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Determinants of low birth weight in urban Pakistan

Naveed Zafar Janjua[1,2,*], Elizabeth Delzell[1], Rodney R Larson[3], Sreelatha Meleth[4], Sibylle Kristensen[1], Edmond Kabagambe[1] and Nalini Sathiakumar[1]

[1]Department of Epidemiology, University of Alabama at Birmingham, 1665 University Blvd, RPHB 430, Birmingham, AL 35294, USA: [2]Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan: [3]University of Utah, Salt Lake City, UT, USA: [4]Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

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Abstract

Objective: To identify determinants of low birth weight (LBW) in Karachi, Pakistan, including environmental exposures and nutritional status of the mother during pregnancy.

Design: Cross-sectional study.

Participants: Five hundred and forty mother–infant pairs. We interviewed mothers about obstetric history, diet and exposure to Pb. We measured birth weight and blood lead level (BLL). We performed multiple log binomial regression analysis to identify factors related to LBW.

Results: Of 540 infants, 100 (18·5 %) weighed ≤2·5 kg. Umbilical cord BLL was not significantly associated with LBW. Maternal poor self-rated health (adjusted prevalence ratio (adjPR) = 1·83; 95 % CI 1·09, 3·07) and none or one prenatal visit (adjPR = 2·18; 95 % CI 1·39, 3·43) were associated with LBW. A statistically significant interaction between mothers' mid upper-arm circumference (MUAC) and dietary vitamin C intake was noted. Compared with mothers with MUAC above the median and dietary vitamin C intake above the 3rd quartile (>208·7 mg/d), infants of mothers with MUAC less than or equal to the median and dietary vitamin C intake >208·7 mg/d (adjPR = 10·80; 95 % CI 1·46, 79·76), mothers with MUAC above the median and vitamin C intake ≤208.7 mg/d (adjPR = 10·67; 95 % CI 1·50, 76·02) and mothers with MUAC less than or equal to the median and vitamin C intake ≤208·7 mg/d (adjPR = 13·19; 95 % CI 1·85, 93·79) more likely to give birth to an LBW infant.

Conclusions: In Pakistan, poor nutritional status and inadequate prenatal care were major determinants of LBW in this setting. Environmental factors including umbilical cord BLL were not significantly associated with LBW.

Keywords
Low birth weight
Lead
Vitamin C
Mid upper-arm circumference
Pregnancy
Newborn
Pakistan

Low birth weight (LBW) remains a significant public health problem in many parts of the world and is associated with both short- and long-term adverse consequences. Globally, more than 20 million infants are born with LBW, about 15·5 % of all live births[1]. The prevalence of LBW is high in developing countries (18·5 %), with the highest prevalence in South Asia (27 %) including Pakistan (19 %)[1]. LBW infants have an increased risk of mortality during the neonatal period, infancy, childhood and during later during adulthood[2,3].

Previous research has shown that birth weight is influenced by length of gestation, parity, prenatal care, education level of the mother and father, socio-economic status, maternal malnutrition, maternal smoking, environmental tobacco smoke (ETS), short stature of the mother, short birth intervals, maternal and fetal medical problems, as well as certain infections and exposure to environmental agents such as Pb and pesticides[4–13].

Risk factors for LBW in developing countries are different from those in developed countries. In the USA and European countries, the prevalence of LBW is relatively low (5–7 % of live births) and the main determinants of LBW are exposure to environmental toxins such as Pb, ambient air pollution, lack of prenatal care and low socio-economic status. In contrast, most developing countries have a high prevalence of both LBW and maternal malnutrition and dietary deficiencies[14]. In addition, developing countries have high levels of rising urban environmental pollutants such as Pb. Thus, there is a need to evaluate the relationship between Pb exposure and LBW in regions with high prevalence of other potential risk factors for LBW. The present study examined the determinants of LBW including Pb exposure,

*Corresponding author: Email naveed@uab.edu

nutritional status and prenatal care during pregnancy in Karachi, Pakistan.

Methods

Study setting

The study was conducted in Karachi which is the largest city, the main port and the industrial and trade centre of Pakistan. Karachi has a population of more than 10 million, about 40 % of whom live in squatter settlements. Karachi has potential for high Pb exposure from various environmental sources such as automobiles, industrial emissions and occupational exposures. The subjects for the present study were recruited at two tertiary-care hospitals located in the inner city, and comprised low- and middle-income patients from various parts of the city.

Study design

The present study was a cross-sectional study conducted between January and August 2005. Study subjects were mothers and their infants born during the study period.

Study participants

Eligible subjects were women who: (i) were willing to participate in the study; (ii) were residents of Karachi for at least 1 year; (iii) were admitted for delivery in one of the two study hospitals; and (iv) planned to deliver a singleton at term (37–42 weeks of gestation). Mothers were excluded if they had physician diagnoses of psychiatric morbidity, kidney or cardiac disease, history of repeated urinary tract infections, sickle cell anaemia, thyrotoxicosis, autoimmune diseases such as Crohn's or coeliac disease, drug dependence, steroid intake during pregnancy, antepartum haemorrhage, placental abnormalities such as abruptio placentae, pre-eclampsia or a fetus with congenital anomalies.

