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Original article

Discrepancies among different tools evaluating Mediterranean diet adherence during pregnancy, correlated to maternal anthropometric, dietary and biochemical characteristics

Tatiana Papazian [a, b], Aya Serhal [b], Hala Hout [b], Hassan Younes [b, c], Georges Abi Tayeh [d], Joseph Azouri [e], Fabienne Hajj Moussa Lteif [a], Assaad Kesrouani [d], Lydia Rabbaa Khabbaz [a, *]

[a] *Laboratoire de pharmacologie, pharmacie clinique et contrôle de qualité des médicaments, Faculty of Pharmacy, Saint-Joseph University of Beirut, Beirut, Lebanon*
[b] *Department of Nutrition, Faculty of Pharmacy, Saint-Joseph University of Beirut, Beirut, Lebanon*
[c] *Department of Nutrition and Health Sciences, Institut Polytechnique LaSalle Beauvais, France*
[d] *Department of Gynecology and Obstetrics, Hôtel-Dieu de France Hospital, Beirut, Lebanon*
[e] *Department of Gynecology and Obstetrics, Mont-Liban Hospital, Beirut, Lebanon*

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SUMMARY

Background & aims: Scientific evidence confirms the favorable impact of Mediterranean diets (MD) on maternal and neonatal outcomes. However, the assessment of this dietary pattern requires valid indexes with scoring systems adapted to pregnant females. The aim of this cross-sectional study was to compare the adherence to MD, through 5 internationally validated tools, in pregnant women following a Mediterranean eating pattern, correlated to maternal anthropometric, dietary and biochemical markers.
Methods: 100 healthy pregnant females completed a sociodemographic questionnaire, a dietary recall and a food frequency questionnaire compatible with the MD. 10 ml of maternal blood were drawn for the analysis of biological markers such as C-reactive protein (CRP), leptin and adiponectin.
Results: We used the 50th percentile as cut-off of each scale (low or high adherence) to avoid the discrepancies noted in the literature among the large range of cut-offs points for the different tools. The % of agreement was high between the Mediterranean Food Pattern, MD Score, the MD Score and the Short MD Questionnaire. The MD Scale presented small agreement in relation to the other tested tools. All the tested indexes were significantly correlated with CRP levels, except for the MDScale. Significant correlations were reached regarding adiponectin and the MFP (p value = 0.04) and the MDScale (p value 0.03) tools. Pre-gestational body mass index was significantly correlated with all the tested biological markers. **S**ignificant correlations were seen between CRP on one hand and maternal age (p value = 0.033), adiponectin (p value = 0.028), and leptin (p value = 0.003) on the other. Fiber intake was significantly and negatively correlated to CRP (p value = 0.008) and positively to adiponectin levels (p value = 0.000).
Conclusions: None of the tested tools were adapted for pregnancy, since a-priori scores were attributed for components already not consumed by pregnant females such as alcohol or recommended for daily or weekly consumptions such as whole dairy products and fish, respectively. In addition, the lack of inclusion of some traditional food ingredients of the MD implies the urge to create a new index adapted to pregnancy.

Abbreviations: FFQ, Food frequency questionnaires; MD, Mediterranean diet; BMI, Body mass index; MWG, Maternal weight gain; MFP, Mediterranean Food Pattern; CRP, C-reactive protein; WHO, World health organization; IOM, Institute of Medicine; MDS, Mediterranean diet score; MedDietScore, The Mediterranean diet score; SMDQ, Short Mediterranean diet questionnaire; MDScale, Mediterranean diet scale.

* Corresponding author. Laboratoire de Pharmacologie, Pharmacie clinique et Contrôle de qualité des Médicaments, Faculté de pharmacie, Campus des Sciences médicales (CSM), Université Saint-Joseph, Rue de Damas, B.P. 11-5076, Riad el Solh, Beirut, 1107 2180, Lebanon. Fax: +00961 1 421 022.
E-mail address: lydia.khabbaz@usj.edu.lb (L.R. Khabbaz).

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Introduction

The assessment of nutritional status during critical periods of life, such as pregnancy, is of great importance. The majority of studies in this field followed the approach of analyzing and using long dietary assessment tools such as food frequency questionnaires (FFQ) or food records to highlight the intake of every single nutrient. However, people do not eat isolated nutrients, but consume meals consisting of a variety of foods with complex combination of nutrients. Therefore, it has been suggested that global eating patterns and not unique nutrients should be evaluated since foods could have a synergistic and antagonistic effects on health [1]. Several observational and epidemiological studies have proved that high intake of fruits, vegetables, non-refined cereals, fish, nuts and olive oil is beneficial on health (1). The only diet that includes these characteristics is the Mediterranean diet (MD), rich in plant-based proteins, monounsaturated fatty acids, fibers, and antioxidants and containing low levels of cholesterol and saturated fats.

Pregnancy is a critical period in a woman's life, since neonatal and gestational outcomes are under the direct influence of genes, diet, pre-gestational body mass index (BMI), maternal weight gain (MWG), alcohol intake, tobacco use and inflammatory and biological markers [2]. Studies have proven that MD favorably modulates those outcomes with lower incidence of intrauterine growth restriction, prematurity and maternal hypertension/preeclampsia [3–6]. A recent cohort highlights the importance of studying the global eating pattern and not food groups or nutrients analysis in nutrition related epidemiology studies. Results of that study showed an inverse correlation between the high adherence of MD during pregnancy on offspring adiposity and fat mass [7].

