ORIGINAL ARTICLE

Comprehensive maternal characteristics associated with birth weight: Bayesian modeling in a prospective cohort study from Iran

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Background: In this study, we aimed to determine comprehensive maternal characteristics associated with birth weight using Bayesian modeling. **Materials and Methods:** A total of 526 participants were included in this prospective study. Nutritional status, supplement consumption during the pregnancy, demographic and socioeconomic characteristics, anthropometric measures, physical activity, and pregnancy outcomes were considered as effective variables on the birth weight. Bayesian approach of complex statistical models using Markov chain Monte Carlo approach was used for modeling the data considering the real distribution of the response variable. **Results:** There was strong positive correlation between infant birth weight and the maternal intake of Vitamin C, folic acid, Vitamin B3, Vitamin A, selenium, calcium, iron, phosphorus, potassium, magnesium as micronutrients, and fiber and protein as macronutrients based on the 95% high posterior density regions for parameters in the Bayesian model. None of the maternal characteristics had statistical association with birth weight. **Conclusion:** Higher maternal macro- and micro-nutrient intake during pregnancy was associated with a lower risk of delivering low birth weight infants. These findings support recommendations to expand intake of nutrients during pregnancy to high level.

Key words: Bayesian modeling, bioinformatics, birth weight, maternal characteristics, nutritional risk factors

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INTRODUCTION

Birth weight, one of the birth outcome components, is an international problem with important consequences for mortality, health development, incidence of acute and chronic diseases, and the economic output of individuals and societies.[1] The prevalence of low birth weight (LBW) infants in developing countries is more than double than that of developed countries. Overall, 70% all LBW births occur in Asia.[2] There are substantial researches that address the impact of maternal behavior on infant's health. Fetal growth and size are influenced by genes, parental body size, maternal nutrition, and the mother's metabolic and vascular competence during pregnancy. Documents show that the nutritional status of a woman before and during pregnancy is truly important for a healthy birth outcome.[3] There are considerable evidences supporting the role of various macro- and micro-nutrients in determining pregnancy outcomes such as birth weight and maturity.[4] Furthermore, studies presented that a number of biosocial factors such as maternal weight and smoking are strongly associated with poor birth outcomes.[5] In addition, decreased physical activity of women was reported to be associated with LBWs.[6] Women of low socioeconomic status are at increased risk for delivering LBW babies, where socioeconomic status is defined by income, occupation, and education.[7]

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Although studies on investigating nutritional, socioeconomical, and anthropometric risk factors associated with birth weight have been published extensively, none of which considered the true distribution of birth weight, methodologically. Using the routine statistical methods, assuming normally distribution medical responses could affect the accuracy of the medical inferences.[8] There are some applied researches which investigated the deviation from normality assumption considering flexible (Bayesian) modeling using nonnormal distribution leading to more reliable results.[9-11] Bayesian modeling not only utilizes prior information which in a medical setting is all around and is unbiased in small sample sizes but it also relaxes the normality assumption of the response variable.[12] Bayesian modeling could manage uncertainty, which is part of the clinical medicine,[13] better than other inferences, and the confidence intervals of the parameters are appropriately wide.[14]

To our knowledge, these flexible methods have not yet been used for LBW analysis in the literature. Considering the fact that determining true risk factors affecting birth weight could prevent many of the adverse outcomes of LBW children in future, study aimed at investigating the risk factors associated with birth weight based on an updated statistical method using a prospective cohort study data from Iran.

