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Influence of an exercise intervention plus an optimal Mediterranean diet adherence during pregnancy on the telomere length of the placenta. The GESTAFIT project

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ABSTRACT

We aimed to investigate whether the effects of exercise on placental relative telomere length (RTL) after delivery are modulated by the Mediterranean diet [MD] adherence in 65 pregnant women (control n = 34, exercise n = 31). No differences were found in placental RTL between the exercise and the control groups ($p = 0.557$). The interaction-term between exercise and MD adherence with placental RTL was significant ($p = 0.001$). Specifically, women in the exercise group showed longer placental RTL after birth compared to controls (referent group), only for those women with a high MD adherence (mean difference = 0.467, p=0.010). A concurrent-exercise training plus an optimal MD adherence during pregnancy might prevent the placental RTL shortening.

1. Introduction

Telomeres are nucleoprotein structures that serve as guardians of genome stability by ensuring protection against both cell death and senescence [1]. Previous evidence has implicated shortened placental relative telomere length (RTL) in the pathogenesis of pregnancy complications including preeclampsia [2], gestational diabetes [3], intrauterine growth restriction [4], spontaneous preterm birth [5], and unexplained stillbirths [6]. In this context, exercise and healthy diets such as the Mediterranean diet (MD) might partially offset telomere shortening measured in blood cells [7–10]. The traditional MD is characterized by a high intake of vegetables, legumes, fruits, nuts, cereals and olive oil, a low intake of saturated lipids, a moderately-high intake of fish, a low-to-moderate intake of dairy products and a low intake of meat and poultry [11]. However, the extrapolation of these benefits to placental RTL has not been investigated to date. Therefore, the purposes of the present study were [1]: to explore the effects of an exercise intervention delivered during pregnancy on placental telomere length; and, 2) to investigate whether MD adherence during pregnancy moderates the effects of the exercise intervention on placental RTL.

2. Methods

These are secondary analyses from the GEStation and FITness (GESTAFIT) project where a concurrent exercise program consisting of aerobic and resistance exercises from the 17th g.w. until birth was conducted [12] (Identifier: NCT02582567). The GESTAFIT project was initially designed as a randomised control trial (computer-generated simple randomisation). Nonetheless, the randomised component was partially broken in the second and third waves of participants because of difficulties related to the adherence of control women to their intervention regime; which represents a frequent methodological barrier in

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antenatal exercise research [13,14] Thus, half of the women were not randomised but allocated to the control/exercise group accordingly to their personal convenience to attend the exercise sessions. Pregnant women in the control group did not take part in the exercise training program and were asked to continue with their usual activities [12]. A total of 65 pregnant women (exercise n = 31, control n = 34) who had valid data in placental RTL and dietary habits during pregnancy were included in this study.

At the 16th g.w. dietary habits were assessed with an adult-validated food frequency questionnaire [15]. MD adherence were derived from it using the MD adherence score [16]. Participants were classified as having a high MD adherence if they had a score of ≥30 points in the MD score as previously done in this study sample [17].

Placental samples were collected immediately after delivery. RTL (T/S ratio) was assessed by a quantitative real time polymerase chain reaction (QRT-PCR)-based method developed by Cawthon et al. [18] with some modifications [19] (Further detailed in **Appendix A**).

3. Statistical analyses

Differences in placental RTL between the control and exercise groups were explored by a one-way analysis of covariance. Placental RTL was included as dependent variable, exercise group as fixed factor, and maternal age, gestational week at birth, sex of the baby, and smoking habits as covariates. The association between MD adherence and placental RTL was investigated with linear regression analyses after adjusting for the same covariates. Additionally, the interaction term between group (i.e., exercise versus control) and MD adherence (i.e., low versus high) was investigated. As initially designed [12], statistical analysis was conducted on a per-protocol basis including women who attended more than 75% of exercise sessions. All analyses were conducted using the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 22.0, Armonk, NY) and the level of significance was set at $p \leq 0.05$.

