

Association of Maternal Dietary Patterns in Early Pregnancy with Risk of Delivering a Small or Large-For-Gestational Age Infant: Yazd Birth Cohort

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Abstract Introduction: Maternal dietary pattern is one of the most important birth outcomes determinants. We aimed to evaluate association of dietary patterns with risk of small-for-gestational age (SGA) and large-for-gestational age (LGA) newborns for weight, height, and head circumferences (HC). **Methods:** The Yazd Birth Cohort (YBC) includes 1666 mother-child pairs which their dietary intakes were obtained food frequency questionnaire (FFQ) at 4-12 weeks of gestation. By using principal component analysis (PCA), we derived two dietary patterns: fruit/vegetables and western pattern. Multinomial regression model was used for analyses. **Results:** Of 1666 newborns, 263 SGA and 71 LGA for weight, 115 SGA and 182 LGA for height and 86 SGA and 279 LGA for HC, were born. Lower scores of western pattern are associated with lower risk of LGA newborns (OR: 0.34; 95% CI: 0.15-0.78) and higher risk of SGA newborns (OR: 1.53; 95% CI: 1.01-2.32) for weight and also higher risk of LGA infants (OR: 1.67; 95% CI: 1.36-2.71) for height. While, lower adherence to fruit/vegetable is associated with higher risk of LGA infants (OR: 1.69; 95% CI: 1.02-2.8) for height too. **Conclusion:** Western pattern in early pregnancy may have higher risk of LGA and lower risk of SGA infants for weight.

Keywords: diet, pregnancy, newborn, Small-for-Gestational Age, birth outcome

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1. Introduction

An estimated 32.4 million live births in middle- and low-income countries are small for gestational age (SGA) (below the 10th percentile of the birth weight curve); in fact, 27% of all children born are small for gestational age [1]. On the other hand, previous studies have shown an increasing trend of obesity and gestational diabetes mellitus (GDM) which causes a higher prevalence of macrosomia and large-for-gestational-age (LGA) (above the 90th percentile of the birth weight curve) newborns in developing countries [2]. Whereas abnormalities in weight of newborns at birth may predict a higher risk of mortality,

morbidity, and defective growth [3,4,5,6], in 2009 Institute of Medicine (IOM) reported weight gain during pregnancy (inadequate or excessive gain) affect long term maternal and offspring health, such as maternal postpartum weight retention, adiposity in childhood [7] and coronary heart disease (CHD) [8].

Adequate intake of certain micro-nutrients during pregnancy, such as iron, folic acid, and vitamin D, is crucial for proper fetal growth and development [9,10,11]. As mothers follow different diets and any diet includes thousands of minerals, vitamins, and substances with complex combinations, these are likely to be interactive or synergistic [12]. Rather than single or a few nutrients or foods, maternal dietary pattern provides in depth understanding of the whole diet and in addition, it is

an important modifiable risk factor that could be a applicable method to reduce non communicable diseases in offspring [13].

Many studies have evaluated a priori dietary patterns, e.g., the Healthy Eating Index (HEI) [14] and Mediterranean dietary patterns [15,16]. These studies illustrate that adherence to these patterns in pregnancy were associated with a lower risk of preterm newborns. In addition, in a systematic review and meta-analysis, healthy dietary patterns were associated with a lower risk of SGA and low birth weight (LBW; under 2500 gr) [17]. In Japan, wheat products dietary pattern, including bread, confectionaries, and soft drink increased the risk of SGA for weight and head circumferences but not for height [18] while, others found no such association [19]. Earlier studies have also shown that high-quality diet in the first trimester of pregnancy is positively associated with birth size including birth weight and birth length [20].

Dietary patterns are strongly associated with population's culture and cooking recipes in a particular manner. Therefore, concept of "healthy" and "unhealthy" differs, making comparison between populations difficult. Hence, comparison among different populations and attribute results from one study to another is challenging. In addition to population differences, inconsistent finding in studies may be due to the use of different outcome definitions because there is no international consensus on growth standard and SGA and LGA definition. However, because the definite relationship between early maternal dietary pattern and birth weight in developing countries (Iran) are not fully known, we decided to evaluate the relationship between SGA and LGA for weight, height, and head circumferences at birth and mothers' major dietary patterns.

2. Materials and Methods

2.1. Study Population

Yazd birth cohort is a prospective, population-based pregnancy cohort which is a part of a bigger project (PERSIAN birth cohort) [21]. Briefly, this study was conducted in five cities of Iran on the association between pregnancy and post-pregnancy outcomes and environmental exposure, socioeconomic status, and diet from June 2016 and it still goes on. Sample size calculated 15,000 mother-offspring pair ($n=3,000$ for each city), sufficient to study the events as rare as those with incidence of less than 0.4% in the study population, which is acceptable for most of the outcomes studied in this cohort. The first phase of data collection was conducted on pregnant women in Yazd. Ethics approval was obtained [IR.SSU.SPH.REC.1399.201] from School of Public Health, Shahid Sadoughi University of Medical Sciences.