MATERIALS AND METHODS

This population-based prospective cohort study was conducted on a group of 620 Iranian pregnant women aged 15–49 years whose delivery was in hospital. It was performed by compliance sampling from public health centers and private offices in Isfahan. Data collection tool was questionnaires completed through interviews with eligible mothers. Content validity of the questionnaire was confirmed by experts. The exclusion criteria were smoking and drug addiction, having digestive and metabolic diseases, hemoglobinopathies, eating disorders, allergies, mental diseases, and malignancy affecting pregnancy outcome. We then excluded women who reported pregestational or gestational diabetes, had an average daily energy intake <500 or >5000 kcal, or for whom most items in the questionnaires were missing or unknown. After these exclusions, 526 participants were available for analysis. Written informed consent was obtained from all participants. The study was approved by the Research Ethics Committee of Isfahan University of Medical Sciences, complying with the Declaration of Helsinki. Data were collected through face-to-face interview by qualified nurses using validated questionnaires in the local language. The general questionnaire covered demographic socioeconomic characteristics of pregnant women and medical history.

The anthropometric data were recorded for each participant. The measurements were made on the participants wearing a minimum amount of clothing. The weights of pregnant women were recorded at the early first trimester during their first visit and continued at every trimester using a digital weighing balance with a sensitivity of 100 g. The height was measured when the horizontal headpiece was lowered onto the women's head. Fundal height was measured by a midwife as the distance between the symphysis pubis and the highest point of the uterine fundus defined with a gentle pressure on a plain at a right angle of the abdominal wall. The following characteristics were also considered for the infants: comprised gestational age, weight at birth, and gender. Gestational weight gain was taken in relation to pregnancy birth weights of neonates within 24 h after birth using a standard procedure. A beam balance with an accuracy of 50 g was employed for weighing the infants. The infants were weighed with minimum clothing while the child was restful.

Nutrient intake was determined using a quantified single 24-hour dietary recall at the 11th–15th, 26th, and 34th–37th weeks of gestation through interviews with pregnant women, prenatal and obstetric care-related records. Iron, folic acid, multivitamins, calcium, and omega-3 supplements administered for the participants by their caregivers (gynecologists and midwives) were also considered in the final analysis. Physical activity was considered as any physical movement due to skeletal muscles resulting in energy consumption. Physical activity data were collected using a standard pregnancy physical activity questionnaire consisted of four parts including physical activity at home, exercise, leisure activities, and workplace activity. The physical activities were assessed within 48 h at the 11th–15th, 26th, and 34th–37th weeks of gestation. Physical activity was measured in metabolic equivalent of task-hours (MET-hours). MET-hours is a unit for estimating the metabolic cost or oxygen consumption of a particular physical activity, according to a standard questionnaire. Total amount of activity was calculated by summing up the activities in the three trimesters and was used for further analysis. Data obtained from the 48-hour dietary recalls were analyzed using NUTRITIONIST-IV software (N-Squared Computing, Salem, OR).

Statistical analysis

In the present study, birth weight was considered as the dependent variable. The intake of macro- and micro-nutrients, supplement consumption during the pregnancy, demographic characteristics, socioeconomic characteristics, anthropometric measures, physical activity, and pregnancy outcomes were measured as independent variables. Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages

for the categorical variables. The comparison between two LBW and normal was performed using the independent sample *t*-test for the continuous variables and Chi-square test for the categorical variables.

Flexible regression modeling was used to determine the effect of different independent variables on the birth weight as continuous response. Having fitted conventional model with the normality assumption, it was revealed by the diagnostic plots that the normality assumption resulted in unreliable results. The alternative flexible models were fitted on the data based on Student's *t*-test and Laplace distribution. The hierarchical Bayesian approach was used for the estimation of the posterior distributions and the model parameters. A Gibbs sampling algorithm based on the Markov chain Monte Carlo (MCMC) approach was used to find posterior densities of the parameters. Having compared different nonnormal flexible modeling, the Akaike information criterion (AIC) was used for the comparison among the selected nonnormal flexible models. Accordingly, models with lower AIC values were selected.