The main difficulty in assessing the adherence to MD in the general population and specifically in pregnant women is choosing the most suitable questionnaire to use, since there is no international consensus on which MD questionnaire best reflects adherence among pregnant women. The disparities among the tools created in different research settings don't permit to rely on a single tool as a gold standard, since dietary patterns that make up MD may vary among countries and subgroups of populations [8].

Research examining MD adherence in pregnancy are limited and when published, authors used the questionnaire in the form adapted to the general population, without excluding questions not applicable to pregnant women, such as alcohol or without specifying if the question was removed and cut-off scores recalculated accordingly [9]. One exception is the tool created by Martinez-Gonzalez [10], the Mediterranean Food Pattern (MFP) that was used in pregnancy by Gesteiro et al., after excluding the question related to alcohol and readjusting the score accordingly [11]. However, in this study, authors did not change the cut-off, even though the original questionnaire of 14 items was reduced to 13.

The presence of systemic inflammation can be detected by measuring the levels of acute phase proteins, such as C-reactive protein (CRP). During pregnancy, physiological transformations, metabolic disturbances and MWG alter hormonal secretions from adipose tissue. Leptin and adiponectin are hormones implicated in fetal programming and are influenced by dietary patterns. Leptin is a hormone involved in satiety, obesity and cardiovascular disease, and increases during pregnancy; adiponectin enhances insulin sensitivity and tends to be negatively correlated with MWG, and decreases across gestational weeks [12].

The primary objective of this research was to compare the results of adherence to MD of pregnant Lebanese females, using five different internationally and widely published tools, of adherence to MD. As a second step, the research team decided to examine correlations between the results of each of those scores with maternal outcomes such as age, pre-gestational BMI, MWG, inflammatory marker (IM) CRP, and obesity and appetite related hormones such as leptin and adiponectin.

Materials and method

Study design

This present research is part of an ongoing cross-sectional one studying the impact of nutritional status and the adherence of MD during pregnancy on neonatal and gestational outcomes and IMs.

Study population

374 Lebanese pregnant women presenting to 5 private clinics in Beirut during their prenatal consultation were examined for eligibility, irrespective of their eating habits. 121 Lebanese singleton pregnant women, in their second trimester of pregnancy (between 14th and 27th week of gestation) and aged between 18 and 40 years were considered potentially eligible. After examining the following exclusion criteria: gestational diabetes, preeclampsia, chronic diseases affecting the nutritional status, flu-like symptoms, acute respiratory infection and dental problems (two weeks prior to the enrollment), 104 women were conformed eligible and participated in the study. However, 4 were excluded from the final analysis, because the follow-up conducted via telephone calls, throughout gestation, revealed that 3 patients developed gestational diabetes and 1 preeclampsia (flow chart provided as supplementary material 1). The sample size was determined by applying the formula published by Tabachnick and Fidell, taking into account the number of independent variables included in the regression model, as follows: $N = 50 + 8\,m$ (m being the number of independent variables) [13]. Pregestational BMI, lipids, fibers, adiponectin and leptin were the 5 independent variables used in the model. This lead to a minimum required sample size of 90 subjects. This number is similar to sample sizes in other comparable studies: Abreu et al. [14] assessed the predictors of MD adherence among 102 pregnant females in their second trimester; Pereira-da-Silva et al. studied the effect of pregestational BMI, dietary intakes during pregnancy and gestational weight gain on neonatal outcomes in 100 mother and infant pairs [15]. The research team decided to target pregnant women in their second trimester of pregnancy. This period was selected, because women are less prone to hormonal disturbances such as nausea and vomiting affecting their nutritional status. In addition, the first and last trimester of pregnancy are known as proinflammatory periods, where high levels of T helper and cytokines are observed, which is not the case during the second trimester of pregnancy where the immune response is no longer the predominant endocrine feature, and a symbiotic environment is present between the mother and the fetus [16].

Recruitment dates were from October 2016 and March 2017. Field work was conducted by a registered dietitian.

Study material

The research team had previously developed and validated a 157 item FFQ, composed of foods highly representative of the Mediterranean eating pattern, among pregnant Lebanese females [17]. It includes 12 categories of food groups subdivided as follows: Bread and cereals (12 items), Rice, pasta, potato and legumes (14 items), Milk and dairy products (9 items), Fruit and fruit juices (10 items), vegetables (12 items), Meat, poultry, fish, eggs and ham (25 items), nuts and condiments (16 items), Sugar based sweets, desserts and jams (23 items), Bakery products (11 items), Salty snacks (3 items), Oils and fats (9 items), and Beverages (13 items).

MD tools were selected after a thorough literature review of articles measuring the adherence to this dietary pattern. Electronic searches were carried out using the following international databases: MEDLINE, Scopus, Web of Science and EMBASE. The search strategy was designed to obtain original studies about the development or validation of scores measuring adherence to MD, published until September 2016.

