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ORIGINAL ARTICLE

Maternal diets with low healthy eating index or mediterranean diet adherence scores are associated with high cord-blood insulin levels and insulin resistance markers at birth

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BACKGROUND/OBJECTIVES: Few studies have used healthy eating index (HEI) and mediterranean diet adherence (MDA) scores to evaluate the diet quality during pregnancy. To determine the relationship between first trimester diet quality and insulin sensitivity/resistance biomarkers at birth.

SUBJECTS/METHODS: Cord-blood insulin sensitivity/resistance biomarkers of the offspring of 35 women whose diets were 'adequate' or 'inadequate' according to their HEI score (>70 or $\leqslant 70$, respectively) and their 13-point MDA score ($\geqslant 7$ or <7, respectively).

RESULTS: Low HEI-score diets contained less (g/1000 kcal) carbohydrates (CHO; $P=0.027$) and fibre ($P=0.011$), and more fats ($P<0.001$) and cholesterol ($P<0.001$), and contributed (percentage contribution to total energy (%En)) fewer CHO ($P=0.005$), more fats ($P=<0.001$) and saturated fatty acid (SFA; $P=0.002$) than their high HEI-score counterparts. Low MDA-score diets contained less (g/1000 kcal) fibre ($P<0.001$) and more cholesterol ($P=0.05$), had lower polyunsaturated fatty acids + monounsaturated fatty acid/SFA (PUFA + MUFA/SFA; $P=0.05$) and higher SFA/CHO ($P=0.021$) and ω-6/ω-3 PUFA ratios ($P=0.044$) than their respective counterparts. Women consuming the low HEI- or low MDA-score diets had low-fasting glycaemia ($P=0.016$ or $P=0.025$, respectively) but delivered infants with high insulinaemia ($P=0.048$ or $P=0.017$, respectively), homeostatic model assessment for insulin resistance (HOMA-IR; $P=0.031$ or $P=0.049$, respectively) and glycaemia ($P=0.018$ or $P=0.048$, respectively). The relative risk (RR) of high-neonatal glycaemia and insulinaemia were 7.6 ($P=0.008$) and 6.7 ($P=0.017$) for low vs high HEI-score groups. High HOMA-IR and high glucose RR were, respectively, 3.4 ($P=0.043$) and 3.9 ($P=0.016$) in neonates from the <7 MDA- vs $\geqslant 7$ MDA-score group. These RRs were not affected by potential confounders.

CONCLUSION: Maternal diets with low HEI- or MDA-scores during the first trimester of pregnancy negatively affect insulin resistance markers at birth.

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Keywords: pregnancy; neonates; HEI score; mediterranean diet adherence; insulin sensitivity/resistance markers

INTRODUCTION

Diet during pregnancy is an important factor that affects maternal, fetal and infant health and wellbeing.[1,2] Food and energy-adjusted nutrient intakes from foods did not change appreciably from the first to the second trimester[3] or from early to late pregnancy.[4]

The quantity and quality of dietary carbohydrates (CHO),[5] dietary fibre[6] and fats affect glucose metabolism and insulin resistance/sensitivity. Individuals with high-fat intake are more likely to develop glucose metabolism disorders than those who consume a low-fat diet.[7–9] In addition, ω-3 polyunsaturated fatty acids (PUFA) and monounsaturated fatty acids (MUFA) affect insulin sensitivity/resistance and fasting plasma glucose levels in different population groups.[7]

The homeostatic model assessment for insulin resistance (HOMA-IR) has been widely used to evaluate the degree of insulin resistance in different populations.[10–12] Our group has published the normal range for insulin resistance/sensitivity biomarkers at birth.[13] HOMA-IR correlates with the saturated fatty acid/CHO (SFA/CHO) ratio,[14,15] suggesting that dietary quality greatly affects this insulin resistance biomarker. Kastorini *et al.*[16] showed that the adherence to the mediterranean diet adherence (MDA) decreases the metabolic syndrome risk.

The healthy eating index (HEI) and the MDA scores have been largely employed to assess diet quality[17] during pregnancy.[18–20] HEI score reflects the complexity of dietary patterns[18] and its validity has been demonstrated in studies using plasma biomarkers.[21,22] MDA score has been used to assess diet quality and its relationship with degenerative diseases.[17,23] PREDIMED, one large scale epidemiological study, uses the 14-point MDA score.[24,25] To our knowledge, there have been no studies on the possible association between diet quality during pregnancy, based on maternal HEI and MDA scores, and insulin sensitivity/resistance markers at birth.

Author's hypothesis was that an 'adequate' diet (based on its HEI or MDA scores) during the first trimester of pregnancy results in lower values of insulin resistance biomarkers at birth than an 'inadequate' diet.

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The aims of the current study were to analyse the quality of the maternal diet based on HEI and MDA scores during the first trimester of pregnancy and determine its influence on (a) maternal glycaemia and (b) insulin sensitivity/resistance biomarker levels in newborns. In addition, the authors compared the relative risk (RR) of displaying high-birth levels of glucose, insulin and HOMA-IR, and low values of the quantitative insulin sensitivity check index (QUICKI) between neonates whose mothers had consumed low HEI- or MDA-score diets in the first trimester of pregnancy and those whose mothers had followed adequate-score diets.

SUBJECTS AND METHODS

Subjects

The subjects of the present study were 35 women who gave birth at the Mérida Hospital (Mérida, Extremadura, Spain), a regional hospital having 400 beds, placed in a town of approximately 54 000 inhabitants, giving medical support to 150 000 people. In all, 89 women were interested and contacted us through advertisements in the hospital. They were first informed about the study aims. A total of 23 future mothers were excluded. A total of 70 women completed the survey just before the first ultrasound pregnancy test at 12–15 week pregnancy, and were requested about their interest in performing an extra survey after delivery on major dietary changes occurring during the second and third trimesters. At weeks 24–28 of pregnancy, coinciding with their O'Sullivan glucose tolerance test,[26] information about twin pregnancies and gestational diabetes was obtained. A total of 16 mothers were excluded. After delivery, a total of 35 women with their respective children were finally selected after excluding 19 mothers/neonates more. Exclusion factors in each stage of the study are summarized in Figure 1. After delivery, participant mothers were surveyed by telephone on major dietary changes occurring through second and third trimesters (Table 1). The participation rate was about 16% of participating women in the Mérida Cohort study. All infants studied were Caucasian: The study was performed in accordance with the Helsinki Declaration and approved by the Management and Ethical Committee of the Mérida Hospital.

