-1β had increased significantly compared to 15 weeks, while CRP levels dropped from 24 to 32 weeks (all $p < 0.05$). Adiponectin levels dropped throughout pregnancy ($p < 0.05$), while leptin remained constant.

3.1. Associations between sedentary behavior and glucose and lipid metabolism

In univariate analyses, higher total cholesterol and LDL levels were found in the 3rd tertile of sedentary time, compared to the 1st and 2nd tertile at 24 weeks of gestation. Also higher levels of HDL were found in the 3rd compared to the 1st tertile (Fig. 2). No other differences were found between tertiles of sedentary behavior. In cross-sectional multivariate analyses, the percentage of sedentary time was positively associated with total cholesterol at 24 weeks (beta 0.06; 95% CI 0.02–0.10) and HDL at 24 weeks (beta 0.02; 95% CI 0.01–0.03) (Table 3). The ratio HDL-C:total cholesterol did not change with sedentary time (data not shown). No associations were observed in the multivariate models with LDL, triglycerides or with glucose metabolism. In longitudinal analyses, changes in the percentage of sedentary time throughout pregnancy were not related to changes in glucose or lipid metabolism.

3.2. Association between sedentary behavior and cytokines

At 32 weeks of gestation significantly higher levels of leptin were found in the 2nd and 3rd tertile of sedentary time compared to the 1st tertile (Fig. 3). In cross-sectional multivariate analyses adjusted for maternal age, BMI, and MVPA, more sedentary time was associated with lower IL-6 levels at 24 weeks and with higher IL-10, TNF-α and leptin levels at 32 weeks (Table 3). No other cross-sectional associations were observed. In longitudinal analysis, changes in percentage of sedentary time throughout pregnancy were not related to changes in cytokines.

4. Discussion

We hypothesized that obese and overweight women who spend less hours in sedentary behavior would have lower fasting glucose and insulin levels, higher insulin sensitivity, have a healthier lipid profile, and a less pro-inflammatory cytokine profile. The study results confirm this hypothesis in part. Less sedentary time was associated with decreased lipid levels in middle pregnancy and with increased IL-6, and decreased IL-10, TNF-α and leptin levels in middle or late pregnancy. However, despite the association of sedentary behavior with lipid profile and inflammatory markers, no significant relationships with glucose or insulin outcomes were found at any time point in pregnancy.

As far as we know, only five previous studies have assessed the role of sedentary time for maternal metabolism in pregnancy [27,33–35,38], of which only two assessed sedentary time objectively [33,38]. One of those two studies assessed only glucose metabolism [33], and the other one combined all gestational ages [38]. The present study is the first to determine the association of objectively measured sedentary behavior with diverse aspects of maternal metabolic health at multiple time points in pregnancy. How our results compare to those previous studies is discussed below.

Outside of pregnancy, more sedentary time was associated with a more inflammatory cytokine profile, e.g. higher CRP, TNF-α, and leptin levels [24–26], which is partly (TNF-α, leptin) in line with our findings. The absence of an association between CRP and sedentary time confirms another study, which also analyzed the three trimesters of pregnancy separately [27], but is in contrast to a study that found a positive association between sedentary behavior and CRP levels in a population with mixed gestational ages and a mean BMI of 29 [38]. The positive association of sedentary time with the anti-inflammatory cytokine IL-10 that we observed might reflect a counterbalancing response to the increase in TNF-α [28]. As far as we know, other cytokines have not been studied in pregnancy in relation to sedentary behavior.

High maternal leptin is associated with higher fetal leptin levels [29] and with reduced fetal insulin sensitivity [29,30]. Therefore, preventing high levels of maternal leptin might be beneficial for fetal metabolism. Whether leptin levels will indeed decrease as a result of a reduction of sedentary time needs assessing in experimental studies. In addition, the relevance of those changes for mother and offspring health needs to be determined.

Although we observed a cross-sectional association between time spent sedentary and IL-6, TNF-α, and leptin levels, all factors