The combination of the following keywords was used: Mediterranean diet, Mediterranean score and adherence to Mediterranean diet. The tools elaborated in Canada, USA and Japan, were disregarded since the eating habits and food groups do not represent our population's. Finally, tools selected were elaborated in 4 different countries where eating habits are similar to Lebanon. The first and most widely used score (MDScale) created by Trichopoulou et al. initially in 1995 and then updated in 2002 was selected. The scores created by Panagiotakos et al. in Greece (MedDietScore) and Martinez-Gonzalez et al. in Spain (MFP) were also selected because their concurrent and predictive validity is well reported in previous publications. The Mediterranean diet score (MDS), created and applied by Leighton et al. in the Chile was also selected because avocado, olive and canola oil are included separately as food components only in that tool and those food items are common in the Lebanese modern cuisine. Finally, we selected the SMDQ score created by Zito et al. because it represents Italian food habits and because it is the shortest one, thus not-time consuming and practical to be used. A comparative table presents the details regarding the food categories and the scoring system of each of the tested tools (Table provided as supplementary material 2).

A written approval was solicited by email from each corresponding author of those scales.

Face-to-face interviews conducted by a registered dietitian with the participants, helped in collecting basic sociodemographic data, dietary intakes thru the validated questionnaires, FFQ and a 24 h dietary recall. Even though no direct question about palatability of the different components was asked, palatability would be reflected by a change in the dietary habits of the pregnant women, which was taken into account in the general questionnaire. Anthropometrical measurements such as weight before conception and height were taken from the medical files. BMI was calculated as the ratio of pre-gestational weight in kilograms to the square of height in meter. It was then categorized according to the WHO cut-off points (underweight<18.5, normal 18.5 to 24.9, overweight 25 to 29.9 and obese > 30) [18].

Participants were provided pictures of local food portions, plastic food models, measuring cups and spoons to estimate usual quantity of foods consumed. Values of serving sizes and frequency of consumption obtained from the dietary data (FFQ and dietary recall) were converted into nutrients and caloric intake estimates, by a special software (Nutrilog 2.30). Briefly, the weight in grams of each food was multiplied by its frequency of consumption, and divided for example by 7, if it was consumed just once a week, and incorporated in the software data. Following this analysis, serving sizes of each food item were derived and inserted in the calculation of the score for the different tools.

A follow-up via telephone calls once a month was maintained with all the participants, during the course of their pregnancy to note health related complications such as preeclampsia and gestational diabetes. MWG was calculated as the difference between the weight at the delivery and the weight before conception. It was then categorized according to the 2009 Institute of Medicine (IOM) guidelines as insufficient, adequate or excessive weight gain [19]. Gestational and neonatal outcomes were copied directly from the medical files, post-delivery, in order not to end-up with irrelevant data.

Methods of calculating each score

Mediterranean food pattern (MFP) [10]

Martinez-Gonzalez et al. introduced this tool in 2012, after being used in a large Spanish cohort, the PREDIMED study, between 2003 and 2009, with over 7000 participants. It addresses 14 questions related to the Mediterranean eating pattern. A value of 1 is attributed for each positive response directly, without referring to a FFQ, since this scale addresses direct questions concerning specific serving sizes for nuts, olive oil, butter, margarine, animal protein sources, wine, fruit, beans, legumes, sugar sweetened beverages, pastries and fish. A score of 9 or above is an indicator of adequate MD adherence. In the PREDIMED study, values were distributed as follows: 0–5, 6–9, and greater or equal to 10 respectively for low, average and high adherence. We omitted the question regarding alcohol intake, as done by Gesteiro et al., who used the same questionnaire in pregnant women, excluding the question regarding wine intake and suggested a single cut–off point equal or less than 7 [11].

Mediterranean diet score (MDS) [20]

Although this tool was created and applied by Leighton F. et al. in a country far away from the Mediterranean region, the Chile, it is a validated questionnaire measuring adherence to the MD. Our research team was interested in testing it on our sample, since avocado, olive and canola oil and vegetable oil were included separately as food components in that tool; those food items are common in our Lebanese modern cuisine. The grading system was different compared to the other scores, since it permitted to assign a value of 0, 0.5 or 1 depending on the serving consumed per day or per week. No cut-off points were assigned by the developers of this tool, only a mention of a final score ranging from 0 to 14, indicating respectively low and high adherence to MD. Once more, the question related to wine intake (≤1 glass/day) was deleted in our study, ending up with scores ranging from 0 to 13.

The Mediterranean diet score (MedDietScore) [21]

Created by Panagiotakos et al., in 2006, this tool has been validated among more than 3000 Greeks, during 2001 and 2002, in ATTICA study. 11 food groups representative of the MD pyramid were consigned values ranging from 0 to 5 depending on their frequency of consumption per month, distributed as follows: never, 1–4, 5–8, 9–12, 13–18, and more than >18 serving. Food components selected were non-refined cereals, potatoes, fruits, vegetables, legumes, fish, red meat and products, poultry, full fat dairy products and olive oil. Reverse scaling was reserved for meat, poultry, and full fat dairy products. As for alcohol, excessive (>700 ml/day) or no alcohol consumption was assigned a value of 0, while consuming 300 ml per day was assigned a value of 5. Alcohol intake was omitted from the initial questionnaire, during the calculations. The final score ranges from 0 to 55, higher values suggesting a greater adherence, but no specific cut-offs were suggested by the authors. In another study published by the same authors, 3 tertiles were defined as follows: less than 20, between 21 and 35 and more than 36 as low, medium and high adherences, respectively. Parlapani et al. used this tool in pregnant women, without specifying if alcohol intake was omitted or not, and using the 50th percentile as cut-off [9].