We enrolled pregnant women regardless of pregnancy time within the first trimester, gravida number, parity or use of fertility treatment and also who signed the informed consent form, planned to give birth in hospitals in which the cohort study was being undertaken, had Iranian nationality, and did not plan to change their city of residence for five years. Pregnancies ended in both natural vaginal deliveries or cesarean section were included in the

study. The pregnant women were recruited by two catchment processes 1: when they referred to hospital outpatient clinics or when our experts phoned them by using mother and child databank from the National Health Service. 2: distribution of invitation advertisements in the city. A total of 3,110 pregnant women were enrolled in the YBC at the first invitation and completed the demographic baseline questionnaire and the validated FFQ [22] in face-to-face interview. After recruitment (baseline questionnaire), protocol of study includes three time follow up: first trimester (13th-15th weeks), second trimester (24th-27th weeks) and third trimester (one week before estimated delivery date).

At the time of analysis, the dietary patterns of 1,666 pregnant women who have given birth to a healthy baby were extracted. The missing values of birth weight were because of miscarriage, immigration, lack of corporation with the researchers, or the birth of the child in other hospitals (1,026 attrition). After excluding women with daily calorie intakes of under 800 Kcal and above 5000 Kcal ($n=203$) [23], 1,881 women remained. Thirty-six pregnant women who were older than 45 or younger than 18 years were eliminated. Also, 10 pregnant women were removed because of smoking and alcohol abuse during pregnancy. Pregnant women suffering from diabetes (except GDM), cancers, fibromyalgia, chlamydia, arthritis rheumatoid, systematic lupus erythematosus, autoimmune diseases, syphilis, gonorrhea, toxoplasmosis, epilepsy, and multiple sclerosis (MS) ($n=151$) were also eliminated from the analysis. Finally, 18 mothers who had twins were removed from the data, and the analysis was performed on 1,666 women. (Figure 1)

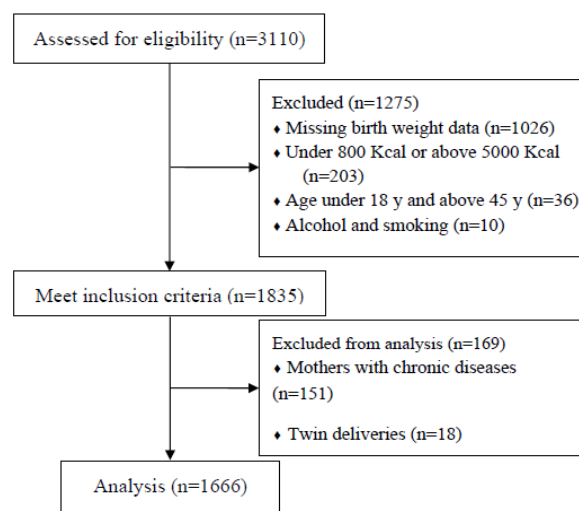


Figure 1. Flow chart of study population

2.2. Dietary Assessment

Dietary information was obtained from a 88-item semiquantitative FFQ which the validity and reliability of the FFQ had been previously evaluated [24]. The psychometric properties of this FFQ were investigated and confirmed by Sharifi among pregnant female in Iran. In the study of Sharifi et al., Pearson correlation coefficients between test and retest for foods was $r=0.845$. The Kaiser-Meyer-Olskin measure of sampling adequacy was 0.584, P values for the Bartlett test of sphericity were all less

than 0.001. This questionnaire was filled out by pregnant women one time in the first trimester of pregnancy (4-15 weeks of pregnancy). Mothers were asked to fill out the questionnaire by themselves regarding their usual intake during the past year. This FFQ asked the participants about the consumption frequency of standard units commonly used by Iranians for each food item (on a daily, weekly, monthly, or yearly basis). After completing FFQ, each food item was calculated for daily intake and then, we converted the FFQ information into gram using household measurements. Energy intake and the amounts of other nutrients were computed by Nutritionist 4 (N4) designed for Iranian foods. All the items in FFQ were divided into 34 groups based on similar characteristics and culinary use (Supplemental Table 1, online supplementary material). Then, to reduce the basic error in dietary intake assessments (energy effects), we computed the energy-adjusted gr for each group [25]. By using principal component analysis (PCA) with the Varimax rotation, dietary patterns were extracted. The breakpoint of the scree plot depicted two major factors (dietary patterns) that could be extracted. The factor loading for each food group showed the correlation of that food group with the dietary patterns; we considered the factor loading of 0.2 or higher than 0.2 (Table 1).