Methods

Dietary data collection. Participants, conducted by a trained dietician, completed a food frequency questionnaire (FFQ) that included 169 items classified according to food groups and based on FFQs used and validated in the enKid study.[27] Photographs of sample portions were used to estimate the serving size and volumes consumed.[28] The dietician reviewed together with the volunteer the usual consumption frequency of each food (per day/week/month), together with the normal food helping size, and specific information for mineral–vitamin supplements. Daily energy, nutrient intakes and HEI were calculated using a computer programme (DIAL, Madrid, Spain)[29] to evaluate diet quality consumed during the first pregnancy trimester. Dietary data were adjusted to 1000 kcal to reduce measurement error and to adjust for confounding. The HEI is based on a 10-component, 100-point scale and is a slight modification for the Spanish population of that of Kennedy *et al.*,[18] taking into account recommended energy intakes of for 1600, 2200 and 2800 kcal[29,30] and the required servings.[29,31] Diets with HEI scores of $\leqslant 70$[(refs 18,32)] were labelled 'inadequate', whereas those with HEI scores of >70 were considered 'adequate'.

The MDA score of 14 points used in the PREDIMED study[24] was modified to 13-point MDA score taking into account that wine should be not consumed through the whole pregnancy. Each of the 13 components comprising the MDA score contributes a maximum of one point to the final score. An extra survey based on the 13 MDA points was performed to search on major dietary changes occurring during late pregnancy. Table 1 presents specific details considered in the surveys for HEI or MDA scores. Based on different studies[32,33] and considering that the average MDA score of the mothers was 6.87, and about 1/3 of them consumed diets with MDA score <7, the cutoff point for the MDA score <7 was selected to define low adherence to the mediterranean diet.

Maternal and neonatal data. Anthropometrical measurements were taken by trained personnel following hospital's standard procedures. Data concerning mothers (age, gestational weight gain, O'Sullivan test basal and after 1 h glycaemia, gestational diabetes, type of delivery, primarity/multiparity, education degree, place of residence) and neonates (weight, height, gender, gestational age, first and fifth minute Apgar indices) were obtained from hospital records. Data concerning of physical activity, seasonality, dietary habits and major dietary habits changes were obtained from the nutritional survey records.

Cord-blood measurements. After delivery, the umbilical cord was cut and arterial blood collected in BD Vacutainer SST II tubes (Becton Dickinson, Plymouth, UK). Blood was centrifuged at 3500 r.p.m. for 5 min, and serum aliquots frozen at $-18\,^{\circ}C$ until processed. Serum glucose and insulin were measured by the glucose hexokinase and electrochemiluminescence immunoassay (ECLIA) methods both supplied by Roche Diagnostics (Basel, Switzerland). Our laboratory is certified by AENOR and participates in the Spanish Clinical Chemistry Society (SEQC) External Quality Evaluation Program, which follows UNE-EN-ISO 9001:2000 standards. Intra-assay and inter-assay variation coefficients were 1% and 1.7% for glucose, 1.5% and 4.9% for insulin, respectively.

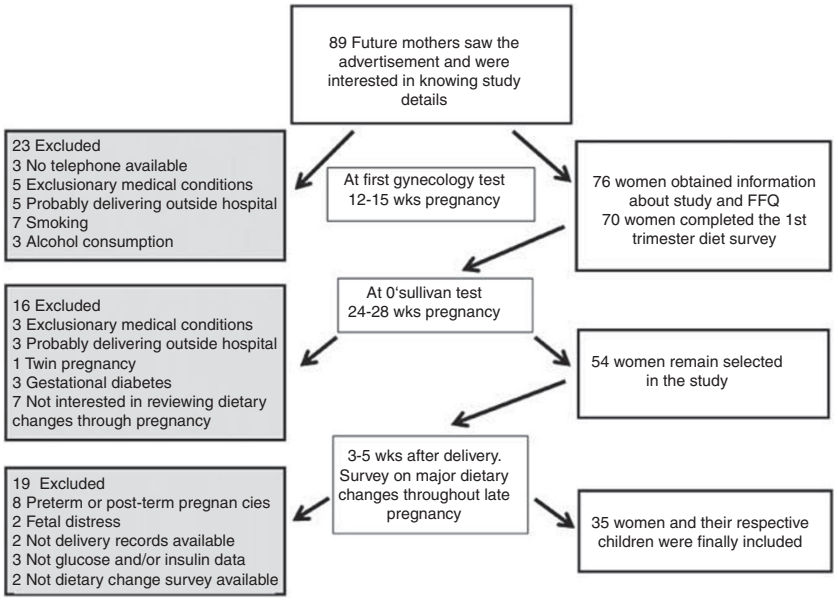

Figure 1. Study flow diagram. Data obtained, recruited and exclusion reasons are detailed.

