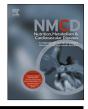
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Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd



# Influence of the degree of adherence to the mediterranean diet and its components on cardiometabolic risk during pregnancy. The GESTAFIT project



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Received 27 January 2021; received in revised form 7 April 2021; accepted 19 April 2021 Handling Editor: Dr. A. Siani Available online 4 May 2021

# **KEYWORDS**

Cardiometabolic risk; Dietary intake; Gestation; Mediterranean diet **Abstract** Background and aims: Studies regarding dietary patterns and cardiometabolic risk markers during pregnancy are scarce. The aim of the present study was to analyse whether different degrees of adherence to the Mediterranean diet (MD) and the MD components were associated with cardiometabolic markers and a clustered cardiometabolic risk during pregnancy. Methods and results: This study comprised 119 pregnant women from the GEStation and FITness (GESTAFIT) project. Dietary habits were assessed with a food frequency questionnaire at the 16th and 34th gestational weeks (g.w.). The Mediterranean Diet Score was employed to assess MD adherence. The following cardiometabolic markers were assessed: pre-pregnancy body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting glucose, triglycerides and high-density lipoprotein cholesterol (HDL-C). A greater MD adherence was associated with a better cardiometabolic status in cross-sectional (16th g.w. and 34th g.w.) and prospective analyses (MD adherence at the 16th g.w. and cardiometabolic markers at the 34th g.w.; SBP, DBP and HDL-C; all, p < 0.05). Participants with the highest MD adherence (Tertile 3) had a lower clustered cardiometabolic risk than those with the lowest MD adherence (Tertile 1) at the 16th and 34th g.w. (both, p < 0.05). A higher intake of fruits, vegetables and fish and a lower intake of refined cereals and red meat and subproducts were associated with a lower cardiometabolic risk during pregnancy (all, p < 0.05).

*Conclusion:* A higher MD adherence, a greater intake of fruits, vegetables and fish and a lower intake of refined cereals and red meat and subproducts showed a cardioprotective effect throughout gestation.

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Abbreviations: BMI, Body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein-cholesterol; MD, Mediterranean diet.

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https://doi.org/10.1016/j.numecd.2021.04.019

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## Introduction

During pregnancy, essential cardiometabolic changes occur in order to allow foetal growth [1]. Nevertheless, an inadequate adaptation to these changes (i.e. adverse cardiometabolic markers, including high level of triglycerides, glucose, high blood pressure, maternal obesity and low levels of high-density lipoprotein cholesterol [HDL-C]), may result in an increased risk of cardiometabolic diseases, such as gestational hypertension, preeclampsia and gestational diabetes mellitus [1–3].

Dietary patterns during gestation are potential modifiable behaviours that may exert a positive influence on pregnancy cardiometabolic markers [1]. In this regard, the Mediterranean diet (MD) has been associated with a better cardiometabolic status and a lower cardiometabolic risk in adult population [4–9]. Notwithstanding, studies regarding dietary patterns and cardiometabolic risk markers during pregnancy are scarce [1,10]. For instance, a Mediterraneanstyle diet in pregnancy has been associated with a lower risk of gestational diabetes [10]: a dietary pattern characterized by a high intake of fruits, vegetables, whole grains, low fat dairy, breakfast bars and water has been associated with lower maternal glucose levels and insulin resistance [1]; the Dietary Approaches to Stop Hypertension scorebased method has been associated with lower levels of maternal triglycerides [1], better glucose tolerance, blood pressure and overall lipid profile [11]; and a dietary pattern comprising a high intake of vegetables, vegetable oils, pasta, rice, fish and legumes, a moderate intake of alcohol and a low intake of sweets has been associated with lower maternal blood pressure [12]. Importantly, pregnant women with a worse metabolic profile are more likely to have adverse maternal (preterm delivery, preeclampsia or gestational diabetes mellitus) and foetal (small/large for gestational age, neonatal asphyxia or foetal demise) outcomes [2]. Therefore, the main aim of the present study was to explore whether different degrees of adherence to the MD were associated with cardiometabolic markers and a clustered cardiometabolic risk in pregnant women. A secondary, exploratory aim was to study the association of specific MD components with this clustered cardiometabolic risk.