Table 1. Factor loading of energy adjusted food groups in patterns using PCA in Yazd birth cohort (n=1666)

Food Or Food Groups	Fruit/Vegetables pattern	Western pattern
Fruits	.61	-
Leafy vegetables	.53	-
Dried fruits	.51	-
Date	.49	-
Cruciferous vegetables	.42	-
Natural fruit juice	.36	-
Olive	.35	-
Tomato	.31	-
Fish	.3	-
Refined grain	-.29	.25
Nuts	.22	-
Processed meat	-	.47
Chips/puffs	-	.45
Soft drink	-	.44
Pickles	.25	.41
Hydrogenated fat	-	.4
Legumes	-	.38
Dairy	-	-.37
Tea	-	.33
Whole grain	-	-.32
Salt	-	.31
Soybean protein	-	.3
Tuna	-	.29
Sugar	-	.29
Sweet desserts	-	.23
Poultry meat	-	.21
Potatoes	-	.2

Values are factor loading (correlation coefficients) between factors (dietary patterns) and food frequency variable. Foods are sorted by size of loading factors and minus values show lower frequency of foods in pattern. Absolute values <0.20 are disappeared to simplifying. PCA: Principal Component Analysis

2.3. Birth Outcomes

The mothers' gestational age was estimated during the first interview by calculating the first day of the last menstrual period. Information on birth outcomes was extracted from the mentioned hospitals which measured weight (g), height (cm), and head circumference (cm) immediately after birth. SGA, Appropriate-for-Gestational Age (AGA), and LGA were categorized based on the birth week in the Fenton growth chart [26]. SGA was defined for weight, height, and head circumference as measurements below the 10th percentile on the sex- and age-specific Fenton growth chart. LGA was defined as newborns whose anthropometric measurements were above the 90th percentile curves, and normal newborns were placed in the AGA category [27].

2.4. Covariates

Potential confounding covariates were asked during interviews from previously reported determinants of fetal growth [28,29]. We treated maternal age, Body Mass Index (BMI), and height (which were measured at first trimester) as continuous variables. BMI calculated by dividing the early pregnancy maternal body weight (kg) by the square of body height (m²) (BMI = kg/m²). The International Physical Activity Questionnaire (IPAQ) was used for physical activity measurements [30]. The scores of IPAQ are divided into three levels. Based on the IPAQ guideline, physical activity is classified as follows: at least 600 MET-minutes/week: low, 600-3000 MET-minutes/week: moderate, and above 3000 MET-minutes/week: high physical activity. The consumption of folic acid supplements and other multivitamin supplements that contain folic acid was asked during the first and second interviews (yes or no). During the first interview, the use of oral contraceptive pills (OCP) in the four months before pregnancy was reported by the mothers. Morning sickness during pregnancy was divided into three levels (no nausea, nausea, and acute vomiting for a long time) and analyzed as dichotomous data (yes/no). In the third and fourth interviews, the mothers self-reported GDM based on screening on the 20-24th week as an overall protocol in Iran. Financial level was reported in three levels: very poor, poor, and favorable. Another important covariate for analysis was the gravida number which was classified into nulliparous mothers or mothers with more than 1 gravidity. Education was divided into three levels of illiterate, low literacy, and university (Table 2). Weight gain (kg) during pregnancy was obtained by subtracting the weight before birth from the first weight of the mothers and after that it was converted to ounces (oz). Mothers according to gestational weight gain guidelines, divided into three categories: below, within and above. Pregnancy BMI was categorized into four groups and a specific weight gain range is defined for each group: underweight <18.5 (28-40 oz); normal 18.5–24.9 (25-35 oz); 25-29.9 (15-25); overweight, ≥30 (11-20 oz). Some of other important micro and macro nutrients provided in Table 3.

Table 2. Baseline characteristics of 1666 pregnant mothers across quartiles of two dietary patterns identified by principal component analysis in Yazd Birth Cohort (Mean values and standard deviation; percentage)