Table 1. Detailed criteria taken into account in the 10-point HEI and 13-point MDA score

HEI score	*Value (score range)*[a]	*MDA score*[b]	*Criteria to obtain one point*[b]
Cereals, grains and legumes (6, 8 and 10 servings, respectively).[a] One serving: bread = 30–40 g; biscuits and plain fairy cakes, rolls and others = 40–50 g; breakfast cereals = 30–40 g	0 to 10 (0–10)[a]	Use of olive oil as main culinary fat	Yes
Vegetables (3, 4, and 5 servings, respectively). One serving: Swiss chard, lettuce, spinach and others = 100–150 g; potatoes, tomatoes, carrots and others = 100–150 g	0 to 5 (0–10)[a]	Amount of olive oil consumed per day including oil used for frying, salads, meals away from home and others	$\geqslant$4 table spoons
Fruits (2, 3, and 4 servings, respectively); one serving: fruits = 150–200 g or natural fruit juices = 100–150 g	0 to 4 (0–10)[a]	Servings of vegetables per day (one serving = 200 g). Consider side dishes as half a serving	$\geqslant$2; $\geqslant$1 raw or as salad
Milk and dairy products. One serving: milk = 200–250 ml, yoghurt = 125 ml, fresh cheese = 60 g; old or partially old cheese = 30–40 g	0 to 3 (0–10)	Units of fruits, including natural fruit juices per day	$\geqslant$3
Meat, eggs and fish (2, 2.4 and 2.8 servings, respectively). One serving: meat and viscera = 100–125 g; fish = 100–150 g; egg = 1 unit	0 to 3 (0–10)[a]	Serving of red meat, hamburger or meat products (ham, sausage and others) per day	$<$1
Total fat (%En)	$>$45 to $<$30 (0–10)	Servings of butter, margarine or cream consumed per day (one serving = 12 g)	$<$1
Saturated fat (%En)	$>$15 to $<$10 (0–10)	Sweet or carbonated beverage number per day	$<$1
Cholesterol (mg/day)	$>$450 to $<$300 (0–10)	Servings of legumes per week (one serving = 150 g)	$\geqslant$3
Sodium (g/day)	$>$4.8 to $<$2.4 (0–10)	Servings of fish or shellfish consumed per week (one serving = 100–150 g of fish or 4–5 units or 200 g of shellfish)	$\geqslant$3
Dietary variety (number per 3 days)	$<$6 to $>$16 (0–10)	Servings of commercial (not home-made) sweets or pastries such as cakes, cookies, biscuits or custards per week	$<$3
		Servings of nuts (including peanuts) per week (one serving = 30 g)	$\geqslant$3
		Consumption of chicken, turkey or rabbit meat instead of veal, pork, hamburger or sausage	Yes
		Times per week of vegetables, pasta, rice or dishes seasoned with *sofrito*, sauce made with tomato, onion, leek or garlic and simmered with olive oil	$\geqslant$2

Abbreviations: HEI, healthy eating index; MDA, mediterranean diet adherence. Survey performed after birth (a) Change with respect to the first survey (first pregnancy trimester)—irrelevantly; a little; a few and quite a lot. (b) Number of serving of the following foods decreased/increased (only in case of a few or quite a lot dietary changing)—use of olive oil (yes/not); olive oil (decrease, $>$2; 1–2; 0–1 spoons; increase, 0–1; 1–2, $>$2 spoons); vegetables per day (decrease, $>$2; 1–2; 0–1 half servings; increase, 0–1; 1–2, $>$2 half servings); fruits, including natural fruit juices, per day (decrease, $>$2; 1–2; 0–1 units; increase, 0–1; 1–2; $>$2 units); red meat, hamburger or meat products (ham, sausage and others) per day (decrease, 0–1; 1–2; $>$2 half servings; increase, 0–1; 1–2; $>$2 half servings); butter, margarine or cream consumed per day (decrease, 0–1; 1–2; $>$2 servings; increase, 0–1; 1–2; $>$2 servings); sweet or carbonated beverage number per day (decrease, 0–1; 1–2; $>$2 servings; increase, 0–1; 1–2; $>$2 servings); servings of legumes per week (decrease, 0–1; 1–2; $>$2 servings; increase, 0–1; 1–2; $>$2 servings); servings of fish or shellfish consumed per week (decrease, 0–1; 1–2; $>$2 servings; increase, 0–1; 1–2; $>$2 servings); servings of commercial sweets or pastries per week (decrease, 0–1; 1–2; $>$2 servings; increase, 0–1; 1–2; $>$2 servings); servings of nuts (including peanuts) per week (decrease, 0–1; 1–2; $>$2 servings; increase, 0–1; 1–2; $>$2 servings); consumption of chicken/turkey/rabbit meat instead of veal/pork/hamburger/sausage (decrease, 0–1; 1–2; $>$2 servings; increase, 0–1; 1–2; $>$2 servings); times per week of vegetables, pasta, rice or dishes seasoned with sofrito, sauce made with tomato, onion, leek or garlic and simmered with olive oil (decrease, 0–1; 1–2; $>$2 times; increase, 0–1; 1–2; $>$2 times). [a]Adapted by Ortega *et al.*[29] to recommended energy intakes of 1600, 2200 and 2800 kcal. For more details see Material and methods. Values correspond to food edible part. [b]This MDA is an adaptation of the 14-point MDA score of Estruch *et al.*[24] as red wine consumption should be avoided by all future mothers.

QUICKI, calculated by the formula 1/[(log insulin)(mIU/l) + (log glucose) mg/dl)];[34] HOMA-IR, calculated as: glucose (mmol/l) $\times$ insulin(mIU/l)/22.5,[35] and the glucose/insulin ratio were used as insulin sensitivity/resistance indices. The prevalence of neonates presenting high insulin, glucose and HOMA-IR, and low QUICKI values was calculated using Gesteiro *et al.*[13] newborn reference data for high-insulin (percentile 75th, males $\geqslant$4.8 mUI/l, females $\geqslant$6.4 mUI/l), high-glucose (percentile 75th, males $\geqslant$81.25 mg/dl, females $\geqslant$82.5 mg/dl) and high HOMA-IR levels (percentile 75th, males $\geqslant$0.92, females $\geqslant$1.09), and low QUICKI levels (percentile 25th, males $<$0.39, females $<$0.37).