The data were analyzed using the Statistical Package for the Social Sciences version 20.0 (SPSS, Inc., Chicago, IL, USA) and OpenBUGS 3.2.2, an open source computer program for the Bayesian analysis of complex statistical models using MCMC approaches. The classical statistical analysis was performed with a two-sided alpha level of 0.05. Based on the Bayesian analysis of modeling count data, the significance of variables was determined using the 2.5th and the 97.5th percentile of marginal posterior distribution or 95% high posterior density (HPD) regions for parameters in the Bayesian model.

Normality is one of the important preassumptions checked in linear regression. Diagnostic plots, not shown here, revealed that Student's *t*-test and Laplace distributions, as two suitable heavy-tailed distributions, had better fitting on the data. Posterior distributions of the parameters were estimated using the OpenBUGS software. For the fundamental models, 7000 iterations were discarded as burn-in sample to eliminate the impact of starting values and then 1000 iterations were followed to obtain Bayes estimates (posterior means and SDs) of the regression coefficients. Visual assessment of the Markov chain for all parameters was used for convergence assessing. Monte Carlo errors and trace plots of the model parameters were also checked. As a rule of thumb, ratios of the Monte Carlo errors relative to the respective SDs of the estimates should be <0.05.

Definition of categorical variables

Body mass index was classified as underweight (<19.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (24.9–29.9 kg/m^2), and obese (30 kg/m^2). The monthly income of family was categorized into three groups as low (lower than 5 million Iranian Rial (IRR), middle (Between 5–10 million IRR), and high (more than 10 million IRR). Based on Iranian educational system, maternal education was categorized as low (0–5 years), intermediate (6–12 years), and high education (more 12 years). Physical activity measured in MET-hours of each activity multiplied by the duration of the activity in the day was categorized into three following classes: low, (0–10) middle (10–15), and high (15–21). The pregnancy outcome including preeclampsia, premature rupture of membranes (PROM) before the onset of labor, and preterm PROM (PPROM) before completion or the 37th week of pregnancy were considered as binary variables: positive (Yes) and negative (No). Prematurity was categorized into (i) birth after 37 weeks and (ii) birth before 37 weeks, and finally, the infant gender was classified as (i) male and (ii) female.

RESULTS

A number of 526 pregnant women participated in this study. There were not significant differences in the average maternal age, weight, the number of pregnancies, and family for normal and LBW groups [Table 1]. The average infant birth weight was 3.16 kg with SD of 0.44 kg. The incidence of LBW was 5.9% (31). Birth outcomes and maternal characteristics during prepregnancy were presented in Tables 2 and 3. The descriptive statistics showed that the incidence of LBW for girls (6.8%) was higher than that of boys (4.9%). As shown in Table 2, there was a significant association between preeclampsia, PROM and prematurity status of infants, and the incidence of LBW ($P < 0.05$). There were significant differences between LBW and normal groups based on the following maternal characteristics during pregnancy categorical variables: physical activity hours and monthly ($P < 0.05$) [Table 3].

For heavy-tailed distribution model selection, the results of AIC revealed that the t-model (AIC = 29614) had better fitting to the data than the Laplace model (AIC = 30,362). Results of the Gibbs sampling for the t-model were presented in Table 4 based on 95% HPD.

Table 1: Quantitative characteristics of the study participants by birth weight groups based on the mean±standard deviation

Quantitative variables	Normal birth weight (*n*=495)	LBW (*n*=31)	*P*†
Age of mother (years)	25.69±4.37	25.29±3.99	0.62
Maternal weight	11.87±4.19	11.91±4.31	0.96
Number of pregnancy	1.56±0.75	1.48±0.67	0.59
Number of family	2.57±0.92	2.55±0.99	0.92

†*P* values obtained from independent sample *t*-test. LBW = Low birth weight

Table 2: Study participants' birth outcomes by the n (%), totally and in low birth weight group