Characteristics	Dietary Patterns										
	All participants	Fruit/vegetables dietary pattern					Western dietary pattern				
		Q1 N=416	Q2 N=417	Q3 N=417	Q4 N=416	P- value*	Q1 N=416	Q2 N=417	Q3 N=417	Q4 N=416	P- value*
Age, y±sd	28.65±5.34	28.6±5.5	28.1±5.2	28.6±5.3	29.2±5.3	0.04	29.5±5	28.7±5.2	28.8±5.3	27.6±5.7	<0.001
Weight, kg±sd	65.18±11.98	64±11.54	63.76±11.8	66.15±12.1	66.9±12.1	<0.001	66.2±12	65.5±11.6	65.3±12	63.8±12.1	0.03
Height, cm±sd	159.58±5.63	159±5.8	159.6±5.6	160±5.6	159.5±5.4	0.09	160±5.8	159.4±5.6	159.5±5.8	159.2±5.1	0.17
BMI, kg/m ²	25.57±4.44	25.3±4.3	24.9±4.5	25.8±4.2	26.3±4.5	<0.001	25.8±4.3	25.7±4.3	25.6±4.4	25.1±4.7	0.13
Education											
Illiterate, n (%)	80 (4.8)	30 (37.5)	21 (26.3)	15 (18.8)	14 (17.5)	<0.001	16 (20)	11 (13.8)	21 (26.3)	32 (40)	<0.001
Low literacy, n (%)	742 (44.5)	231 (31.1)	183 (24.7)	170 (22.9)	158 (21.3)		155 (20.9)	164 (22.1)	190 (25.6)	233 (31.4)	
University, n (%)	844 (50.7)	155 (18.4)	213 (25.2)	232 (27.5)	244 (28.9)		245 (29)	242 (28.7)	206 (24.4)	151 (17.9)	
GDM											
Yes, n (%)	155 (9.3)	40 (25.8)	35 (22.6)	41 (26.5)	39 (25.2)	0.89	45 (29)	34 (21.9)	38 (24.5)	38 (24.5)	0.61
No, n (%)	1511 (90.7)	376 (24.9)	382 (25.3)	376 (24.9)	377 (25)		371 (24.6)	383 (25.3)	379 (25.1)	378 (25)	
Financial level											
Low, n (%)	259 (15.5)	101 (39)	72 (27.8)	43 (16.6)	43 (16.6)	<0.001	54 (20.8)	53 (20.5)	75 (29)	77 (29.7)	<0.001
Medium, n (%)	339 (20.3)	97 (28.6)	103 (30.4)	87 (25.7)	52 (15.3)		67 (19.8)	87 (25.7)	84 (24.8)	101 (29.8)	
High, n (%)	1068 (64.1)	218 (20.4)	242 (22.7)	287 (26.9)	321 (30.1)		295 (27.6)	277 (25.9)	258 (24.2)	238 (22.3)	
Nulliparous											
Yes, n (%)	1125 (68.1)	291 (25.8)	283 (25.1)	280 (24.8)	273 (24.2)	0.62	307 (27.2)	286 (25.4)	278 (24.7)	256 (22.7)	0.003
No, n (%)	531 (31.9)	123 (23.2)	133 (25)	135 (25.4)	140 (26.4)		107 (20.2)	129 (24.3)	139 (26.2)	156 (29.4)	
Folic acid											
Yes, n (%)	788 (47.3)	188 (23.9)	193 (24.5)	183 (23.2)	224 (28.4)	0.01	209 (26.5)	212 (26.9)	195 (24.7)	172 (21.8)	0.02
No, n (%)	878 (52.7)	228 (26)	224 (25.5)	234 (26.7)	192 (21.9)		207 (23.6)	205 (23.3)	222 (25.3)	244 (27.8)	
Physical activity											
Low, n (%)	962 (57.7)	233 (24.2)	246 (25.6)	251 (26.1)	232 (24.1)	0.66	245 (25.5)	256 (26.6)	241 (25.1)	220 (22.9)	0.06
Medium, n (%)	495 (29.7)	135 (27.3)	116 (23.4)	116 (23.4)	128 (25.9)		121 (24.4)	103 (20.8)	123 (24.8)	148 (29.9)	
High, n (%)	209 (12.5)	48 (23)	55 (26.3)	50 (23.9)	56 (26.8)		50 (23.9)	58 (27.8)	53 (25.4)	48 (23)	
Morning sickness											
No nausea, n (%)	613 (36.8)	137 (22.3)	137 (22.3)	169 (27.6)	170 (27.7)	<0.001	171 (27.9)	171 (27.9)	142 (23.2)	129 (21)	<0.001
Nausea, n (%)	530 (31.8)	139 (26.2)	127 (24)	124 (23.4)	140 (26.4)		150 (28.3)	130 (24.5)	112 (21.1)	138 (26)	
Acute vomiting long time, n (%)	523 (31.4)	140 (26.8)	153 (29.3)	124 (23.7)	106 (20.3)		95 (18.2)	116 (22.2)	163 (31.2)	149 (28.5)	
Gestational weight gain											
Below	440 (26.4)	118 (26.8)	133 (30.2)	90 (20.5)	99 (22.5)	0.002	128 (29.1)	91 (20.7)	107 (24.3)	114 (25.9)	0.18
Within	606 (36.4)	157 (25.9)	138 (22.8)	174 (28.7)	137 (22.6)		141 (23.3)	164 (27.1)	154 (25.4)	147 (24.3)	
Above	454 (27.3)	100 (22)	113 (24.9)	109 (24)	132 (29.1)		110 (24.2)	112 (24.7)	121 (26.7)	111 (24.4)	

SD, standard deviation; BMI, body mass index; GDM, gestational diabetes mellitus; Q, quartile.

* P-values for continuous variables were calculated by ANOVA test and chi-square test used for categorical variables.