4. Results

Descriptive characteristics of study participants are shown in Table 1. No differences were found in placental RTL after adjusting for maternal age, gestational week at birth, sex of the baby and smoking habit between control and exercise groups ($p = 0.557$) (Fig. 1). No associations were found between maternal MD adherence and RTL (B = −0.013 [95% CI: 0.033 to 0.006], p = 0.181). The maternal MD adherence during gestation was found to be a moderator on the effects of the exercise intervention on placental RTL ($p = 0.001$). In particular, those participants who received the exercise intervention and had a high MD adherence showed a longer placental RTL after birth (RTL difference = 0.467 [95% CI: 0.113–0.802], p = 0.010).

Table 1
Anthropometric and sociodemographic characteristics of the study sample.

Variable	Total women (n = 65)	Control (n = 34)	Exercise (n = 31)
Age (years)	33.3 (4.2)	33.3 (4.4)	33.3 (4.1)
Pre-pregnancy body mass index (kg/m^2)	23.6 (3.7)	23.4 (3.2)	23.9 (4.2)
Gestational week at birth	39.7 (1.1)	39.6 (1.2)	39.7 (1.0)
Percentage of attendance	–	–	86.3 (7.2)
Mediterranean Diet adherence	28.4 (4.1)	27.6 (4.2)	29.3 (3.8)
Low Mediterranean diet adherence (n [%])	45 (69.2)	25 (73.5)	20 (64.5)
High Mediterranean diet adherence (n [%])	20 (30.8)	9 (26.5)	11 (35.5)
Educational status (n [%])			
University studies	41 (63.1)	24 (70.6)	17 (54.8)
No university studies	24 (36.9)	10 (29.4)	14 (45.2)
Working status (n [%])			
Working	43 (66.2)	23 (67.6)	20 (64.5)
Not working	22 (33.8)	11 (32.4)	11 (35.5)
Marital status n [%])			
Married	36 (55.4)	19 (55.9)	17 (54.8)
Single/divorced/widow	29 (44.6)	15 (44.1)	14 (45.2)
Sex of the baby (n [%])			
Male	34 (47.7)	16 (47.1)	15 (48.4)
Female	34 (52.3)	18 (52.9)	16 (51.6)
Smoking habit (yes, n [%])	6 (9.2)	5 (14.7)	1 (3.2)

Values shown as mean (standard deviation) unless otherwise is indicated.

5. Discussion

Our results showed that a concurrent-exercise training combined with an optimal MD adherence during pregnancy might be a useful strategy to promote longer placental RTL.

It has been reported that placental RTL progressively shorten throughout the gestation [20]. The rate of telomere shortening can be accelerated by factors that affect the mother and result in oxidative stress [20,21]. Lifestyle factors including exercise and diet have shown to positively influence the oxidation-inflammation pathway [22,23]. Telomeres are particularly sensitive to oxidative stress [21]. Exercise training seems to have an antioxidant effect [23], it seems plausible that diet and exercise are related to telomere length. However, we did not observe effects of the exercise intervention on placental RTL. Regarding diet, dietary antioxidants and consumption of antioxidant-rich, plant-derived foods help maintain telomere length [24]. The MD is considered to be one of the most recognized diets for disease prevention and healthy aging, partially due to its demonstrated anti-inflammatory and antioxidative properties which may exert a positive impact on telomere length [7]. This may, at least in part, explain our findings that participants who received the exercise intervention and had a greater MD adherence (i.e., MD Score≥30) showed longer placental RTL relative to participants in the control group and with a low MD adherence. This is in agreement with previous evidence suggesting that MD adherence is associated with longer telomeres measured in blood cells in the non-pregnant population [24]. Regarding placental RTL, only one previous observational study conducted by Vahter et al. [25] suggested that placental telomere length is associated with variations in maternal nutrition during pregnancy. Notwithstanding, they did not assess dietary habits nor dietary patterns but concentrations of essential trace elements in maternal serum [25]. This approach based on blood, serum, plasma, and urine nutritional biomarkers can be complemented by the assessment of the actual dietary patterns used in the GESTAFIT project. The dietary approach better reflect food and nutrient consumption, and may therefore be suitable for assessing the relation between the diet quality and telomere length and for providing practical recommendations directly on the dietary habits of pregnant women [26].