Statistics. Sample size was adequate to estimate absolute differences of 2.5 in HOMA-IR and 4 mUI/l in insulinaemia with a power of 82 and 70% (nominal alpha = 0.05) between neonates belonging to $\leqslant$70 and $>$70 HEI scores and $<$7 vs $\geqslant$7 MDA scores, respectively. A standard deviation of 3 and 1 for HOMA-IR and 6 and 2 mUI/l for insulin in neonates belonging to the low- and high-score diet groups, respectively, was assumed for this calculation. The Mann–Whitney *U* test was employed to compare diet characteristics and insulin sensitivity/resistance biomarkers in the different neonate groups. RR for neonates presenting high levels of glucose, insulin or HOMA-IR, or low QUICKI values in 'inadequate' vs 'adequate' diet groups and the exact one-tailed *P*-values for significant RR values (RR$>$1) were calculated. The effect of several confounders that could modify dietary habits and/or insulin sensitivity was also tested. The relationship between different parameters was obtained using the Spearman's rank test. Statistical significance was set at $P<0.05$ using the SPSS (version 15.0) and the SAS (version 9.2) statistical software packages.

Table 2. Maternal and neonatal variables in neonates belonging to total mothers and in those following an inadequate diet (HEI score ⩽70) or an adequate diet (HEI score >70) or a low adherence to the mediterranean diet (MDA<7) or a high adherence (MDA ⩾7)

	ALL (N = *35*)	*HEI ⩽70* (N = *19*)	*HEI >70* (N = *16*)	P *HEI*	*MDA <7* (N = *13*)	*MDA ⩾7* (N = *22*)	P *MDA*
Mothers, <35/⩾35 years	19/16	13/6	13/3	0.319	12/1	14/8	0.066
Vaginal/caesarean delivery	34/1	19/0	15/1	0.457	12/1	22/0	0.370
Male/female neonate	23/12	14/5	9/7	0.234	7/6	16/6	0.220
<10/⩾10 kg weight gain	17/18	12/7	5/11	0.061	9/4	7/15	0.062
Positive/negative O'Sullivan test	27/8	14/5	13/3	0.452	10/3	18/5	0.645
Maternal				P* *HEI*			P**MDA*
Age (years)	30.4 ± 0.9 (28.6–32.3)	29.5 ± 1.5 (26.3–32.7)	31.5 ± 0.8 (29.8–33.2)	0.271	27.8 ± 1.6 (24.7–30.8)	31.8 ± 1.6 (29.7–34.2)	0.055
Pregestational weight (kg)	63.5 ± 1.7 (60.1–67.0)	62.6 ± 2.6 (57.1–68.0)	64.7 ± 2.1 (60.2–69.1)	0.605	63.4 ± 3.2 (56.5–70.3)	63.6 ± 1.9 (59.5–67.7)	0.957
Pregestational BMI	23.0 ± 0.6 (21.8–24.3)	23.6 ± 0.7 (22.0–25.5)	22.5 ± 0.6 (21.0–24.0)	0.125	23.7 ± 1.1 (21.5–25.8)	22.6 ± 0.7 (21.2–24.0)	0.295
Weight gain (kg)	10.1 ± 0.8 (8.4–11.8)	9.1 ± 1.2 (6.5–11.6)	11 ± 1.1 (9.0–13.6)	0.117	7.9 ± 1.8 (4.1–11.8)	11.5 ± 0.6 (10.1–12.8)	0.017
Weight gain at 12–15 weeks (kg)	2.9 ± 0.3 (2.4–3.3)	2.8 ± 0.5 (2.0–3.5)	3.0 ± 0.5 (2.1–3.6)	0.856	2.7 ± 0.5 (1.8–3.7)	3.1 ± 0.3 (2.5–3.6)	0.331
Glucose (mg/dl)[a]	83.0 ± 1.3 (80.3–85.6)	80.1 ± 1.6 (76.8–83.4)	87.0 ± 1.7 (83.2–90.8)	0.016	80.1 ± 2.0 (75.6–85.6)	84.3 ± 1.6 (80.6–87.7)	0.025
Glucose 1 h (mg/dl)[a]	120.1 ± 5.4 (109.1–131.1)	118.4 ± 5.9 (105.9–131)	122.4 ± 10.2 (100–144.9)	0.845	117.6 ± 11.7 (93.0–141.3)	128.4 ± 6.4 (111.0–135.1)	0.617
Neonatal							
GA (weeks)	39.5 ± 0.2 (39.0–40.0)	39.4 ± 0.4 (38.6–40.1)	39.6 ± 0.3 (39.0–40.3)	0.857	39.1 ± 0.4 (38.1–40.0)	39.7 ± 1.3 (39.1–40.3)	0.448
Weight (kg)	3.22 ± 0.07 (3.08–3.35)	3.21 ± 0.10 (3.01–3.42)	3.22 ± 0.09 (3.04–3.40)	0.987	3.20 ± 0.13 (2.89–3.44)	3.23 ± 0.07 (3.09–3.39)	0.745
Height (cm)	49.9 ± 0.2 (49.5–50.3)	50.0 ± 0.2 (49.6–50.4)	49.8 ± 0.4 (49.1–50.6)	0.707	49.7 ± 0.1 (49–50)	50.0 ± 0.3 (49.6–50.7)	0.284
Apgar first minute	9.1 ± 0.1 (8.9–9.3)	9.2 ± 0.2 (8.8–9.5)	9.0 ± 0.1 (8.8–9.2)	0.333	9.3 ± 0.1 (9.0–9.6)	9.1 ± 0.1 (8.9–9.3)	0.284
Apgar fifth minute	9.9 ± 0.04 (9.9–10)	9.9 ± 0.1 (9.8–10)	9.9 ± 0.1 (9.8–10)	0.961	10 ± 0.0 (10–10)	9.9 ± 0.1 (9.8–10)	0.676
BMI (kg/m^2)	12.9 ± 0.2 (12.4–13.4)	12.9 ± 0.4 (12.1–13.6)	13 ± 0.3 (12.3–13.6)	0.832	13 ± 0.5 (11.9–14.0)	12.9 ± 0.3 (12.3–13.4)	0.841
PI (kg/m^3)	25.9 ± 0.5 (24.8–26.9)	25.7 ± 0.8 (24.1–27.3)	26 ± 0.6 (24.7–27.3)	0.832	26.1 ± 1.0 (24.0–28.2)	25.7 ± 0.5 (24.5–26.9)	0.486
Insulin (mUI/l)	6.6 ± 1.4 (3.5–9.7)	9.2 ± 2.0 (3.6–14.8)	3.6 ± 0.6 (2.2–5.0)	0.048	11.8 ± 4.0 (3.2–19.3)	3.8 ± 0.7 (2.5–5.3)	0.017
Glucose (mg/dl)	76.9 ± 4.9 (80.3–85.6)	85.5 ± 6.4 (76.8–83.4)	66.8 ± 6.9 (83.2–90.8)	0.018	93.6 ± 10.8 (68.1–117.5)	68.6 ± 3.5 (61.6–75.8)	0.048
Glucose/insulin	31.2 ± 7.9 (15.1–47.2)	32.0 ± 13.8 (3.0–60.9)	30.2 ± 6.4 (16.6–43.8)	0.441	17.0 ± 3.2 (8.8–22.8)	40.2 ± 11.6 (15–65.5)	0.024
HOMA-IR	1.6 ± 0.5 (0.54–2.8)	2.5 ± 1.0 (0.5–4.5)	0.6 ± 0.1 (0.3–0.91)	0.031	3.5 ± 1.5 (0.4–6.2)	0.7 ± 0.1 (0.43–1.0)	0.049
QUICKI	0.44 ± 0.02 (0.39–0.48)	0.42 ± 0.03 (0.35–0.49)	0.45 ± 0.03 (0.40–0.50)	0.271	0.41 ± 0.0 (0.35–0.47)	0.45 ± 0.0 (0.39–0.51)	0.298