## Methods

## Study design and participants

The present longitudinal study is part of the GEStation and FITness (GESTAFIT) project, where a novel exercise intervention was conducted [13]. The complete methodology of this project (including the eligibility criteria and the sample size calculation) has been published elsewhere [13]. The sample size was only determined for the primary outcome of the GESTAFIT project (maternal weight gains and maternal/neonatal glycaemic profile) resulting in 52 pregnant women (26 per group) [13]. This study was approved by the Ethics Committee on Clinical Research of Granada, Regional Government of Andalusia, Spain (code:

GESFIT-0448-N-15). Of the 384 pregnant women assessed for eligibility, 159 were recruited (Supplementary Fig. S1) and signed a written informed consent.

The evaluation procedures were performed on 2 nonconsecutive days. At the 16th gestational week (g.w.), data on nutritional and clinical information (e.g. smoking habit and alcohol intake) were gathered through face-to-face interviews by trained staff. In addition, blood pressure and body composition were assessed (in the same order as mentioned). On the second appointment, participants attended our research centre for blood sample extractions. At the 34th g.w., a second assessment was carried out where trained staff gathered the same information as they previously did.

## **Exercise** intervention

The exercise program carried out in the GESTAFIT project was designed following the standards of the American College of Obstetricians and Gynecologists [14] and has been previously detailed [15,16]. Briefly, women randomized into the exercise group followed a concurrent exercise program (60 min/session, 3 days/week of combined aerobic and strength training) from the 17th g.w. until delivery.

## **Control group**

Pregnant women allocated to the control group did not participate in the training sessions and were asked to continue with their usual activities. For ethical reasons, the research team held a series of conferences to address the importance of physical activity and healthy dietary habits during pregnancy (Appendix A).

Both the control and exercise groups attended these conferences.

#### Maternal anthropometry and body composition

At the first evaluation, height was measured using a stadiometer (Seca 22, Hamburg, Germany). Pre-pregnancy body weight (kg) was self-reported. These values were used to calculate the pre-pregnancy body mass index (BMI), as weight (kg) divided by squared height (m<sup>2</sup>). The pre-pregnancy weight status classified based on the selfreported pre-pregnancy weight and height has been previously validated [17].

## Vascular function

A blood pressure monitor (M6 upper arm blood pressure monitor Omron. Omron Health Care Europe B.V. Hoolddorp, The Netherlands) was used to assess systolic blood pressure (SBP) and diastolic blood pressure (DBP), which were measured after 5 min of rest on two separate occasions (with 2 min between trials) with the person seated. Both values were recorded, although only the lowest value of the two trials was selected for the analysis.

## **Biochemical markers**

Venous blood samples (5 mL) after all night fasting were collected in serum tubes. The blood sample was allowed to clot (coagulation) at room temperature for 30 min. Then, samples were centrifuged at 1750 rpm during 10 min at 4 °C in a refrigerated centrifuge (GS-6R Beckman Coulter, Brea, CA, USA) to obtain serum. Glucose, triglycerides and HDL-C were assessed with standard procedures using an auto-analyser (AU5822 Clinical Chemistry Analyzer, Beckman Coulter, Brea, CA, USA).

## **Clustered cardiometabolic risk**

A clustered cardiometabolic risk (Z-score) was created as the mean of the standardized scores [(value - mean)/ standard deviation] of pre-pregnancy BMI, mean blood pressure [defined as (SBP + DBP)/2], serum fasting glucose, triglycerides and HDL-C, since these factors have been previously employed as a cluster of metabolic risk factors during pregnancy [2]. For variables characterized by a lower metabolic risk with increasing values (HDL-C), zscores were multiplied by - 1. A higher clustered cardiometabolic status indicates a higher cardiometabolic risk.

# Physical activity levels

Participants were asked to wear a tri-axial accelerometer attached to their waist (Actigraph GT3X+, Pensacola, Florida, US) for 9e consecutive days, 24 h/day [18]. The total physical activity (min/day) was calculated.

## Dietary assessment and mediterranean diet adherence

A validated food frequency questionnaire designed by Mataix et al. [19] was administered to participants by a trained nutritionist at the 16th and 34th g.w. asking about their dietary habits.