Altogether, it seems that the diet quality, in combination with exercise, might prevent the placental RTL shortening in pregnant women, which might have implications for clinical pregnancy outcomes [2–6]. For instance, previous studies have shown associations of the RTL with intrauterine growth restriction, preterm birth and placental abruption [2–6]. In this study sample, we observed that women giving birth through cesarean section presented shorter RTL than their peers. However, our findings should be considered with caution given the non-randomized design of the trial and our limited sample size. Future research is needed to confirm or contrast our findings.

6. Conclusion

This study indicates that placental telomere length might be positively influenced by lifestyle factors such as diet combined with exercise during gestation. Future studies should elucidate the concerning potential role of placental RTL for child health. The interaction between exercise and MD could lead to longer placental RTL, although larger randomized controlled trials should formally test this hypothesis.

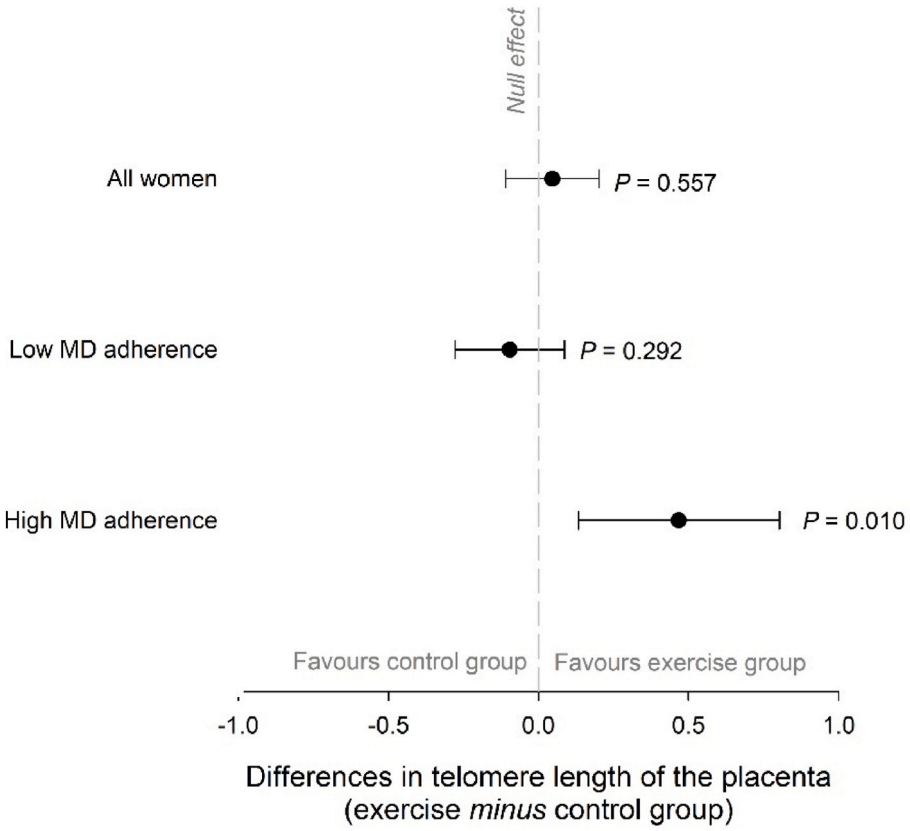

Fig. 1. Differences in placental relative telomere length (RTL) according to exercise intervention and the degree of adherence to the Mediterranean diet (low Mediterranean diet adherence vs high Mediterranean diet). Model adjusted for maternal age, gestational week at birth, sex of the baby and smoking habit. MD, Mediterranean diet.

Trial registration

NCT02582567; Date of registration: 20/10/2015. https://clinicaltrials.gov/ct2/show/NCT02582567?term=GESTAFIT&rank=1.

Ethical statement

The study was conducted following the ethical guidelines of the Declaration of Helsinki, last modified in 2013. This study was approved by the Ethics Committee on Clinical Research of Granada, Regional Government of Andalusia, Spain (code: GESFIT-0448-N-15).

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Declaration of competing interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.placenta.2023.04.002.

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