Table 3. Macro and micro nutrients intakes in early pregnancy (Adjusted mean values and standard error)

Dietary intakes	Dietary Patterns									
	Fruit/vegetables dietary pattern					Western dietary pattern				
	Q1 N=416	Q2 N=417	Q3 N=417	Q4 N=416	P- value*	Q1 N=416	Q2 N=417	Q3 N=417	Q4 N=416	P- value*
Energy intake, kcal $\pm$ se ^a	2581 $\pm$ 33.38	2223 $\pm$ 33.47	2233 $\pm$ 33.21	2448 $\pm$ 33.29	<0.001	2655 $\pm$ 33.47	2164 $\pm$ 33.37	2189 $\pm$ 33.33	2477 $\pm$ 33.37	<0.001
Carbohydrate, gr $\pm$ se ^b	344.6 $\pm$ 2.08	330.6 $\pm$ 2.07	333.7 $\pm$ 2.05	339.9 $\pm$ 2.05	<0.001	336 $\pm$ 2.1	335 $\pm$ 2.08	336 $\pm$ 2.07	340 $\pm$ 2.06	0.2

Dietary intakes	Dietary Patterns									
	Fruit/vegetables dietary pattern					Western dietary pattern				
	Q1 N=416	Q2 N=417	Q3 N=417	Q4 N=416	P-value*	Q1 N=416	Q2 N=417	Q3 N=417	Q4 N=416	P-value*
Protein, gr±se ^b	68±0.6	71.6±0.6	72.6±0.59	75.6±0.59	<0.001	71.2±0.6	72.2±0.6	71.6±0.59	72.9±0.59	0.1
Fat, gr±se ^b	83.1±0.93	87.8±0.93	86.3±0.92	82.7±0.92	<0.001	86.2±0.95	85.5±0.93	85.1±0.93	83.1±0.93	0.1
Fiber, gr±se ^b	15.1±0.3	18.6±0.3	21.6±0.3	26.9±0.3	<0.001	18.3±0.3	20±0.3	21.3±0.3	22.7±0.3	<0.001
Sodium, mg±se ^b	3261±98.7	3396±98.3	3445±97.5	3379±97.4	0.6	2691±99.9	3084±98.6	3512±98.2	4193±97.7	<0.001
Calcium, mg±se ^b	749±11	789±10.9	798±10.8	849±10.8	<0.001	932±11.1	794±11	751±10.9	709±10.9	<0.001
Vitamin c, mg±se ^b	69.7±3.1	106.3±3.1	132.2±3	191.3±3	<0.001	118.7±3.1	120.1±3.1	129.7±3.1	130.9±3	<0.001
Folic acid, µg±se ^b	206±3.8	249±3.8	273±3.8	334±3.8	<0.001	231±3.9	251±3.8	270±3.8	310±3.8	<0.001
Iron, mg±se ^b	8.2±1.2	9.3±1.2	10±1.2	11.2±1.2	<0.001	9.7±1.2	9.4±1.2	9.3±1.2	10.2±1.2	<0.001
Polyunsaturated fat, gr±se ^b	20.4±0.5	23.5±0.5	23.9±0.5	22.7±0.5	<0.001	19.2±0.5	23.3±0.5	24.2±0.5	24±0.5	<0.001
Linolenic acid, gr±se ^b	0.2±0.006	0.26±0.006	0.27±0.006	0.28±0.006	<0.001	0.25±0.006	0.27±0.006	0.27±0.006	0.23±0.006	<0.001

SE, standard error; Q, quartile.

* P-values were calculated by ANCOVA test

^a: adjusted for age, ^b: adjusted for age and energy intake

2.5. Statistical Analysis

The distribution of maternal characteristics in the quartile of dietary patterns was analysis by the chi-square test for categorical measurements, an analysis of variance (ANOVA) for comparing the means of normal quantitative measurements, and the Kruskal-Wallis test for nonnormal quantitative measurements. Means of dietary variables that were adjusted for age and energy used to compare them across quartiles in patterns were calculated by an analysis of covariance (ANCOVA) with Bonferroni's correction. To remove confounding effect of energy, we adjusted the gram of food groups by using linear regression (residual method) [31], and the residual amounts in each group were added to a constant number to eliminate minus numbers. PCA was performed on residual amounts to extract dietary patterns with the Varimax rotation. We also evaluated Bartlett's test of sphericity and Kaiser-Meyer-Olkin (KMO) measure to sampling adequacy. As determining the number factors to be retained, the three selection criteria that are typically used include 1) retaining factors with an eigenvalue greater than one, 2) the scree plot, and 3) the interpretable variance percentage. The dietary pattern score for each participant was calculated by summing the standardized frequency of food groups weighted by their factor loadings. The scores of each pattern were categorized into quartiles and last quartile consider as the reference. The response variable was divided into three groups (SGA, AGA, and LGA); so we used multinomial logistic regression and AGA was considered as reference [32]. All data analyses were performed in SPSS 21.0 (IBM Corporation).

3. Results

A total of 1,666 pregnant women were selected for this study. There were 261 (15.8%) SGA and 71(4.1%) LGA newborn for weight, 115 (6.9%) SGA and 182 (10.9%)

LGA newborn for height and 86 (5.2%) SGA and 279 (16.7%) LGA newborn for head circumference in this study.