Factors	Total, *n* (%)	LBW, *n* (%)	*P*†
Sex of infant			
Male	263 (50.0)	13 (4.9)	0.459
Female	263 (50.0)	18 (6.8)	
Preeclampsia			
No	502 (95.4)	27 (5.4)	**0.046**
Yes	24 (4.6)	4 (16.7)	
PROM			
No	446 (84.8)	25 (5.6)	0.449
Yes	80 (15.2)	6 (7.5)	
PPROM			
No	506 (96.2)	23 (4.5)	**<0.001**
Yes	20 (3.8)	8 (40)	
Delivery type			
Vaginal	208 (39.5)	13 (6.2)	0.85
Cesarean	318 (60.5)	18 (5.7)	
Prematurity			
No	488 (92.8)	13 (2.7)	**<0.001**
Yes	38 (7.2)	18 (47.4)	

†*P* value obtained from Chi-square test; significant associations are in bold; comparing LBW and normal groups. PROM = Premature rupture of membranes; PPROM = Preterm premature rupture of membranes; LBW = Low birth weight

Table 3: Basic maternal characteristics during prepregnancy by the *n* (%), totally and in low birth weight group

Factors	Total, *n* (%)	LBW, *n* (%)	*P*†
Education			
Low	187 (35.6)	12 (6.4)	0.482
Intermediate	267 (50.8)	17 (6.4)	
High	72 (13.7)	2 (2.8)	
BMI			
Underweight	41 (7.8)	3 (7.3)	0.124
Normal weight	314 (59.7)	23 (7.3)	
Overweight	149 (28.3)	3 (2)	
Obese	22 (4.2)	2 (9.1)	
Monthly income			
Low	300 (57.0)	19 (6.3)	**0.01**
Middle	188 (35.7)	6 (3.2)	
High	38 (7.2)	6 (15.8)	
Physical activity			
Low	112 (21.3)	12 (10.7)	**0.048**
Middle	266 (50.6)	13 (4.9)	
High	148 (28.1)	6 (4.1)	

†*P*-value obtained from Chi-square test; significant associations are printed in bold; comparing LBW and normal groups. LBW = Low birth weight; BMI = Body mass index

According to the regression coefficients, there was strong positive correlation between infant birth weight and the intake of the following macro- and micro-nutrients intake containing: vitamin C (posterior mean = 11.71), folic acid (posterior mean = 13.51), Vitamin B3 (posterior mean = 7.22), Vitamin A (posterior mean = 15.16), selenium (posterior mean = 8.74), calcium (posterior mean = 16.31), iron (posterior mean = 6.62), phosphorus (posterior mean = 16.59), potassium (posterior mean = 19.24), magnesium (posterior mean = 12.91), fiber (posterior mean = 7.19), and protein (posterior mean = 10.95). Except the type of the delivery, there were no significant differences between other maternal characteristics variables and birth weight.

DISCUSSION

We found that the average protein intake during pregnancy in pregnant women was significantly related to neonate's birth weight [Table 4]. However, the controversial results were obtained in the literature about the effect of protein on LBW. Kathleen and DroraQuting mentioned that the association between protein intake and birth outcomes was unlikely to be found in well-nourished populations, especially if diet was assessed in the second trimester or later and was not evaluated for type or quality of protein intake.[15]

Moreover, maternal fiber intake was significantly related with birth weight in our study [Table 4]. Bang and Lee showed that fiber intake was significantly higher in pregnant women whose neonates were in the high birth weight group, which is in agreement with our findings.[16]

Another results obtained in this study were that higher calcium and phosphorous received in mothers resulted in babies with more weight in compared to others [Table 4]. Calcium and phosphorous are the most important elements of the primary bone forming minerals. At birth, an infant contains approximately 20–30 g calcium and 16 gr phosphorus, of which approximately 98% and 80%, respectively, are in the skeleton.[17]

It has been hypothesized in the literature that the effect of dairy products on fetal bone and femur length was due primarily to calcium consumption. However, this effect may also be partially attributed to other nutrients in dairy, such as phosphorus, magnesium, zinc, and Vitamin D. In agreement with our finding, Bang and Lee showed that the phosphorus intake was significantly higher in the high birth weight group.[16]