Abbreviations: BMI, body mass index; GA, gestational age; HEI, healthy eating index; HOMA-IR, homoeostatic model assessment; MDA, mediterranean diet adherence; N, number of cases; *P, Mann–Whitney *U* test; *P*, χ^2 test; PI, Ponderal index; QUICKI, quantitative insulin sensitivity check index. Data are mean ± s.e. (95% confidence intervals). [a]Glucose at O'Sullivan test.

RESULTS

Table 2 shows that no significant differences were found between maternal and neonatal age, and anthropometric characteristics of groups classified according to the HEI and MDA score. Low HEI-score women had lower ($P = 0.016$) glycaemia than their high HEI-score counterparts. Neonates whose mothers had consumed low HEI-score diets displayed significantly higher glycaemia ($P = 0.018$), insulinaemia ($P = 0.048$) and HOMA-IR ($P = 0.031$) than those whose mothers had followed an 'adequate' diet. Women with MDA scores <7 had lower ($P = 0.025$) glucose levels and weight gain during pregnancy ($P = 0.017$) than their MDA ⩾7 score counterparts. Neonates whose mothers followed low MDA-score diets had higher insulinaemia ($P = 0.017$), glycaemia ($P = 0.048$) and HOMA-IR ($P = 0.049$) than neonates of mothers with adequate MDA diets. The mother or neonate distributions according to HEI or MDA score were not significantly affected by potential confounders.

Table 3 indicates that low HEI-score diets displayed lower (g/1000 kcal) CHO ($P = 0.027$) and fibre values ($P = 0.011$) but higher fat ($P < 0.001$) and cholesterol ($P < 0.001$) levels, and SFA/CHO ratios ($P < 0.001$) than the high HEI-score diets. Low HEI-score diets had higher contribution to total energy (%En) of fats ($P < 0.001$) and SFA ($P = 0.002$) and lower of CHO ($P = 0.005$). Diets with MDA score <7 vs ⩾7 contained (per 1000 kcal) more ($P < 0.05$) cholesterol but less fibre ($P < 0.001$) and had higher SFA/CHO ($P = 0.021$), ω6/ω3 ($P = 0.044$) and lower PUFA + MUFA/SFA

Table 3. Dietary energy, macronutrient and fatty acid energy contribution in the total of mothers and in those following an inadequate diet (HEI score $\leqslant 70$) or an adequate diet (HEI score >70) or a low adherence to the mediterranean diet (MDA <7) or a high adherence (MDA $\geqslant 7$)