3.1. Dietary Patterns

Fourteen components had the eigenvalue above 1 but, there was a clear break after second factor (Supplemental Figure 1, online supplementary material). Based on breaking point and interpretability, we decided to retain two factors [33]. Two distinct dietary patterns with as well as factor loading above 0.2 [34], were retained. These patterns explained 12.8% of the variance of total intakes. The first pattern included higher factor loading for fruits and vegetables such as leafy vegetables, fruits, dried fruits, dates, cruciferous vegetables, fruit juice, olives, tomatoes, nuts, and fish as the only animal source. Refined grains had only negative factor loading in the fruits/vegetables pattern. The second pattern (Western pattern) included processed meat, chips/puffs, soft drinks, pickles, hydrogenated fat, legumes, tea, salt, soybean protein, canned fish, sugar, sweet desserts, poultry, and potatoes. Dairy and whole grains in the Western pattern had negative scores (Table 1). The Kaiser-Meyer-Olkin statistic was 0.43 and Bartlett's test of sphericity means that the data is sufficient for the PCA (P-value < 0.0001).

3.2. Association of Dietary Patterns with Maternal Characteristics

As shown in Table 2, in the fruits/vegetables across pattern quartiles, means of age, weight, and BMI decreased which is opposite to the Western pattern in which age and weight decreased in higher quartiles and BMI was not different across quartiles. In education level, more adherence to fruits/vegetables pattern is associated to lower number of illiterate and low-literacy pregnant women and higher number of university-educated mothers. In contrast, illiterate and low-literacy pregnant women have higher adherence to western pattern and university-educated women have lower adherence to western dietary

pattern. No significant difference was observed in the frequency of GDM in the quartiles of two patterns.

The financial level was stratified into three levels; in low and medium levels, the number of mothers decreased by increasing the quartiles of the fruits/vegetables pattern, while the number of high-income families in quartile 4 was higher than the first quartile. On the other hand, since the adherence to western dietary pattern increased also, frequency of pregnant women in low- and medium-financial levels increased. In addition, the number of women in the high financial level decreased when quartiles increased. The frequency of nulliparous mothers declined in higher adherence to the Western dietary pattern, while in the fruits/vegetables pattern, there was no significant difference.

Furthermore, pregnant women with higher scores of the fruits/vegetables pattern had higher folic acid supplement consumption and vice versa, i.e., pregnant women with higher scores of the Western dietary pattern, consumed less folic acid supplement. There was no significant association between the number of pregnant women in physical activity levels and quartiles of dietary patterns. Additionally, mothers who had more adherence to the fruits/vegetables dietary pattern had less acute vomiting for a long time, and mothers in higher quartiles of this pattern had a lower risk of nausea. Although there is no association among gestational weight gain categories (below, Whitin and above) across quartiles of western dietary pattern, mothers in the higher quartiles of fruit/vegetable dietary pattern are more likely to be in the

above category of gestational weight gain categories.

3.3. Association of Dietary Patterns and Birth Outcomes

A total of 263 SGA and 71 LGA newborns for weight were born among 1,666 newborns. There was no significant association between quartiles of dietary patterns and SGA and LGA in the crude model of multinomial regression for weight. After adjusting for morning sickness, education level, acid folic, physical activity, age, BMI, OCP usage, nulliparous, financial level, GDM, height, energy intake, and weight gain during pregnancy in the Western pattern, the second quartile compared to the reference showed a higher risk for SGA newborns (OR: 1.53; 95% CI: 1.01-2.32). Again, in the Western dietary pattern in the adjusted model, less adherence to the pattern reduced the risk of LGA in quartiles 1 compared to quartile 4 (OR: 0.34; 95% CI: 0.15-0.78) (Table 4).

There was another significant association in the third quartile compared to the fourth quartile of western pattern in LGA newborns for height that showed lower adherence to western pattern increased risk of LGA infants (OR: 0.167; 95% CI: 1.36-2.71). Also, in fruit/vegetables pattern lower adherence to pattern was significantly associated with higher risk of LGA newborns (OR: 1.69; 95% CI: 1.02-2.8). For crude and adjusted models in head circumference, there was no significant association between head circumference and dietary patterns.

Table 4. Association between dietary patterns quartiles and SGA and LGA for birth outcomes (weight, height and head circumference)