In the current study, a significant difference was found between the mean of manganese intake during pregnancy and newborn weight. We were not able to find any manuscript in the literature indicating the association between manganese intake and birth weight, as confirmed in Abu-Saad and Fraser study.[18] However, it was shown that lower maternal blood manganese is associated with fetal intrauterine growth retardation and lower birth weight.[19]

Table 4: Estimates of posterior mean, standard deviation, Monte Carlo error, and 90% credible intervals for determining the effect of different independent variables on birth infant weight according to the *t*-model

Variable	Mean±SD	Mc error	95% HPD
Age	0.155±3.081	0.044	−5.902, 6.134
Weight	0.108±3.062	0.053	−5.832, 6.017
Number of pregnancy	0.008±3.12	0.056	−6.063, 6.250
Number of family	0.002±3.146	0.050	−6.168, 6.116
Iron supplement	5.435±3.207	0.047	−0.914, 11.86
Folic acid supplement	5.476±3.167	0.053	−0.773, 11.73
Multivitamin supplement	3.528±3.171	0.048	−2.839, 9.962
Calcium supplement	2.276±3.136	0.046	−3.847, 8.475
Omega-3 supplement	1.482±3.198	0.054	−4.871, 7.828
PROM	0.701±3.144	0.044	−5.431, 6.852
PPROM	0.181±3.135	0.042	−5.833, 6.537
Preeclampsia	0.248±3.187	0.051	−6.010, 6.346
Premature	0.2962±3.17	0.054	−5.867, 6.447
Sex of infant			
Male	Reference		
Female	2.703±3.175	0.056	−3.498, 8.961
Education			
Low	Reference		
Intermediate	2.901±3.162	0.051	−3.422, 9.136
High	0.753±3.161	0.046	−5.280, 6.975
BMI			
Underweight	Reference		
Normal weight	3.314±3.195	0.051	−2.918, 9.639
Overweight	1.642±3.116	0.050	−4.476, 7.665
Obese	0.260±3.201	0.047	−6.104, 6.481
Monthly income			
Low	Reference		
Middle	2.06±3.205	0.057	−4.058, 8.296
High	0.422±3.182	0.042	−5.825, 6.605
Physical activity			
Low	Reference		
Middle	2.732±3.119	0.044	−3.279, 8.854
High	1.442±3.191	0.043	−4.739, 7.656
Time of follow-up			
First trimester	Reference		
Second trimester	1.879±3.083	0.054	−4.162, 8.042
Third trimester	1.808±3.143	0.047	−4.335, 7.970
Vitamin E (mg)	−0.582±3.185	0.052	−6.779, 5.501
Vitamin D (μg)	1.375±3.147	0.047	−4.762, 7.594
Vitamin C (g)	11.71±3.243	0.051	**5.145, 17.901**
Vitamin B12 (g)	2.354±3.151	0.050	−3.974, 8.396
Folic acid (g)	13.51±3.209	0.056	**7.180, 19.770**
Vitamin B6 (g)	0.589±3.158	0.042	−5.535, 6.702
Vitamin B3 (g)	7.226±3.326	0.052	**0.7436, 13.81**
Vitamin B2 (g)	0.897±3.132	0.056	−5.376, 7.075
Vitamin B1 (g)	1.018±3.177	0.053	−5.186, 7.223
Vitamin A (IU)	15.16±3.176	0.057	8.811, 21.440
Zinc (g)	4.678±3.199	0.052	−1.595, 10.93
Selenium (g)	8.744±3.224	0.052	**2.399, 15.010**
Manganese (g)	3.937±3.196	0.049	−2.271, 10.21
Copper (g)	1.202±3.113	0.054	−4.752, 7.201
Calcium (g)	16.31±3.146	0.049	**9.961, 22.450**
Sodium chloride (g)	−0.023±3.205	0.055	−6.392, 6.079
Iron (g)	6.919±3.204	0.055	**0.764, 13.301**
Phosphorus (g)	16.94±3.241	0.063	**10.31, 22.850**
Potassium (g)	19.24±3.191	0.045	**13.03, 25.430**
Magnesium (g)	12.91±3.213	0.053	**6.736, 19.340**
Fat (g)	−0.043±3.247	0.053	−6.336, 6.467
Cholesterol (mg)	−0.001±3.205	0.049	−6.166, 6.360
Linoleic acid (g)	−0.076±3.149	0.046	−6.262, 6.032
Oleic acid (g)	0.032±3.146	0.056	−6.064, 6.301
Sugar (g)	0.059±3.211	0.057	−6.284, 6.428
Fiber (g)	7.19±3.187	0.047	**0.8638, 13.47**
Protein (g)	10.95±3.167	0.046	**4.915, 17.280**
Constant	5.579±3.162	0.049	−0.6054, 11.81