## Mediterranean diet adherence

The Mediterranean Diet Score was used to assess MD adherence [20]. It was calculated by using dietary data obtained from a food frequency questionnaire [19]. The Mediterranean Diet Score consists of eleven variables (whole-grain cereals, potatoes, fruits, vegetables, pulses, fish, olive oil, red wine, red meat and subproducts, poultry and whole dairy products) ranging from 0 to 5 according to their position in the MD pyramid [21]. The total score ranges from 0 to 55, with higher values indicating a greater adherence to the MD, and therefore, higher diet quality. A moderate alcohol intake, also typical of the MD, was not considered for calculating the index in this group of women, as they must not drink alcohol during this period. Therefore, the maximum score considered for these analyses in pregnant women was 50 points. Because there are no available pre-specified cut-off points for pregnant population, the Mediterranean Diet Score was divided into tertiles with participants being categorized as having low, medium or high MD adherence (Tertile 1, Tertile 2 and Tertile 3, respectively).

## Statistical analysis

Descriptive statistics (mean  $\pm$  standard deviation for quantitative variables and number of women [%] for categorical variables) were used to describe sociodemographic and clinical characteristics of the study participants at baseline (16th g.w.). Nominal variables were analysed by using the chi-squared test.

Linear regression analyses after adjusting for maternal age, smoking habit (at the 16th and 34th g.w.) and the exercise intervention (at the 34th g.w.) were used to explore cross-sectional associations of MD adherence with cardiometabolic risk biomarkers and clustered cardiometabolic risk at the 16th (n = 119) and 34th g.w (n = 103). In addition, prospective analyses (n = 107) were performed to analyse the association of the MD adherence at the 16th g.w. with cardiometabolic risk biomarkers and the 34th g.w. The statistical power analyses showed statistical power of 95% to detect small-to-medium association sizes at the 16th g.w. (n = 119, minimum detectable  $f^2 = 0.11$ ) and at the 34th g.w. (n = 103, minimum detectable  $f^2 = 0.13$ ) [22].

The Mediterranean Diet Score was divided into tertiles. Subsequently, the clustered cardiometabolic risk was compared across the tertiles by a one-way analysis of covariance (ANCOVA) after adjusting for maternal age, smoking habit (at the 16th and 34th g.w.) and the exercise intervention (at the 34th g.w.) for both, crosssectional and prospective associations. Post-hoc multiple comparisons (Bonferroni's correction) were applied to examine pairwise differences between groups (e.g. Tertile 1 vs. Tertile 3).

Linear regression analyses after adjusting for maternal age, smoking habit (at the 16th and 34th g.w.) and the exercise intervention (at the 34th g.w.) were used to explore cross-sectional and prospective associations of the MD adherence with the clustered cardiometabolic risk at the 16th and 34th g.w.

A paired Student's t-test was performed to explore differences in total physical activity levels, body weight, MD components and MD adherence of pregnant women by g.w. (16th versus 34th g.w.).

The Benjamini–Hochberg procedure [23] was applied to account for the random effect in multiple comparisons for all the tests included in the primary analysis (i.e. MD adherence associations with cardiometabolic risk biomarkers and clustered cardiometabolic risk), and separately for all the tests included in the dietary habits analysis (i.e. dietary habits associations with clustered cardiometabolic risk) with q = 0.05.

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  $p \leq 0.05$ .

## Results

The total sample size for the present analyses comprised 119 Caucasian pregnant women  $(33.2 \pm 4.4 \text{ years}, \text{ pre-pregnancy BMI } 24.1 \pm 4.1 \text{ kg/m}^2)$  who had valid data in the food frequency questionnaire [19], vascular function, biochemical markers and body composition measurements (Supplementary Fig. S1). The descriptive characteristics of the study sample according to the tertiles of MD adherence are shown in Table 1.

Differences in total physical activity, body weight, dietary habits and MD adherence of pregnant women by g.w. (16th versus 34th g.w.) are shown in Supplementary Table S1. At the 34th g.w. pregnant women had lower levels of total physical activity (p=0.001), higher body weight (p=0.001), a higher intake of fruits (p=0.007) and vegetables with evidence of statistical significance (p=0.057) compared to the 16th g.w.