SGA & LGA			Dietary patterns							
			Fruit/vegetables pattern				Western pattern			
			Q1	Q2	Q3	Q4 ^b	Q1	Q2	Q3	Q4 ^b
Weight										
SGA (263)	Crude		1.12 (0.77-1.63)	1.01 (0.69-1.47)	0.85 (0.58-1.25)	1 Ref.	0.97 (0.66-1.42)	1.27 (0.88-1.84)	0.98 (0.67-1.44)	1 Ref.
	Adjusted ^a		0.94 (0.62-1.42)	0.84 (0.56-1.28)	0.77 (0.5-1.18)	1 Ref.	1.16 (0.75-1.78)	1.53 (1.01-2.32) *	1.11 (0.72-1.69)	1 Ref.
LGA (71)	Crude		1.37 (0.72-2.62)	1.04 (0.52-2.05)	0.74 (0.35-1.55)	1 Ref.	0.52 (0.26-1.05)	0.61 (0.31-1.2)	0.82 (0.44-1.52)	1 Ref.
	Adjusted ^a		1.99 (0.93-4.25)	1.59 (0.73-3.46)	1 (0.44-2.26)	1 Ref.	0.34 (0.15-0.78) *	0.51 (0.23-1.11)	0.78 (0.39-1.52)	1 Ref.
Height										
SGA (115)	Crude		1.31 (0.75-2.27)	1.27 (0.73-2.2)	1.13 (0.64-1.98)	1 Ref.	0.71 (0.41-1.22)	0.87 (0.52-1.48)	0.89 (0.52-1.51)	1 Ref.
	Adjusted ^a		1.31 (0.7-2.44)	1.37 (0.74-2.53)	1.19 (0.63-2.25)	1 Ref.	1.05 (0.57-1.96)	1.18 (0.65-2.15)	1.12 (0.61-2.02)	1 Ref.
LGA (182)	Crude		1.69 (1.07-2.6) *	1.24 (0.77-1.99)	1.37 (0.86-2.18)	1 Ref.	1.15 (0.72-1.82)	1.14 (0.72-1.82)	1.52 (0.98-2.37)	1 Ref.
	Adjusted ^a		1.69 (1.02-2.8) *	1.45 (0.86-2.43)	1.55 (0.94-2.56)	1 Ref.	1.14 (0.68-1.9)	1.19 (0.7-2)	1.67 (1.36-2.71) *	1 Ref.
HC										
SGA (86)	Crude		0.82 (0.43-1.58)	0.98 (0.52-1.82)	1.09 (0.59-1.99)	1 Ref.	0.7 (0.37-1.33)	0.9 (0.49-1.65)	0.87 (0.47-1.61)	1 Ref.
	Adjusted ^a		0.59 (0.28-1.22)	0.84 (0.43-1.66)	1.01 (0.57-2.12)	1 Ref.	0.99 (0.49-2.01)	1.39 (0.72-2.68)	1.08 (0.55-2.11)	1 Ref.
LGA (279)	Crude		0.87 (0.61-1.25)	0.78 (0.54-1.13)	0.73 (0.5-1.06)	1 Ref.	0.78 (0.54-1.12)	0.81 (0.56-1.16)	0.77 (0.53-1.11)	1 Ref.
	Adjusted ^a		0.93 (0.62-1.4)	0.85 (0.57-1.28)	0.76 (0.51-1.15)	1 Ref.	0.79 (0.52-1.2)	0.87 (0.58-1.32)	0.77 (0.51-1.16)	1 Ref.

Values were calculated by multinomial regression coefficients (95% CIs) with reference to AGA for LGA and SGA birth outcomes.

^a: adjusted for morning sickness, educational level, acid folic, physical activity, age, BMI, OCP usage, nulliparous, financial level, GDM, height and energy intake

^b: reference category

HC, Head Circumference; LGA, Large for Gestational Age; Q, quartile; Ref, reference; SGA, Small for Gestational Age.

4. Discussion

We found two major dietary patterns in this study using the PCA. Lower adherence to the Western pattern was associated with a higher risk of SGA and a lower risk of LGA in newborns for weight. Also, western dietary pattern has a negative association with LGA infants for height. On the other hand, the fruit/vegetables pattern that was an almost healthy pattern, is negatively associated with LGA newborns for height.

Many developing countries are experiencing a nutrition transition which decreases poverty and increases the prevalence of overweight and obesity [35]. Getting pregnant with overweight and obesity may result in higher risks of SGA and LGA newborns [36]. Furthermore, a global estimate of SGA in 2012 in low- and middle-income countries reported that 19.3% of total live births were SGA, which means that 1 out of every 5 newborns was SGA [37]. Other risk factors for SGA and LGA infants have been identified, included weight, body mass index (BMI), gravida number, history of delivery, gestational age at delivery and dietary pattern [38,39,40].

The maternal dietary pattern in early pregnancy and its relationship with birth size has received attention in recent researches. Thompson et al. in New Zealand assessed dietary patterns in early pregnancy and found that higher scores of the traditional pattern (including apples/pears, citrus fruit, kiwifruit/feijoas, bananas, green vegetables, root vegetables, peas/maize, dairy food/yogurt, and water), which was similar to our fruit/vegetables pattern, could likely reduce the delivery of SGA newborns, which is in contrast with our finding [41]. In Thompson et al. study, women filled out the FFQ shortly after delivery which causes a change in reporting compared to the pregnancy period. Similarly, Garay et al. identified two patterns named Western and health-conscious, the latter was characterized by salad/vegetables, dried fruits, fruits, supplements, meat alternatives, fish, and cheese/yogurt. None of the patterns and LGA showed any association, and just a negative relationship was observed only between the health-conscious pattern and SGA compared with AGA [42]. However, the sample size was small (n=303) and adjustment was limited in this study. Again, in the ProcriAr cohort study in Sao Paulo, Brazil (n=299), which just analyzed SGA infants, an unhealthy pattern that contained snacks, sandwiches, sweets, and soft drinks was reported to possibly increase the risk of SGA [43].