Significance based on the 95% HPD is printed in bold. Weight = Maternal weight gain during the pregnancy; BMI = Body mass index; PROM = Premature rupture of membranes; PPROM = Preterm premature ruptures of membranes; SD = Standard deviation; HPD = High posterior density; Mc = Monte Carlo

Our findings showed that mothers who received higher amount of iron intake had larger babies. Baker *et al*. found that the risk of small for gestational age birth was also higher for participants with low iron intake but not when intake included iron from supplements.[20] In agreement with our findings, Bony and Lee showed that iron intake was significantly higher in the high birth weight group in comparison with the LBW group.[16]

We also showed that average selenium intake during pregnancy was positively related to birth weight. It was shown that selenium is involved in maintaining normal glucose uptake, regulating cellular glucose consumption, and decreasing the severity of insulin resistance and therefore has a biological function similar to that of insulin.[21] It might explain the role of selenium in fetal growth. Bo *et al*. reported a significant inverse association between dietary intakes and serum levels of selenium with gestational hyperglycemia.[22]

Another result obtained in this study was that lower potassium intake in mothers ended up with smaller neonates. The relationship between maternal intake of potassium and total body area-adjusted bone mineral content (BMC), spinal BMC, and bone mineral density (BMD) affect body weight. Researchers also revealed that maternal potassium intake was significantly related to birth weight.[23] Furthermore, it was found that birth weight was positively associated with BMC and BMD, in large parts due to the strong relationship between birth weight and body size.

Our results showed that folic acid, Vitamins A, B_3, and C were significantly related to birth weight. In a meta-analysis, Fekete *et al*. demonstrated significant dose–response relationship between folate intake and birth weight.[24]

Another study showed that the folic acid intake of the high birth weight group was significantly higher than that of the LBW group.[16]

It was shown in the literature that thiamin (Vitamin B_1), riboflavin (B_2), and niacin (B_3) are essential cofactors for energy metabolism. Their deficiency in pregnancy might result in marked metabolic effects in mothers and impaired fetal growth.[25]

In our study, Bayesian modeling was used to identify significant factors affecting LBW. Bayesian inference has a decision-theoretic foundation.[26,27] The purpose of most of statistical inference is to facilitate decision-making, and the optimal decision is the Bayesian decision.[27] Furthermore, Bayesian inference through MCMC that was used in our study is unbiased with respect to sample size. However, Bayesian modeling often comes with a high computational cost, and it requires skills to translate subjective prior beliefs into a mathematically formulated prior.[28] Our future work will be focused on designing the causal network for the identification of causal LBW mechanisms.

CONCLUSION

Higher maternal macro- and micro-nutrient intake during pregnancy was associated with a lower risk of delivering LBW infants. These findings support recommendations to expand intake of nutrients during pregnancy to high level.

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Conflicts of interest

There are no conflicts of interest.

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