The association of MD adherence, cardiometabolic risk biomarkers and clustered cardiometabolic risk are shown in Table 2. The cross-sectional analyses showed that a greater adherence to the MD at the 16th g.w. was associated with lower pre-pregnancy BMI, SBP, greater HDL-C and a lower clustered cardiometabolic risk (all, p < 0.05). At the 34th g.w. a higher MD adherence was associated with lower SBP, DBP, higher HDL-C and a lower clustered cardiometabolic risk (all, p < 0.05). Regarding the prospective analyses, a greater MD adherence at the 16th g.w. was associated with lower pre-pregnancy BMI, SBP, DBP, triglycerides, higher HDL-C and a lower clustered cardiometabolic risk at the 34th g.w. (all, p < 0.05). We

**Table 1** Descriptive characteristics of the study participants at baseline (n - 119)

performed an additional analysis adjusting for objectively measured total physical activity (min/day) and educational status but results remained the same (data not shown). After correcting for multiplicity, we observed that the cross—sectional associations between MD adherence (at the 16th g.w.) and BMI and the prospective associations between MD adherence (at the 16th g.w.) and BMI, DBP and triglycerides (at the 34th g.w.) became non-significant.

The clustered cardiometabolic risk profile (Z-score) by the tertiles of the Mediterranean Diet Score is shown in Fig. 1. In the cross-sectional analyses, the group with the highest MD adherence (Tertile 3) had a lower cardiometabolic risk than the group with the lowest MD adherence (Tertile 1) at both, the 16th and 34th g.w. (*Ptrend* = 0.028 and *P*-*trend* = 0.002, respectively). In addition, the prospective analyses showed that participants with the highest adherence to the MD (Tertile 3) had a lower cardiometabolic risk than those participants with low (Tertile 1) and medium (Tertile 2) MD adherence (*Ptrend*<0.001).

The associations of MD components with the clustered cardiometabolic risk (Z-score) at the 16th and the 34th g.w. are shown in Table 3. In the cross-sectional analyses, a higher intake of fruits and fish and a lower intake of red meat and subproducts were associated with a lower clustered cardiometabolic risk at the 16th g.w. (all, p < 0.05). At the 34th g.w., a greater intake of fruits was associated with a lower clustered cardiometabolic risk and subproducts and white bread and rice were associated with a higher clustered cardiometabolic risk (all, p < 0.05). The prospective

Variable	Total cohort ( $n = 119$ )	Tertile 1 $(n = 40)$	Tertile 2 ( $n = 45$ )	Tertile 3 ( $n = 34$ )	р
Age (years)	33.2 (4.4)	32.9 (4.1)	34.1 (4.4)	32.6 (4.8)	0.269
Pre-pregnancy weight (kg)	65.1 (12.2)	66.9 (13.4)	64.1 (10.7)	64.3 (12.6)	0.520
Pre-pregnancy BMI (kg/m <sup>2</sup> )	24.1 (4.1)	24.8 (4.7)	24.2 (3.9)	23.2 (3.7)	0.240
Underweight	3 (2.5)	1 (2.5)	1 (2.2)	1 (2.9)	0.888
Normal weight	74 (62.2)	22 (55.0)	29 (64.4)	23 (67.6)	
Overweight	30 (25.2)	11 (27.5)	11 (24.4)	8 (23.5)	
Obese	12 (10.1)	6 (15.0)	4 (8.9)	2 (5.9)	
Mediterranean diet adherence (0–50)	29.0 (4.0)	24.7 (2.1)	29.6 (1.1)	33.5 (1.6)	< 0.001
Vascular function					
Systolic blood pressure (mmHg)	107.8 (9.3)	109.0 (9.9)	108.2 (8.8)	105.9 (9.2)	0.336
Diastolic blood pressure (mmHg)	64.3 (7.9)	65.2 (8.9)	64.9 (7.7)	62.3 (6.8)	0.226
Glycaemic and lipid profile					
Fasting glucose (mg/dL)	77.4 (15.9)	77.0 (6.7)	78.3 (15.4)	76.7 (23.1)	0.897
HDL-cholesterol (mg/dL)	68.2 (11.4)	63.2 (9.9)	70.9 (11.3)	70.4 (11.7)	0.003
Triglycerides (mg/dL)	121.3 (48.9)	130.2 (50.4)	117.7 (49.8)	115.5 (45.5)	0.362
Educational Status	n (%)				
Low educational status	13 (10.9)	6 (15.0)	2 (4.4)	5 (14.7)	0.125
Medium educational status	36 (30.3)	13 (32.5)	10 (22.2)	13 (38.2)	
High educational status	70 (58.8)	21 (52.5)	33 (73.3)	16 (47.1)	
Smoking habit					
Current smoker	10 (8.4)	5 (12.5)	3 (6.7)	2 (5.9)	0.088
Former smoker	44 (37.0)	9 (22.5)	23 (51.1)	12 (35.3)	
Never smoker	65 (54.6)	26 (65.0)	19 (42.2)	20 (58.8)	
Alcohol consumption (no)	119 (100)	-	-	-	
Taking nutritional supplements (yes)	102 (85.7)	31 (77.5)	39 (86.7)	32 (94.1)	0.123