	All (N = *35*)	*HEI* $\leqslant$*70;* (N = *19*)	*HEI* $>$*70;* (N = *16*)	P *HEI*	*MDA* $<$*7* (N = *13*)	*MDA* $\geqslant$*7* (N = *22*)	P *MDA*
Mothers, $<35/\geqslant 35$ years	19/16	13/6	13/3	0.319	12/1	14/8	0.066
Primarity/multiparity	13/22	7/6	12/10	0.621	2/11	11/11	0.043
Low/medium/high education degree	6/22/7	4/11/4	2/11/3	0.889	2/8/3	4/14/4	0.783
$<1000/1000$–$10\,000/>10\,000$ inhabitants	1/9/25	0/6/13	1/3/12	0.562	0/3/10	1/6/15	1.000
Seasonality spring-summer/ autumn-winter	20/15	9/10	11/5	0.176	9/4	19/3	0.226
No dietary change/change[a]	27/8	16/3	11/5	0.248	10/3	17/5	0.645
Maternal diet				*P* HEI*			*P* MDA*
Energy (kcal)	2166 ± 89 (1974–2343)	2289 ± 143 (1988–2590)	2004 ± 94 (1804–2203)	0.005	2327 ± 137 (2010–2542)	2059 ± 115 (1795–2330)	0.055
Protein (g/1000 kcal)	43.8 ± 1.2 (41.1–46.0)	43.2 ± 1.8 (39.3–47.1)	44.0 ± 1.5 (40.8–47.3)	0.731	41.1 ± 2.2 (36.4–45.8)	45.3 ± 1.3 (46.2–47.9)	0.075
CHO (g/1000 kcal)	101.3 ± 2.3 (96.2–105.5)	96.0 ± 3.4 (88.9–103.1)	106.9 ± 2.2 (102.2–111.6)	0.027	102.3 ± 3.2 (95.3–109.3)	100.8 ± 3.1 (93.5–106.6)	0.668
Fats (g/1000 kcal)	44.1 ± 1.0 (42.4–46.5)	47.0 ± 1.2 (44.5–49.6)	41.4 ± 1.3 (38.6–44.2)	<0.001	45.3 ± 0.9 (43.2–47.3)	43.5 ± 1.5 (40.8–47.1)	0.603
Fibre (g/1000 kcal)	10.5 ± 0.5 (9.4–11.4)	9.4 ± 0.6 (8.1–10.6)	11.7 ± 0.8 (10.0–13.3)	0.011	8.3 ± 0.3 (7.5–9.0)	11.8 ± 0.6 (10.3–13.0)	<0.001
Cholesterol (mg/1000 kcal)	172 ± 6.3 (159.6–185.7)	192.3 ± 8.8 (173.9–210.7)	149.3 ± 5.3 (138.1–160.4)	<0.001	176.8 ± 8.8 (162.1–194.5)	166 ± 7.8 (149.9–183.9)	0.050
Protein (En%)	17.4 ± 0.5 (16.4–18.3)	17.2 ± 3.2 (15.7–18.7)	17.5 ± 2.4 (16.2–18.8)	0.756	16.4 ± 0.9 (14.5–18.2)	18.0 ± 0.5 (16.8–19.0)	0.649
CHO (En%)	43 ± 0.9 (41.0–44.6)	40.6 ± 5.6 (37.9–43.3)	45.4 ± 3.4 (43.6–47.3)	0.005	43.0 ± 1.2 (40.4–45.5)	43.0 ± 1.3 (40.1–45.3)	0.974
Fats (En%)	39.5 ± 0.9 (38.0–41.6)	42.1 ± 4.8 (39.8–44.4)	37.0 ± 4.7 (34.5–39.5)	<0.001	40.6 ± 0.8 (38.7–42.4)	38.9 ± 1.4 (36.5–42.2)	0.649
Alcohol (En%)	0.07 ± 0.03 (0.1–0.13)	0.07 ± 0.19 (-0.02 to 0.16)	0.08 ± 0.16 (0–0.17)	0.635	0.07 ± 0.04 (-0.01 to 0.15)	0.07 ± 0.04 (-0.01 to 0.16)	0.397
SFA (En%)	13.5 ± 0.4 (12.7–14.4)	14.7 ± 0.6 (13.6–15.9)	12.2 ± 0.6 (11.0–13.3)	0.002	14.6 ± 0.7 (13.1–16.0)	12.9 ± 0.5 (11.8–14.1)	0.123
MUFA (En%)	17.8 ± 0.5 (16.9–19.0)	18.6 ± 3.3 (17.0–20.2)	17.1 ± 2.7 (15.7–18.5)	0.182	17.5 ± 0.6 (16.1–18.8)	17.9 ± 0.8 (16.6–19.7)	0.697
PUFA (En%)	4.9 ± 0.2 (4.6–5.4)	5.2 ± 1.1 (4.7–5.8)	4.7 ± 0.9 (4.2–5.2)	0.117	5.0 ± 0.3 (4.4–5.6)	4.9 ± 0.2 (4.5–5.5)	0.820
SFA/CHO (g/1000 kcal)	0.34 ± 0.02 (0.31–0.37)	0.41 ± 0.03 (0.36–0.45)	0.27 ± 0.01 (0.24–0.30)	<0.001	0.40 ± 0.04 (0.35–0.46)	0.31 ± 0.03 (0.27–0.36)	0.021
PUFA/SFA	0.38 ± 0.02 (0.34–0.43)	0.37 ± 0.12 (0.31–0.43)	0.43 ± 0.13 (0.33–0.47)	0.523	0.35 ± 0.03 (0.29–0.42)	0.39 ± 0.03 (0.34–0.46)	0.474
PUFA + MUFA/SFA	1.7 ± 0.1 (1.6–1.9)	1.7 ± 0.4 (1.5–1.9)	1.8 ± 0.3 (1.7–2.0)	0.109	1.5 ± 0.1 (1.3–1.8)	1.8 ± 0.1 (1.7–2.0)	0.050
ω-6/ω-3 Ratio	5.1 ± 0.5 (4.4–6.3)	5.4 ± 0.5 (4.4–6.3)	5.0 ± 0.6 (4.4–8.0)	0.584	6.3 ± 0.8 (4.4–8.0)	4.6 ± 0.3 (4.0–5.2)	0.044

Abbreviations: CHO, carbohydrates; En% (in parenthesis), energy contribution; HEI, healthy eating index; MDA, mediterranean diet adherence; MUFA, monounsaturated fatty acids; N, number of cases; **P*, Mann–Whitney *U* test; *P*, χ^2 test; PUFA: polyunsaturated fatty acids; SFA, saturated fatty acids. Data are mean ± s.e. (95% confidence intervals). [a]At least one point on MDA score from early to late pregnancy.

($P = 0.05$) ratios. The mother or neonate distributions according to HEI or MDA score were not significantly affected by most potential confounders.

Table 4 indicates that no significant effect can be attributable to seasonality, maternal dietary habits changes or other confounders on neonatal distribution according to HOMA-IR, glycaemia and insulinaemia.

MDA scores changed from 5.2 ± 0.3 to 5.4 ± 0.3 ($P = 0.083$) and from 7.8 ± 0.2 to 8.0 ± 0.2 ($P = 0.102$) from early to late pregnancy.

A high percentage of neonates whose mothers consumed low HEI- or MDA-score diets presented high insulinaemia, high glycaemia and high HOMA-IR (Figure 2). Compared with newborns at the 'adequate' HEI-score group, those belonging to the 'inadequate' diet presented a RR of 6.7 ($P = 0.017$) for high insulinaemia, 7.6 ($P = 0.008$) for high glycaemia and 2.9 ($P = 0.103$) for high HOMA-IR values (Figure 2a). In comparison with the $\geqslant 7$ MDA-score infants, the <7 MDA-score group presented a RR of 2.1 ($P = 0.177$) for high insulinaemia, 3.9 ($P = 0.016$) for high glycaemia and 3.4 ($P = 0.043$) for high HOMA-IR levels (Figure 2b). RR appear adjusted for major potential confounders as distribution of neonates according to low-normal and high values for insulin resistance/sensitivity markers was not affected by confounders (Table 4).