Short Mediterranean diet questionnaire (SMDQ) [22]

Derived from a validated FFQ, 9 typical Mediterranean food categories such as fruits, vegetables, olive oil, legumes, fish, wine, meat, fruit and vegetables together, white bread, rice or whole grain bread get a value of 1, when consumed above the specified serving portions per day. Wine intake was once again eliminated during the calculations, ending up with a score of 8, representing the highest adherence to MD.

Mediterranean diet scale (MDScale) [23]

Developed by Trichopoulou et al., initially in 1995, this scale was updated in 2002, by adding the fish component. It englobes 9 specific ingredients detailed as follows: vegetables, legumes, fruits and nuts, dairy products, cereals, meat, fish, dairy products, moderate alcohol intake and the ratio of monounsaturated fatty acids to saturated fatty acids. A value of 0 or 1 is assigned to each of the above mentioned components, considering the mean intake of consumption by all participants, as a cut-off, for each component. Favorable food items, pillars of MDs, such as vegetables, legumes, fruits and nuts, cereal and fish are attributed a score of 1, when consumed above the median. Detrimental components such as meat and whole dairy products are assigned respectively a value of 1 when consumed below the median and 0 if above. Fat intake was determined as the ratio of monounsaturated to saturated lipids; 1 point was added to those surpassing the median value of that ratio. For ethanol, 1 point was allocated when the intake was between 5 and 25 g per day for women. However, in our study, alcohol contribution to the final score was omitted, as suggested by Chatzi L. et al., since all the participants in this study abstained from drinking [24]. Hence, the total Mediterranean diet score varies between 0 and 8 meaning respectively a low and a high adherence. As for cut-off scores, authors of this score divided it into 3 categories ranging from 0 to 3, 4–5 and 6–8 indicating respectively low, medium and high MD adherence.

Blood samples and biological analysis

10 ml of maternal fasting blood were drawn by a certified phlebotomist in two separate tubes: a plain VACUTAINER® and an EDTA tube. Samples were kept on ice and centrifuged within an hour post collection. Serum and plasma were aliquot separately and kept at − 20 °C for future analysis. CRP was quantified by latex-enhanced nephelometry. Briefly, sample is mixed with latex particles coated with mouse monoclonal anti-CRP antibodies. CRP present in the test sample forms an antigen–antibody complex with the latex particles. Light scattering, measured by a nephelometric procedure after 6 min, is proportional to the concentration of the analyte present in the sample [25]. Leptin and adiponectin were quantified by a commercially available enzyme-linked immunosorbent assay (Elisa technique), following the steps detailed in the manufacturer's kit (Abcam, UK). The technique consists of a labeled capture antibody and a reporter conjugated detector antibody which immunocapture the sample analyte in solution. In the final step, a colored signal is generated proportionally to the amount of bound analyte and the intensity is measured at 450 nm. Sample content was calculated from the standard curve constructed [26]. All assays were run in duplicate.

Ethics

The study protocol was approved by the Institutional Review Board of Saint-Joseph University at Beirut Lebanon and the Hotel-Dieu Hospital Ethics Committee (CE HDF 624/FP 49). All subjects gave their written consent prior to their recruitment.

Statistics

Statistical analyses were performed using a software program (SPSS for windows, version 22.0, USA). The alpha error was set at 0.05. Mean and standard deviation (SD) were computed for continuous variables and frequencies for categorical variables. The normality of the distribution of the continuous data was evaluated by the Kolmogorov–Smirnov test. Spearman or Pearson correlation coefficients were used to evaluate the association between two continuous variables. Questionnaire scores were dichotomized using the 50th percentile. Student t-test or Mann Whitney tests were performed to compare continuous variables between two groups. Three logistic regression models were carried out with one categorical dependent variable and explanatory independent variables. Explanatory variables that were not related to questionnaire scores in the univariate analysis with p values > 0.200 were not included in the logistic regressions.

Results

Anthropometric, nutritional intake, biochemical results and pregnancy related characteristics of participants are presented in Table 1. We selected for the purpose of this research total calories consumed per day, percentage fat contribution to total caloric intake and fiber intake in grams per day, since those nutrients have well established links with the MD and the selected biochemical markers. Detailed dietary analysis derived from the FFQ and the 24 h dietary recall for energy, macronutrients and micronutrients is presented as supplementary material (Table provided as supplementary material 3). Gestational follow-up was lost for 6 participants during the course of the study.

The 50th percentile was considered the cut-off of each scale, with participants being categorized as having low or high MD adherence. The percentage of agreement and the relationship between the tools were measured by Spearman and Pearson correlation coefficients. All results are detailed in Table 2.

Table 3 summarizes the correlation between maternal age, fiber intake, pre-gestational BMI and biochemical markers, and in between biochemical markers.

Table 1
Anthropometric, nutritional intake, biochemical markers and pregnancy related characteristics of pregnant females (N = 100).