SD, Standard deviation. BMI, body mass index; HDL, high-density lipoprotein.

Table 2 Association of Mediterranean diet adherence, cardiometabolic risk biomarkers and clustered cardiometabolic risk during pregnancy.

	Cross-sectional associations		Prospective associations			
	16th gestational week $(n = 119)$	34th gestational week $(n = 103)$	Diet in week 16th a	and outcomes in week 34th (n	n = 107)	
Cardiometabolic risk biomarkers	Standardized Coefficients (β)	p <sup>a</sup>	Standardized Coefficients (β)	p <sup>b</sup> Standardized Coefficients (β)	p <sup>b</sup>	
Pre-pregnancy BMI	-0.196	0.034	-0.139	0.161 -0.199	0.041	
SBP	-0.225	0.015	-0.284	<b>0.003</b> -0.260	0.007	
DBP	-0.166	0.073	-0.240	<b>0.015</b> -0.198	0.044	
Glucose	-0.022	0.813	-0.145	0.139 -0.171	0.079	
Triglycerides	-0.149	0.109	-0.073	0.465 -0.194	0.047	
HDL-C	0.299	0.001	0.267	<b>0.004</b> 0.348	< 0.001	
Cardiometabolic risk						
Clustered cardiometaboli risk*	<i>c</i> –0.309	0.001	-0.332	<b>0.001</b> -0.428	< 0.001	

<sup>a</sup> Model adjusted for maternal age and smoking habit.

<sup>b</sup> Model additionally adjusted for exercise intervention. Bold values indicate those outcomes which surpassed the multiple comparison test. BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure. \*A higher clustered cardiometabolic status entails higher cardiometabolic risk.

analyses showed that a greater intake of fruits, vegetables, fish and pulses at the 16th g.w. was associated with a lower cardiometabolic risk at the 34th g.w. (all, p < 0.05). Of note, after correcting for multiplicity, we could observe that the associations between fruits and the clustered cardiometabolic risk throughout gestation remained significant. In addition, the cross—sectional association between red meat and subproducts and cardiometabolic risk (at the 34th g.w.) remained significant.

### Discussion

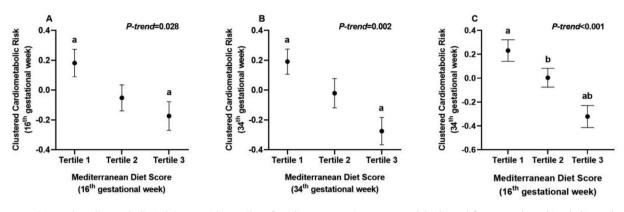
Our results suggest that the MD adherence was associated with most of the studied cardiometabolic markers throughout pregnancy. Moreover, a clear cardioprotective effect was observed across gestation only when the highest MD adherence was reached (Tertile 3) regardless of potential confounders such as age, smoking habit and exercise. In addition, a higher intake of fruits, vegetables and fish and a lower intake of refined cereals and red meat and subproducts were associated with a lower cardiometabolic risk during gestation. Of note, individual associations between food groups and cardiometabolic risk were less significant than the association between the MD adherence and the cardiometabolic risk.