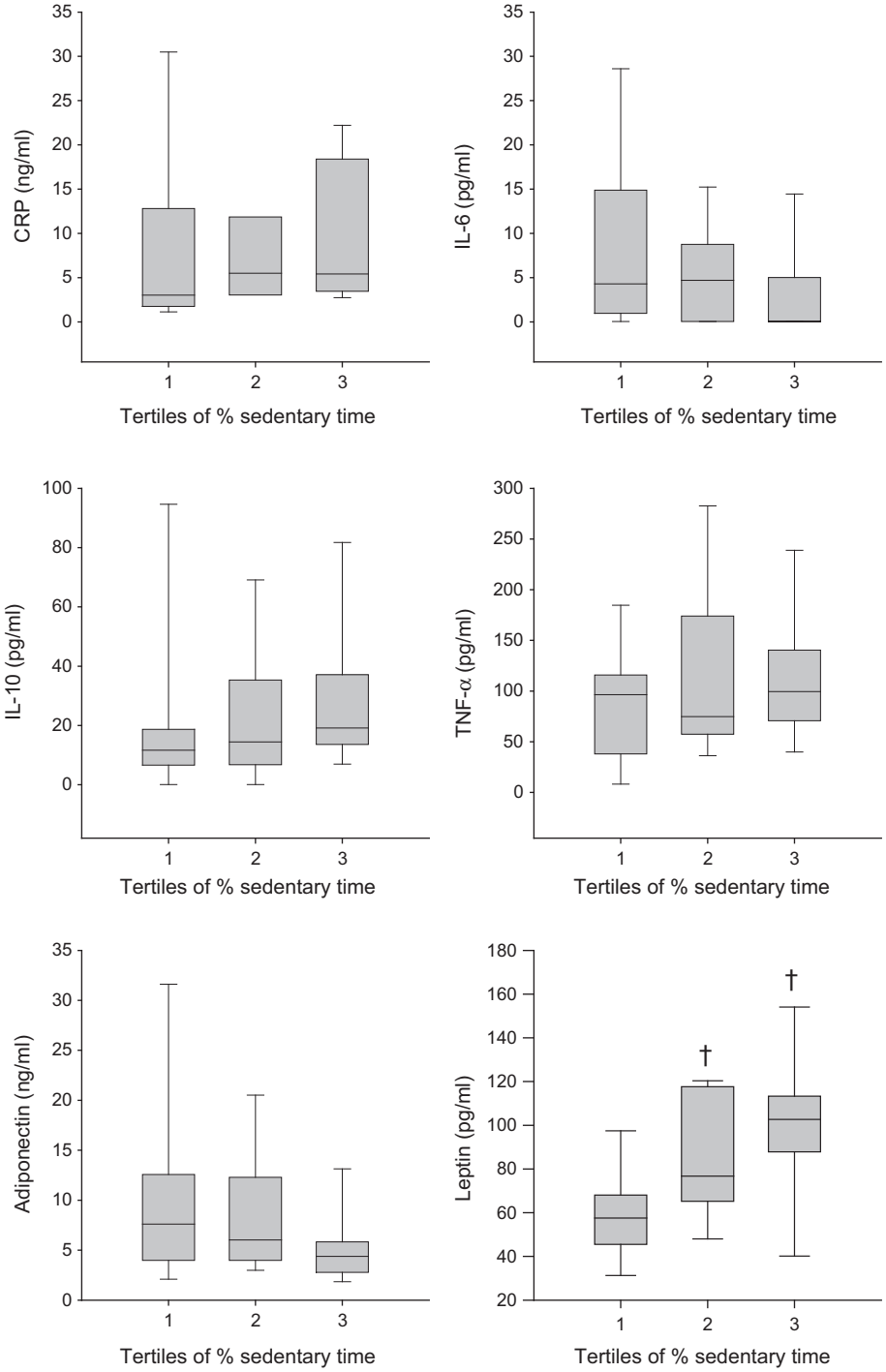

Fig. 3. Cytokine levels per tertile of % sedentary time at 32 weeks of gestation (Box-Whisker plots). † indicates significant ($p < 0.05$) difference with the first tertile (Kruskal-Wallis test).

that have previously been shown to be related to insulin sensitivity [4,31,32], we did not find any association of sedentary time with glucose and insulin outcomes in this population of obese pregnant women. This is conform previous studies in pregnancy [33,34], but in contrast to one other study [35], in which more time in self-reported sedentary behavior during mid-pregnancy was significantly associated with an increased risk of abnormal glucose levels in Latina women of all BMI groups. Of note, this association was not uniform throughout pregnancy, since no statistically significant association was observed in pre-pregnancy or in early pregnancy [35]. The lack of associations between sedentary time and glucose metabolism in our study might be due to our small sample size, due to too little variation in sedentary time in our study population, or due to only small changes in sedentary behavior over time. Furthermore, pregnancy effects might override effects of sedentary behavior on glucose metabolism otherwise found outside of pregnancy.

We found that total cholesterol, HDL-C and LDL-C increased with increasing sedentary time, although the association with LDL-C was not significant when adjusting for possible confounders.

In non-pregnant populations, more time spent sedentary was related to unhealthier lipid profiles, including higher LDL-C and lower HDL-C levels [25,36,37]. A cross-sectional study among pregnant women in all stages of pregnancy and an average BMI of 29 [38] failed to find a significant association of objectively measured sedentary behavior with HDL-C, but found a significant positive association with LDL-C levels, after adjustment for BMI and MVPA. Because of the inconsistent results and scarcity of data in pregnancy, more research on the relationship between sedentary behavior and lipid profile in pregnancy is warranted, preferably in different BMI groups and including the assessment of consequences for fetal metabolism.

Strengths of our study are the objective measurement of sedentary behavior, and having three measurements in pregnancy. Furthermore, in our analyses we had the possibility to adjust for MVPA and BMI. This is a major strength, since not adjusting for these factors might overrate the importance of the independent effect of sedentary time on metabolic outcomes. In previous studies, associations seem to depend on whether or not analyses were adjusted for MVPA and/or BMI. For instance, one study found multiple significant associations of sedentary behavior with cardio-metabolic outcomes without adjustment, most of which disappeared after adjusting for MVPA [23]. In another study, where self-reported sedentary time was associated with higher CRP, leptin, and IL-6 levels after adjustment for MVPA in non-pregnant women, these associations became non-significant when additionally adjusting for BMI [24]. These differences in approach for statistical analyses could be a possible explanation of inconsistent findings in the literature regarding the associations of sedentary behavior with metabolic outcomes.

Furthermore, from our own results and from literature [35], it is clear that associations of sedentary behavior with metabolic outcomes might differ at different time points in pregnancy. Differences between studies might, therefore, also result from differences in timing of measurements in pregnancy.

A limitation of our study is that we were unable to obtain information on types of sedentary behaviors women adopted during pregnancy, since sedentary behavior was measured using accelerometers. Therefore, no distinction could be made between different behaviors, such as TV watching, computer use or sleeping during the day. In addition, our study did not include sedentary behavior pre-pregnancy or in very early pregnancy.

In conclusion, time spent sedentary was associated with higher total cholesterol, HDL-C, IL-10, TNF-α, and leptin levels, and with lower IL-6 levels in second or third trimester. More research is needed on this relative 'new' lifestyle factor in pregnancy. Especially, the effects of sedentary time in different BMI groups and the relevance of reducing sedentary time for neonatal outcomes remain to be studied.

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