Characteristics	Mean	SD
Age (years)	30.8	5.5
Pre-gravid BMI (kg/m^2)	23	3.9
Maternal weight gain (kgs)	12.3	4.6
Caloric intake (Kcal)	1830	452
Lipids (% from total intake)	37.5	5.8
Fibers (g/day)	15.8	6.5
CRP (mg/l)	8.2	7.4
Adiponectin (μg/ml)	7.0	2.5
Leptin (ng/ml)	5.9	4.2
	N	%
Smoking Status		
Active smokers	7	7
Past smokers	4	4
Passive and non-smokers	89	89
Pre-gestational BMI categories		
Underweight	8	8
Normal	67	67
Overweight	19	19
Obese	6	6
Maternal weight gain classification[a]		
Insufficient	30	30
Adequate	45	45
Excessive	19	19
Missing data	6	6
Delivery mode		
Vaginal	34	34
C-section	60	60
Missing data	6	6

[a] According to: Institute of Medicine. Weight Gain during pregnancy: reexamining the guidelines, Washington, DC: National Academies Press; 2009.

Table 2
Scores and percentages of MD adherence derived from five internationally validated tools and percentage of agreement between the scores among 100 pregnant women.

MD scores	Mean	SD	50th percentile	Low adherence (%)	High adherence (%)
MFP	6.67	2.015	6	54	46
MDS	8.05	1.389	8	68	32
MedDietScore	30.68	4.451	30	53	47
SMDQ	4.45	0.869	4	57	43
MDScale	4.51	1.501	4	50	50
Percent agreement		**MFP**	**MDS**	**MedDietScore**	**SMDQ**
MDS	*r*	0.785	1		
	p value	0.000*			
	% of agreement	84			
MedDietScore	*r*	0.756	0.847	1	
	p value	0.000*	0.000*		
	% of agreement	83	85		
SMDQ	*r*	0.662	0.711	0.787	1
	p value	0.000*	0.000*	0.000*	
	% of agreement	81	79	84	
MDScale	*r*	0.257	0.298	0.264	0.178
	p value	0.010*	0.003*	0.008*	0.077
	% of agreement	64	54	57	57

*Statistical analysis was performed using Spearman and Pearson correlation coefficient, with a p value < 0.05 showing a significant association.

Table 3
Correlation between maternal age, fiber intake, pre-gestational BMI and biochemical markers (N = 100).

		CRP (mg/l)	Adiponectin (μg/ml)	Leptin (ng/ml)
Maternal age	*r*	0.213	−0.017	0.061
	p value	0.033*	0.863	0.545
Fiber intake (g/d)	*r*	−0.262	0.350	−0.077
	p value	0.008*	0.000*	0.449
Pre-gestational BMI	*r*	0.294	−0.361	0.525
	p value	0.003*	0.000*	0.000*
CRP (mg/l)	*r*	1.000	−0.220	0.298
	p value	–	0.028*	0.003*
Adiponectin (μg/ml)	*r*	−0.220	1.000	
	p value	0.028*	–	
Leptin ng/ml	*r*	0.298	−0.241	1.000
	p value	0.003*	0.016*	–

*Statistical analysis was performed using Spearman and Pearson correlation coefficient, with a p value < 0.05 showing a significant association.

A significant negative correlation between pre-gestational BMI and total MWG was found (p value = 0.01); women in the underweight and obese BMI categories gained respectively a mean weight of 15 and 6 kg (data not shown). Gestational age at delivery was significantly and negatively correlated to maternal age, pre-gestational BMI, and leptin levels with p values of 0.000, 0.006 and 0.025 respectively (data not shown, Spearman and Pearson correlation coefficient).

The associations between the results of the different scores of MD adherence with maternal anthropometric, dietary and biochemical markers are presented in Tables 4 and 5. The 50th percentile was considered the cut-off of each scale, with participants categorized as having low or high adherence.

Discussion

Studies measuring the impact of MD during pregnancy on maternal and neonatal outcomes are scarce and scattered among different countries such as the French Caribbean [4], Denmark [5], Norway [6], Spain and Greece [3]. In those articles, tools measuring MD adherence were varied, heterogeneous and with different cut-off points, since no consensus is established yet, for this subgroup of the population. The tools used to assess MD adherence are inconsistent regarding the inclusion of specific Mediterranean food. In addition, discrepancies noted in the literature among the large range of cut-offs points for the different scoring tools used to assess adherence of this eating pattern make objective selection hard to achieve, regarding which index to use.

The primary outcome of this study was to compare the adherence to MD by using 5 internationally validated scoring systems, in relation to pre-gestational BMI, caloric, fat, fiber intakes, MWG and 3 biochemical markers (CRP, leptin, and adiponectin) in 100 singleton healthy pregnant females, living in the Mediterranean region. The MD adherence scores were examined as continuous variable, in addition to applying the 50th percentile, with the serving sizes derived from a validated FFQ, as suggested by Martinez-Gonzalez et al. [27]. This second analysis technique permitted to rank our participants as high and low adherent, similarly to what was published by Parlapani E et al., in 2017 [9].

Results observed showed that the percentage of agreement was high between the MFP, the MDS, the MedDietScore and the SMDQ. The MDScale presented small agreement in relation to the other tested tools; this may be due to the particularity of this index, since it relies on the calculation of the median of consumption of the specified Mediterranean food items and the establishment of a cut-off, in each food group, and then to the attribution of scores of 1 or 0.