The lifestyle habits, sociodemographic and clinical characteristics of the study sample were similar to those observed in previous epidemiological studies conducted in Spanish [24–26] and non-Spanish [1] pregnant populations in the same age range. Regarding pre-pregnancy body composition of the study sample (pre-pregnancy BMI (23.2 kg/m<sup>2</sup>)), it was similar to that observed by Martin et al. [1] in which pregnant women with the highest adherence (Tertile 3) to the Dietary Approaches to Stop Hypertension score-based method had a pre-pregnancy BMI of 22.8 kg/m<sup>2</sup> [1]. In addition, a recent study [24] conducted in Spain reported that 37% of

pregnant women were overweight/obese prior to pregnancy, similar to our results (35%). Comparing the early second trimester (16th g.w.) with the third trimester (34th g.w.) we observed a higher intake of fruits and vegetables as previously reported [26]. However, no differences were found regarding MD adherence, suggesting that food behaviours remained unchanged during pregnancy in accordance with previous evidence [26]. Additionally, we found that women had lower total physical activity levels at the third trimester of pregnancy than that at the early second trimester of pregnancy. This is in line with previous evidence that suggested that physical activity levels decrease along gestation [27]. In particular, it has been shown [24] that between the second and the third trimester of pregnancy, there was a decrease in physical activity (assessed with the International Physical Activity Questionnaire), which is highly in agreement with our findings. In this regard, the high prevalence of overweight and obesity prior to pregnancy and the decreasing time spent in total physical activity might imply a higher cardiometabolic risk in this population [1,28,29].

In this context, previous studies [1,3,11,12] have suggested that specific maternal dietary patterns (comprising a high intake of vegetables, fruits, whole grains, fish and nuts and a low consumption of meat, saturated fats and refined grains) are associated with better results in cardiometabolic markers, including triglycerides, glucose, blood pressure and cholesterol. Similarly, we found that the MD adherence was associated with a lower blood pressure and higher HDL-C at the 16th and 34th g.w.

Compelling evidence [30,31] indicates that some dietary strategies were effective for preventing cardiovascular diseases (CVD) in a non-pregnant population, including an increasing intake of omega-3 fatty acids from fish and a high consumption of fruits, vegetables, nuts and wholegrain cereals and with a low intake of refined cereals. A Mediterranean dietary pattern has long been associated with a lower incidence of CVD in the general population



**Figure 1** Clustered cardiometabolic risk (z-score) by tertiles of Mediterranean Diet Score. Model adjusted for age and smoking habit at the 16th gestational week. The model was additionally adjusted for exercise intervention at the 34th gestational week. Dots represent mean and bars represent standard error. <sup>ab</sup>Superscript indicates a significant difference (p < 0.05) between groups with the same letter. Pairwise comparisons were performed with Bonferroni's adjustment (A) Clustered cardiometabolic risk by tertiles of Mediterranean Diet Score at the 16th gestational week (B) Clustered cardiometabolic risk by tertiles of Mediterranean Diet Score at the 34th gestational week. A higher clustered cardiometabolic status entails higher cardiometabolic risk.

[6]. Notwithstanding, a recent systematic review and metaanalysis [32] concluded that there is still some uncertainty regarding the effects of a Mediterranean-style diet on CVD and cardiometabolic risk factors for both primary and secondary CVD prevention. Therefore, it is clinically relevant to determine the appropriate degree of adherence in which the aforementioned cardiovascular protection could be reached in pregnant women. This is especially important as recent studies suggest that pregnant women are drifting away from the MD-like pattern [26,33].

It has been recently proposed that women with several cardiometabolic risk factors during pregnancy have a higher risk of adverse pregnancy outcomes [2]. When we further explored the association between MD and the clustered cardiometabolic risk (Z-score) we found that a

higher MD adherence was associated with a better clustered cardiometabolic status throughout the pregnancy course. This could be explained because this traditional dietary pattern (typical among Mediterranean regions, including Spain) has been suggested as an ideal model for CVD prevention [34,35]. Interestingly, a clear cardioprotective effect throughout pregnancy was only observed when the highest MD adherence was reached (Tertile 3) regardless of potential confounders such as age, smoking habit or exercise. This is in agreement with previous evidence in non-pregnant adult population [36,37], suggesting that a higher adherence to the MD promoted cardioprotective effects.