Mother and child cohort study in Norway (MoBa) was conducted on 65,904 pregnant women and their dietary patterns [39]. Four patterns were found in this study: Western, prudent, traditional, and mixed, and every pattern was compared to the Western diet. Similar to our results, the prudent pattern (including fruits and vegetables) compared to the Western diet increased SGA and decreased LGA. Women in the higher quartile of western dietary pattern consumed more energy dense foods and their food quality characterized by highest amount of total fat, added sugar, trans fatty acids as well as the lowest amount of dietary fiber, all of which may be association with higher risk of LGA. Lower amount of fiber and higher added sugar in diet are correlated to higher postprandial plasma glucose after meals [44] and increased maternal glucose is associated with overgrowth

newborn, even in non-diabetic pregnant women [45].

The role of diet during pregnancy on fetal growth is undeniable [46]. Most previous studies that have measured the relationship between fetal growth and maternal diet have been conducted in Western countries [47,48,49,50]. An Iranian prospective observational study, was performed on major dietary patterns in early pregnancy and birth weight and length. Among three major patterns (healthy, western and traditional patterns), just western pattern showed negative association with weight of newborns [51]. Because the neonates born at various gestational weeks and the sex-differences for anthropometric measurements, usage of SGA and LGA in studies is more appropriate. On the other hand, considering the high nutritional value of fruits and vegetables another finding of this study can be also the importance of the dietary variety and balance. Dietary variety and balance are items to measure food quality that were studied in a study in Spain [20]. Diet quality in this study was inversely associated with small-for-age birth. Further studies are needed to assess the quality of diet in our population.

Although the effects of maternal genetics [52] which covers about 38-80% birth weight and height variance cannot be ignored [53,54], many mechanisms can demonstrate how dietary factors in early pregnancy play a pivotal role on birth anthropometric characters [55]. One of our findings is that lower consumption of foods in Western dietary pattern is associated with a higher risk of SGA newborns for weight and higher risk of LGA for height. Even though this pattern is somehow unhealthy, some foods with high-biological-value proteins exist in this pattern. one study in China clearly illustrated the association between important animal and plant sources of protein separately with LBW, SGA, and intrauterine growth retardation (IUGR) [56]. This study showed that a higher intake of total and animal protein can reduce the risk of SGA, LBW, and IUGR, while plant protein did not. Additionally, in a longitudinal study in Spain, protein was introduced as the most effective macronutrient in the preconception period and during pregnancy on birth weight, independently of the mother's age, smoking, newborn's sex, pregnancy length, BMI, physical activity, and total calorie intake [57]. So western dietary pattern may have conflicting effect on SGA/LGA due to its higher content of protein.

Additionally, maternal nutrition can affect morphology and transporter expression of the placenta as the most important transmitter of macro- and micro-nutrients and other crucial substances between mother and fetus [58]. Although studies show malnutrition impairs the development and function of the placenta which causes lower transfer of nutrients and possibly lead to impairment of fetal growth [59], maternal overnutrition as seen in western dietary pattern caused lower blood level of adiponectin (ADP) and also caused higher blood level of leptin, insulin, insulin-like growth factor-1 (IGF-1) and interleukin 6 (IL-6) which all of them promote anabolism [60]. These changes in hormones and cytokines in response to nutrition up-regulate placental transport of nutrients such as amino acids [61].

In another study, path analysis performed on birth weight and 4 different dietary patterns extracted by PCA: FDP (high intake of fruit, dairy products, poultry and coarse grain), VBP (high intake of vegetables, beans, nuts,

fungi, algae and pork), FS (high intakes of fish, seafood, dietary supplements, coarse grains and soup) and TE (high intakes of potatoes and eggs) with mediated role of cytokines. VBP and FDP patterns negatively related to IL-6 and TE has positively related to ADP. IL-6 and ADP showed significant negative and positive associations with birth weight, respectively [62].

The current study had a prospective design and many coefficients were measured via a questionnaire. The inclusion criteria were not too rigid, and thus, a wide range of age and women with different socioeconomic status participated. Birth outcomes were less affected by reports because at the time of filling out the questionnaire, pregnancy outcome complications did not exist. In our study, alcohol and cigarettes use were removed from the analysis due to their confounding effects.

Still, there were some limitations in this study. As the study was observational, a causal interpretation was not possible. Although we had precision in the known risk factors, other confounders may have remained. The FFQ recall bias is another limitation, whereby people's memories often do not report the exact intake, or mothers may change their diets in late pregnancy; furthermore, the FFQ cannot report the whole diet because the dish composition is different in every family, and the ingredients should be guessed by researchers. Finally, residual confounding linked with both birth weight and dietary patterns cannot be removed, although we adjusted for several factors in the statistical analysis.

5. Conclusion

Even though we found no association between the fruits/vegetables pattern and weight abnormalities (SGA and LGA), higher adherence to the Western pattern was associated with a lower risk of SGA and a higher risk of LGA for weight. This finding implied that the Western pattern may reduce the risk of SGA even it has unhealthy components. Future well-designed controlled trials would be applicable and corroborate the beneficial effects of dietary patterns on pregnancy outcomes.

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