HEI and MDA scores were significantly correlated ($r = 0.446$; $P = 0.007$). In all, 34.3% of mothers followed 'adequate' and 25.7% followed 'inadequate' diets according to both HEI and MDA scores. Both neonatal insulinaemia and HOMA-IR were inversely correlated with the HEI score ($r = -0.365$; $P = 0.031$ and $r = -0.363$; $P = 0.032$, respectively) and with the MDA score ($r = 0.357$; $P = 0.048$ and $r = -0.338$; $P = 0.047$, respectively). Positive correlations, after adjusting data to 1000 kcal, were observed between maternal dietary cholesterol and neonatal glycaemia ($r = 0.541$; $P < 0.001$), insulinaemia ($r = 0.431$; $P = 0.010$) and HOMA-IR ($r = 0.439$; $P = 0.008$); and between dietary fats and neonatal

Table 4. Effect of selected possible confounders affecting the HOMA-IR, glucose and insulin neonatal levels

	Low-normal HOMA-IR (N = 26)	*High HOMA-IR (N = 9)*	P *HOMA-IR*	*Low-normal glucose (N = 25)*	*High glucose (N = 10)*	P *glucose*	*Low-normal insulin (N = 26)*	*High insulin (N = 9)*	P *Insulin*
Maternal									
Age (<35/⩾35 years)	20/6	6/3	0.421	18/7	18/2	0.488	20/6	6/3	0.421
Children number (primarity/multiparity)	11/15	2/7	0.254	10/15	3/7	0.440	12/14	1/8	0.066
O'Sullivan test (negative/positive)	20/6	7/2	0.670	20/5	7/3	0.411	22/7	5/1	0.580
Education level (low/medium/ high)	4/16/6	2/6/1	0.709	4/12/4	2/5/3	0.567	4/15/7	2/7/0	0.219
Delivery type(vaginal/caesarean)	25/1	9/0	0.748	24/1	10/0	0.714	25/1	9/0	0.748
Sex (male/female)	18/5	5/4	0.361	16/9	7/3	0.530	18/8	5/4	0.361
Weight gain (<10/⩾10 kg)	11/15	6/3	0.192	11/14	6/4	0.315	12/14	5/4	0.460
Town inhabitants (<1000/1000–10 000/>10 000)	0/8/18	1/1/7	0.138	0/8/17	1/1/8	0.136	0/8/18	1/1/7	0.138
Seasonality (spring-summer/autumn-winter)	14/12	6/3	0.394	12/13	8/2	0.087	15/11	5/4	0.606
Dietary change (no change/change)[a]	21/6	5/3	0.330	21/6	5/3	0.330	18/5	9/3	0.571

Abbreviations: HEI, healthy eating index; HOMA-IR, homeostatic model assessment for insulin resistance; MDA, mediterranean diet adherence; *P*, probability at contingency tables, χ^2 or Fisher test (*P* HEI or *P* MDA). Probability for different mothers' distribution was considered according to normal/low or high HOMA-IR; normal/low glycaemia or normal/low or high insulinaemia. [a]At least one point on MDA score from early to late pregnancy. For more details see text.

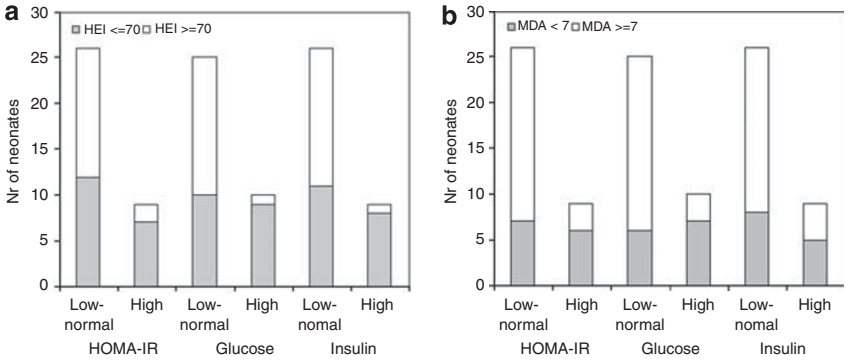

Figure 2. Number of neonates with low-normal (males <4.8 mUI/l, females <6.4 mUI/l) and high insulin cord-blood levels (males ⩾4.8 mUI/l, females ⩾6.4 mUI/l), low-normal (males <81.25 mg/dl, females <82.5 mg/dl) and high glucose cord-blood levels (males ⩾81.25 mg/dl, females ⩾82.5 mg/dl), and low-normal (males <0.92, females <1.09) and high HOMA-IR (males ⩾0.92, females ⩾1.09). (**a**) Neonates belonging to the dietary maternal HEI score (⩽70 or >70). The RR for high insulin level was 6.7 ($P = 0.017$), for high glucose 7.6 ($P = 0.008$) and for high HOMA-IR values 2.9 ($P = 0.103$). (**b**) Neonates from the 13-point MDA score (<7, ⩾7). RR for high insulin levels was 2.1 ($P = 0.177$); for high glucose values, 3.9 ($P = 0.016$); and for high HOMA-IR levels, 3.4 ($P = 0.043$). For more methodological details see text.

glycaemia ($r = 0.357$; $P = 0.035$). Dietary fats inversely correlated with QUICKI ($r = -0.359$; $P = 0.034$) values.

DISCUSSION

Present data suggest for the first time that low HEI- or MDA-score maternal diets negatively affect neonatal insulin and HOMA-IR levels.