A recent systematic review [38], where five MD assessment indices were compared, showed that the

Food groups	Cross-section	Prospective associations					
	16th gestational week (n = 119)		34th gestati (n = 103)	34th gestational week (n = 103)		Diet at the 16th gestational week and cardiometabolic risk at the 34th gestational week ( $n = 107$ )	
	β	P <sup>a</sup>	β	$p^{\mathbf{b}}$	β	$p^{\mathbf{b}}$	
Whole-grain cereals (s/week)	-0.152	0.106	-0.197	0.055	-0.186	0.065	
White bread and rice (s/week)	0.136	0.153	0.263	0.010	0.134	0.176	
Potatoes (s/week)	-0.004	0.963	0.062	0.951	-0.004	0.997	
Fruits (s/week)	-0.255	0.006	-0.341	0.001	-0.318	0.001	
Vegetables (s/week)	-0.022	0.814	-0.108	0.285	-0.255	0.009	
Pulses (s/week)	0.054	0.563	-0.079	0.447	-0.208	0.034	
Fish (s/week)	-0.209	0.032	-0.047	0.657	-0.189	0.064	
Red meat and subproducts (s/week)	0.208	0.025	0.350	< 0.001	0.149	0.131	
Poultry (s/week)	0.159	0.088	0.118	0.257	0.047	0.639	
Dairy products (s/week)	-0.014	0.884	-0.093	0.364	0.064	0.526	
Olive oil (s/week)	0.027	0.785	-0.040	0.703	0.074	0.473	

<sup>a</sup> Model adjusted for maternal age and smoking habit.

<sup>b</sup> Model additionally adjusted for exercise intervention. Bold values indicate those outcomes which surpassed the multiple comparison test. BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure. A higher clustered cardiometabolic status entails higher cardiometabolic risk. Mediterranean Diet Score provides the best evidence of MD adherence. Consequently, we decided to employ this dietary index to assess MD adherence in this study sample. Notwithstanding, to accomplish the second objective of the present study, we analysed the association between individual components of the Mediterranean dietary pattern and a clustered cardiometabolic risk previously employed in pregnant women [2]. We confirmed that components which are suggested to be protective against CVD [30], including fruits, vegetables and fish were associated with a lower clustered cardiometabolic risk, and those supposed to be detrimental for CVD [39], including red meat and subproducts and refined cereals, were associated with a greater clustered cardiometabolic risk in this specific population.

## Limitation and strengths

The present study has some limitations. First, as this is a longitudinal study, causality cannot be concluded. Second, the results should be interpreted cautiously, as we could be limited to detect small association sizes. Larger studies should further explore these associations in order to corroborate our results. Regarding strengths, we assessed dietary habits and cardiometabolic status in both, the 16th and 34th g.w., and we employed a widely used Mediterranean Diet Score. In addition, we included a wide range of cardiometabolic factors within the overall risk score created, which strengthen the usefulness of our results.

## Conclusion

Overall, our results indicate that a higher MD adherence could be associated with better cardiometabolic markers and a cardioprotective effect throughout gestation. Regarding MD components, a higher intake of fruits, vegetables and fish and a lower intake of refined cereals and red meat and subproducts might be associated with lower cardiometabolic risk during pregnancy.

## Role of the funding source

The study was funded by the Regional Ministry of Health of the Junta de Andalucía (PI-0395-2016) and the University of Granada, Unit of Excellence on Exercise and Health (UCEES). MFA was additionally funded by the Spanish Ministry of Education, Culture and Sports (Grant number FPU17/03715). The funders of the study had no role in the design of the study, data collection, data analysis or data interpretation. This study is included in the thesis of MFA enrolled in the Doctoral Programme in Nutrition and Food Sciences of the University of Granada.

# Author contributions

Marta Flor-Alemany: conceptualization, methodology, validation, investigation, data curation, writing – original

draft preparation, writing — review and editing. Pedro Acosta: validation, investigation, data curation, writing review and editing. Nuria Marín-Jiménez: validation, investigation, writing — review and editing. Laura Baena-García: validation, investigation, writing — review and editing. Pilar Aranda: validation, writing — review and editing. Virginia A Aparicio: conceptualization, methodology, validation, resources, data curation, writing — original draft preparation, writing — review and editing, project administration and funding acquisition.

## **Declaration of competing interest**

None of the authors have any conflict of interests.

## Acknowledgments

We are grateful to Ms. Ana Yara Postigo-Fuentes for her assistance with the English language.

# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2021.04.019.

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