Another interesting finding was that at least half of the study population were low adherent to the MD, with all the tested tool. This may be explained by the rapid urbanization undergone in the region, with young women joining the labor market, associated with the nutritional transition influencing eating patterns in traditional societies.

Alcohol consumption was not counted in the scores, because it is prohibited during gestation and data of our participants showed no consumption at all. It is important to highlight some important issues concerning ethanol. First, the traditional dietary pattern of MD concerns wines and not other type of ethanol based drinks. However, the MDScale and the MedDietScore attribute a positive value in their tools, when the consumption of ethanol is between 5 and 25 g/day or 12 g/day, respectively, without specifying the type. This may weaken and not represent the true adherence to traditional MD pattern. Second, it is worth mentioning that researchers were vague in their publications regarding the scoring calculations and the derived cut-offs points, after alcohol omission from their tools measuring MD adherence [9]. This shows the lack of agreement among scientists concerning this issue.

Table 4
Associations between adherence to MD (categorized as low or high according to the 50th percentile) and maternal anthropometric, dietary and biochemical markers.

	MFP		MDS		MedDietScore		SMDQ		MDScale	
	Low Mean ± SD	High Mean ± SD	Low Mean ± SD	High Mean ± SD	Low Mean ± SD	High Mean ± SD	Low Mean ± SD	High Mean ± SD	Low Mean ± SD	High Mean ± SD
Pre-gestational BMI	23.89 ± 4.39 (n = 54) p = 0.023*	22.09 ± 3.14 (n = 46)	23.55 ± 4.26 (n = 68) p = 0.041*	22.02 ± 2.99 (n = 32)	24.14 ± 4.28 (n = 57) p = 0.001*	21.63 ± 2.95 (n = 43)	23.28 ± 4.28 (n = 53) p = 0.557	22.81 ± 4.40 (n = 47)	23.39 ± 4.06 (n = 50) p = 0.417	22.74 ± 3.85 (n = 50)
Maternal weight gain (kgs)	11.75 ± 4.07 (n = 51) p = 0.184	13.01 ± 5.10 (n = 43)	11.88 ± 4.28 (n = 65) p = 0.158	13.33 ± 5.14 (n = 29)	12.05 ± 4.20 (n = 54) p = 0.498	12.70 ± 5.09 (n = 40)	12.18 ± 4.22 (n = 51) p = 0.735	12.50 ± 5.03 (n = 43)	12.45 ± 4.45 (n = 47) p = 0.798	12.20 ± 4.77 (n = 47)
Caloric Intake (Kcal/day)	1828 ± 472 (n = 54) p = 0.958	1832 ± 432 (n = 46)	1860 ± 470 (n = 68) p = 0.340	1766 ± 411 (n = 32)	1821 ± 475 (n = 57) p = 0.828	1841 ± 425 (n = 43)	1835 ± 440 (n = 53) p = 0.909	1825 ± 470 (n = 47)	1800 ± 423 (n = 50) p = 0.517	1860 ± 482 (n = 50)
Fat intake (% of caloric intake)	38.57 ± 6.01 (n = 54) p = 0.044*	36.40 ± 5.52 (n = 46)	37.85 ± 6.44 (n = 68) p = 0.449	36.89 ± 4.44 (n = 32)	38.27 ± 6.54 (n = 57) p = 0.154	36.58 ± 4.74 (n = 43)	38.39 ± 6.54 (n = 53) p = 0.126	36.58 ± 4.89 (n = 47)	38.04 ± 4.93 (n = 50) p = 0.400	37.05 ± 6.70 (n = 50)
Fiber intake (g/day)	13.67 ± 5.69 (n = 54) p = 0.000*	18.25 ± 6.63 (n = 46)	15.22 ± 6.57 (n = 68) p = 0.214	16.96 ± 6.36 (n = 32)	14.49 ± 6.53 (n = 57) p = 0.007*	17.48 ± 6.17 (n = 43)	14.65 ± 6.64 (n = 53) p = 0.031*	17.04 ± 6.21 (n = 47)	13.50 ± 4.85 (n = 50) p = 0.000*	18.04 ± 7.20 (n = 50)
CRP (mg/l)	8.68 ± 6.36 (n = 54) p = 0.042*	6.51 ± 3.98 (n = 45)	8.19 ± 5.88 (n = 68) p = 0.046*	6.17 ± 3.78 (n = 31)	8.59 ± 5.98 (n = 57) p = 0.047*	6.46 ± 4.53 (n = 42)	8.58 ± 6.14 (n = 53) p = 0.038*	6.39 ± 4.10 (n = 46)	8.11 ± 6.46 (n = 49) p = 0.451	7.28 ± 4.37 (n = 50)
Adiponectin (μg/ml)	6.49 ± 1.92 (n = 54) p = 0.024*	7.60 ± 2.88 (n = 46)	6.76 ± 2.27 (n = 68) p = 0.161	7.50 ± 2.87 (n = 32)	6.90 ± 2.05 (n = 57) p = 0.635	7.14 ± 2.93 (n = 43)	6.79 ± 2.36 (n = 53) p = 0.364	7.24 ± 2.57 (n = 47)	6.46 ± 1.84 (n = 50) p = 0.027*	7.54 ± 2.88 (n = 50)
Leptin (ng/ml)	6.50 ± 3.98 (n = 54) p = 0.145	5.27 ± 3.85 (n = 46)	6.42 ± 4.32 (n = 68) p = 0.089	4.89 ± 3.72 (n = 32)	6.78 ± 4.39 (n = 57) p = 0.009*	4.79 ± 3.64 (n = 43)	6.29 ± 4.18 (n = 53) p = 0.369	5.53 ± 4.20 (n = 47)	6.49 ± 4.56 (n = 50) p = 0.184	5.37 ± 3.73 (n = 50)

*Statistical analyses were performed using Student t tests or Mann–Whitney tests, with a p value of less than 0.05 set as significant.