Epidemiological studies show that western-style diets can increase metabolic syndrome risk, whereas mediterranean-style diets have a protective role.[25] During the first trimester of pregnancy, all the women participating in this study followed mediterranean-like diets but with a high contribution of meat and meat derivates and a moderate contribution of cereals and legumes, acceptable of vegetables and fruit and used olive oil as their principal oil for cooking and salads. The average HEI-score (mean (95% confidence intervals)) of the diets of the study participants was 67.5 (63.1–71.9), slightly below the cutoff point of 70 used by some authors to define good-quality diets.[32] HEI scores in the present study were similar to those of Spanish women in general (73.7 ± 10.5; mean ± s.d.) and 25–44 year-old Spaniards (68.8 ± 10.8).[32] A large proportion (approximately 37%) of the participants of the current study displayed MDA scores <7.

Diet of the expectant mothers was similar to the present-day diet of Spaniards, with a high level of dietary fat and a relatively low contribution of CHO to total energy intake.[36,37] Although the energy contribution of SFA was high, the absolute and relative amounts of MUFA, ω-6, ω-3 and the ω-6/ω-3 ratio appear adequate according to current nutritional guidelines.[20,38]

The maternal diet quality, as determined by HEI and MDA scores, significantly affected cord-blood insulin and HOMA-IR values. The smaller portions of vegetables, cereals, legumes and fruits consumed by women in the low HEI-score group explained their low CHO and fibre intakes. Dietary CHO quality and quantity are known to affect glycaemia and insulinaemia. The possible effect of glycemic load on insulin sensitivity markers should be tested in a larger number of pregnant mothers in future studies. Individuals with a high-fat intake (mainly as SFA) are especially prone to alterations of glucose tolerance and insulin sensitivity,[7–9] as diets rich in SFA decreases the number of insulin receptors in most tissues. SFA selectively desensitize the response of peripheral tissue to insulin, whereas unsaturated fatty acids (PUFA + MUFA) may counteract this effect.[39,40] Such phenomena corroborate the

close association between dietary fats and alterations in insulin secretion.[41,42]

Both low HEI- and low MDA-score diets lagged far behind current European nutritional guidelines and recommendations[31,38] with regard to the energy contribution of fats, SFA and CHO and fibre content. In addition, 'inadequate' diets displayed SFA/CHO ratios that were approximately 50 and 22% higher than those of their high-score counterparts. These are important findings, as studies of isocaloric diets in which total fat represented 44 %En confirm that the SFA/CHO ratio is related to HOMA-IR[14,15] and that glucose tolerance was low in individuals consuming diets rich in SFA.[8,9] In addition, the ω6/ω3 ratio in the low MDA-score diets was 37% higher than in the high MDA-score diets, suggesting its impact on neonatal insulin and HOMA-IR levels. Martín de Santa Olalla *et al.*[7] report that the ω6/ω3 ratio affects insulin resistance and sensitivity in certain population groups.

Although no clear evidence is yet available to explain why future mothers consuming high HEI- or MDA-score diets have higher basal glucose levels than their low-score counterparts, it appears that a high CHO intake during pregnancy induces high maternal glucose levels, permitting an adequate fetal glucose uptake. Differences between the diets consumed, as reflected through their HEI or MDA scores, do not appear to have any effect on maternal basal glucose at the O'Sullivan test, as none of the women studied presented fasting glycaemia $\geqslant$120 mg/dl. However, certain neonatal insulin sensitivity/resistance biomarkers were significantly affected by maternal diet. Newborns at the low HEI-score group had 30% higher glycaemia; the insulinaemia and HOMA-IR were 2.5 and 4 times higher, respectively, than infants whose mothers consumed an 'adequate' diet. Similarly, newborns of mothers with <7 MDA-score diets presented HOMA-IR and insulin levels that were 5 and 3 times higher, respectively, than their $\geqslant 7$ score counterparts. The beneficial effect of adherence to the mediterranean diet on HOMA-IR has been suggested.[43] A high percentage of neonates belonging to the low HEI- or low MDA-score diets presented high insulinaemia, glycaemia and HOMA-IR, circumstance that was infrequent in their respective counterparts and explain the significant RR found. Dietary fats, and particularly those containing SFA, are known to increase insulin secretion[44] and insulin resistance.[45] Dietary fat unsaturation greatly influences β-cell function and insulin sensitivity under conditions of low-CHO intake.[46] In addition, a western, low-CHO diet rich in SFA induced significantly higher insulin levels and lower cellular glucose uptake than a mediterranean or National Cholesterol Education Programme (NCEP)-step I diet.[47] Previous epidemiological studies found high correlations between HOMA-IR values and dietary SFA/CHO ratios.[14,15] The lower consumption of fibre by mothers at low MDA- and HEI-score vs their respective high-score counterparts (20% and 30%, respectively) may, at least partially, explain present results as dietary fibre has been found to improve insulin sensitivity.[6,48]

According to our data, after first trimester, except for fruits, fish/shellfish and sweets/pastries, non-remarkable changes occurred in of most food consumption (Supplementary Information). Crozier *et al.*[4] reported that, in practical sense, women's dietary patterns change little during pregnancy, although some differences were found for specific food groups.[4]

It has to be pointed out that present study shows some limitations, as the relatively low number of participating mothers, and the narrow range of neonatal bodyweights. The HEI and MDA scores cutoff points selected suggest acceptable or prudent diets but not optimum diets. Although the mediterranean diet characteristics are well defined, this is not a homogeneous dietary pattern. Timing of the FFQ would be a limitation as it was controlled only at early pregnancy. As the FFQ was completed by a trained dietician using food photographs, it should be accepted that the risk of potential errors due to lack of memory, and lack of precision with regard to food portions was lowered. In addition, dietary pattern showed minor changes during pregnancy. The effect of energy intake on dietary data should be discarded as diets were adjusted to 1000 kcal to reduce measurement error. Confounder influences on the RR of neonatal insulin sensitivity/resistance biomarkers should be also discarded.

In conclusion, notwithstanding study limitations, our data indicate that poor diets, as determined by their HEI or MDA scores, negatively affect neonatal glucose homeostasis and, consequently, HOMA-IR values at birth. Further studies are needed to clarify these relationships and understand the impact that these neonatal values may have later in life.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies the paper on European Journal of Clinical Nutrition website (http://www.nature.com/ejcn)