Table 5
Logistic regression models showing associations between low or high MD adherence and pregestational BMI, dietary and biochemical variables.

MFP	B	Standard error	p value	OR	95% CI for OR	
					Lower	Upper
BMI	−0.13	0.06	0.03*	0.88	0.78	0.99
Lipids	−0.08	0.04	0.04*	0.92	0.86	0.99
Fiber	0.09	0.04	0.03*	1.09	1.01	1.19
CRP	−0.11	0.05	0.03*	0.90	0.82	0.99
Adiponectin	0.18	0.09	0.04*	1.20	1.01	1.44
Leptin	−0.07	0.05	0.15	0.93	0.84	1.03
MDS	B	Standard error	p value	OR	95% CI for OR	
					Lower	Upper
IMC	−0.12	0.06	0.07	0.89	0.78	1.01
Leptin	−0.01	0.06	0.09	0.91	0.81	1.02
CRP	−0.13	0.06	0.04*	0.88	0.78	0.99
Med Diet score	B	Standard error	p value	OR	95% CI for OR	
					Lower	Upper
BMI	−0.18	0.07	0.01	0.83	0.72	0.96
Lipids	−0.06	0.04	0.10	0.94	0.87	1.01
Fiber	0.07	0.03	0.03*	1.07	1.01	1.14
Leptin	−0.13	0.06	0.03*	0.88	0.78	0.99
CRP	−0.12	0.05	0.02*	0.88	0.80	0.98
SMDQ	B	Standard error	p value	OR	95% CI for OR	
					Lower	Upper
Fiber	0.08	0.03	0.02*	1.08	1.01	1.16
CRP	−0.09	0.05	0.04*	0.91	0.83	0.99
Lipids	−0.04	0.04	0.39	0.96	0.89	1.04
MD Scale	B	Standard error	p value	OR	95% CI for OR	
					Lower	Upper
Adiponectin	0.19	0.09	0.03*	1.21	1.02	1.45
Fiber	0.11	0.04	0.00*	1.12	1.04	1.21
Leptin	−0.04	0.05	0.41	0.96	0.86	1.06

*p value of less than 0.05 set as significant.

The study conducted by Fernandez-Barres et al., in 1827 mother-child pairs, created a new tool, “the relative MD score”, excluding alcohol from the scoring system from the start, to avoid inconsistent data at the end [28]. Gesteiro et al. studied the impact of maternal MD adherence on insulin resistance at birth, by modifying the 14 items MFP tool into 13 components, by omitting the question concerning wine intake and considering 6.87 as a cut-off of MD adherence, among their participants [11]. Our results using the 50th percentile of this same tool showed a similar cut-off of 6.

Although olive oil is the main contributor of monounsaturated fatty acids in the traditional MD, recent nutrition transitions led to the inclusion of some new food sources of those fatty acids, such as avocado, canola and sesame oil (tahini paste) in the diet of people living in the Mediterranean region. The tool created by Leighton et al., in 2003 in Chile, was the only one taking into account canola oil and avocado, maybe because the latter is a food originating from South America, but not mentioned in the traditional Mediterranean meal plan (20). This implies the importance of creating tools compatible with the diet transition influencing eating patterns of individuals. It is interesting to pinpoint a second issue: only the tool created by Trichopoulo et al. takes into account the ratio of monounsaturated over fat intake of the diet. This could be an added value of this tool, since total fat contribution to a diet plays a detrimental role in caloric intake and health outcomes.

A decreasing scale was attributed to full fat dairy and red meat consumption in some of the indexes such as the MDS, the MDScale and the MedDietScore. This can be regarded as a controversy, since nutritionists recommend the inclusion of such food items during pregnancy, to ensure adequate intake of high biological value proteins, calcium, vitamin D and iron. Hence, their consumption during pregnancy should not be avoided and considered detrimental on health.

Fish, a major source of omega 3 in the MD, is counted separately in all the calculated indexes. However, our research team is reluctant concerning the attribution of a value of 1 for a daily consumption of 3 servings of fish in the SMDQ score, created by Zito et al. [22], because only a weekly consumption is recommended by health practitioners during pregnancy, to avoid the negative impact of mercury on neonatal health status [29]. In addition, national surveys conducted in Lebanon show that fish consumption is relatively low among our population due to the high cost of this food product and the prohibition against some types of fish in Muslim rites [30].

Another major drawback encountered while scoring the MD adherence was the lack of inclusion of other food ingredients, such as green leafy vegetables, lentils, beans, and chickpeas, frequently consumed and highly representative of the MD eating pattern in the region, but not taken into account. Sesame oil, a monounsaturated fatty acid, present in various recipes of the Mediterranean cuisine, was a missing food component too. Cracked whole wheat, known as burghol, is typically consumed in Eastern Mediterranean countries, in many traditional recipes and was incorporated in our FFQ. However, it was not accounted for, in all the indexes; this may underestimate MD adherence scoring of our participants. Finally, it is worth mentioning the importance of seasonality of local ingredients and cooking techniques due to mixing of spices, herbs, tomato, and olive oil on health of this famous cuisine, taken into account only in the MFP tool established by Martinez-Gonzalez, as a separate component while scoring [10].

Regarding the association between MD adherence and biochemical markers, results of this study prove the beneficial effect of this particular dietary pattern on CRP, adiponectin and leptin levels since all scores except the MDScale showed a significant negative association with CRP levels. Adiponectin levels were significantly and positively associated to MFP and MDScale scores while leptin levels were significantly and negatively associated to the MedDietscore. Hrolfsdottir et al., in 2016 confirmed the favorable impact of fibers and plant based proteins, as in the MD, on all biomarkers of inflammation, similar to our results showing that high fiber intake was significantly associated to low CRP values (p value of 0.008) and high adiponectin levels (p value of 0.000) [2]. The exact mechanism of action of fibers on inflammatory and obesity related markers are not fully elucidated. Some scientists attribute their protective effect to attenuated lipid oxidation, hence reducing inflammation and modifying adipose tissue secretions and hepatic fat circulation [31].

Azzini et al. studied the influence of MD on cytokines, lipid and vitamin profiles by using the MDScale and proved once more the improvement of oxidative stress in high adherent individuals [32].

The mean pre-gestational BMI of participants was 23, with 75% and 25% of the women being respectively in the underweight/normal and overweight/obese weight category. This distribution limits major bias related to overweight and obesity on inflammatory markers and obesity related hormones. In a large longitudinal study, Schoenaker et al. analyzed the impact of pre-gestational BMI and MD adherence, thru the MDScale, on maternal complications, in a sample of 3000 Australian pregnant women. They suggested that this eating pattern, if implemented before pregnancy, optimizes pre-gestational BMI and reduces gestational diabetes and hypertension [33]. In this study, significant correlations were seen between pre-gestational BMI and CRP, leptin as well as adiponectin, similar to the results presented by Madan et al., explained by the fact that obesity and visceral fat are active contributors of low grade inflammation and are implicated in hormonal disturbances [34,35].

It is also worth mentioning the significant positive correlation observed between maternal age and CRP values (p value $= 0.033$), suggesting a rise of CRP with age, as mentioned by Eklund [31].

This paper is the first in the literature comparing scores derived from different indexes in relation to biochemical markers among pregnant women. Despite the presence of variations in calculating the used indexes and their relative cut-off points, our results are coherent, since they are derived from a FFQ composed of Mediterranean food components, validated among pregnant women and were conducted by the same researcher.

Several limitations deserve our acknowledgement. Blood sampling was performed only once, hence biochemical markers might have been influenced by pregnancy induced physiological status [36]. Memory and social bias are frequent in epidemiological studies, since participants often forget or hide their true eating habits. In addition, the FFQ from which the indexes were derived was filled during a single interview; multiple recalls ensure a better estimates of dietary intakes, but due to the limited time frame of the study, this was not realizable. However, the use of our own validated FFQ during pregnancy, with food items highly representative of a Mediterranean eating pattern, was the major strength of this research. The “a priori” scoring criteria can be considered by some researchers as an arbitrary limitation, since it can misclassify individuals. Thus, we created our own cut-off points, depending on the scoring pool calculated. Furthermore, the results of the indexes varied between the different applied tools, since some such as the MDS ranged from 0,0.5 to 1, while the MedDietScore attributed values ranging from 0 to 5, for each food component. However, this last limitation can be neglected, since studies confirmed that regardless of the scoring criteria, higher values obtained from different tools are always associated with a greater MD adherence [37]. In addition, a follow-up was maintained with all participants, to collect neonatal and gestational outcomes for future research purposes.

In conclusion, pregnancy is the perfect period for health professionals to induce preventive nutritional strategies and to promote traditional meals of the Mediterranean cuisine, because pregnant women are more motivated to improve their health by adopting a healthier lifestyle for the benefit of their fetus.

Our findings support the beneficial impact of Mediterranean food components such as fibers, antioxidants and lipids on biological markers such as CRP, leptin and adiponectin during pregnancy. However, discrepancies, gaps and bias generated during the analysis of each index led us conclude that none of the scores present in the literature is the ideal one to be applied to pregnant females, specifically for components such as ethanol, full fat dairy, fish and meat products. There is a pressing need to create and validate a MD assessment tool during pregnancy, taking into consideration the results of this paper.

Authors' contribution

All authors reviewed and approved the submitted manuscript. T.P. conceived the study, supervised the recruitment of the participants, performed face-to-face interviews, conducted the nutrient analysis and prepared the manuscript draft. A.S. did face-to-face interviews, conducted the data collection and the follow-up of participants. H.H. participated in the data analysis. H.Y., G.A., J.A., A.K. helped in the design of the study, reviewed the data and corrected the manuscript. L.R. K., F.H.M., and T.P. took in charge the laboratory analysis. L.R. K. conceived the project, provided complete supervision, critical revision, data interpretation and correction of the manuscript. All authors constituted the research team.

Conflict of interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnu.2018.06.960.

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