Subject selection

We randomly selected ten mothers each day who registered for delivery at the study hospitals. We invited selected mothers for eligibility screening using medical records. Those found eligible at this stage were invited for participation in the study and written consent was obtained.

Exposure assessments

We used maternal interview, medical record review and maternal anthropometric examination, and umbilical cord blood for assessment of potential risk factors.

We used a pre-tested Urdu translated questionnaire to collect information. Registered nurses conducted interviews after training in interviewing and field procedures. Study procedures were pilot-tested before the start of data collection. Maternal interview and measurements were conducted both before and after delivery depending on the mother's condition.

The questionnaire elicited information on sociodemographic factors, obstetric history, diet during pregnancy and sources of Pb exposure. Sociodemographic factors included maternal age, education, occupation, husband's education and occupation, household income and possession of household assets. Socio-economic status was assessed using income and a wealth index based on household possessions with proportionate weighting.

The questionnaire also elicited information on current and past obstetric history including parity, pre-pregnancy weight, prenatal care (number, time of each visit and services provided), history of vaginal discharge, feeling of depressive symptoms (measured on a scale of 1–5, from none to extreme feeling), overall health status (measured on a scale of excellent, very good, good, fair and poor), hours of rest during day and night, total hours spent in the kitchen, perception of work load during pregnancy, potential exposure to indoor pollution (measured by type of kitchen), smoking during pregnancy, exposure to ETS at home or work, use of DDT (dichlorodiphenyltrichloroethane), mosquito coils and rodenticides, anaemia during pregnancy, history of acute upper respiratory tract infection, fever, physician diagnosed high blood pressure, gestational diabetes, and use of calcium/iron/vitamin C supplements with the quantity, duration and brand name during pregnancy.

We assessed dietary intake of Ca, Fe and vitamin C during current pregnancy using an FFQ adapted from a previous study of dietary intake during pregnancy in Karachi[15]. The FFQ elicited information on the intake of foods in the most recent month, including the frequency per week and the quantity according to portion size. To help in recall, pictures and models of standard portion sizes applicable in the local settings were used. Total Ca intake was estimated from questionnaire data on supplements and diet. For supplements, the quantity of Ca was abstracted using manufacturer information provided in a drug index and then the quantity from each supplement taken each day was summed to obtain daily Ca intake from supplements. Dietary Ca intake was derived from the quantity of Ca contained in each food item on the FFQ. Ca content estimates were obtained from Pakistani food tables. If a food was not available in the Pakistani food table, Ca content was derived from Indian or US food tables. The amount of Ca consumed was computed by multiplying Ca contained in a serving of food by the number of servings of food consumed each day. Total Ca intake per day was the sum of Ca from diet and supplements. The same approach was used to compute elemental Fe and vitamin C intake from supplements, diet and daily total intake.

Maternal weight, height, mid upper-arm circumference (MUAC) and biceps and triceps skinfold thickness were measured after delivery. Three measurements of MUAC, biceps and triceps skinfolds were taken on the non-dominant arm. MUAC and the biceps skinfold thickness

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(BSFT) have been shown to predict pre-pregnancy nutritional status, as these indices change very little during pregnancy[16]. Medical records were reviewed for gestational age measured by ultrasound, high blood pressure during pregnancy, glucose intolerance and gestational diabetes.

Pb levels were tested in umbilical cord blood. At delivery, an umbilical cord blood sample was collected into a trace metal-free BD Vacutainer™ sterile glass tube containing Na_2EDTA. The analysis for Pb level was performed at the laboratory of the Pakistan Institute of Scientific and Industrial Research (PCSIR) in Karachi, using graphite furnace atomic absorption spectrophotometry. PCSIR has been participating in the Centers for Disease Control and Prevention (CDC) Blood Lead Laboratory Reference System (BLLRS). For the present study, PCSIR tested BLLRS bovine blood. The intra-class correlation coefficient was 0·999, and the mean (SD) of PCSIR was 29·7 (19·4) μg/dl *v*. the mean (SD) CDC target value of 30·40 (19·17) μg/dl.

Outcome assessment

The outcome of interest was LBW. LBW was defined as infant weight ≤2·5 kg. Infant anthropometrics were measured within 12 h of birth. Birth weight was measured using an infant pan scale, length using a flat board, and head and chest circumferences were measured using a non-stretchable tape.

Sample size

Sample size estimation was based on the relationship of umbilical cord blood lead level (BLL) and LBW. We assumed that about 80 % of women will have BLL ≥ 10 μg/dl as in a previous study on children[17] and umbilical cord BLL will be 75–90 % of maternal levels[18]. By assuming umbilical cord BLL to be 80 % of maternal levels, 64·2 % of newborns were expected to have umbilical cord BLL ≥ 10 μg/dl. Thus the sample size for examining the relationship between BLL and LBW was based on the assumption that 64 % of normal-weight infants would have BLL ≥ 10 μg/dl. With 5 % significance and 80 % power and assuming a 1:3 ratio of normal and LBW babies, to detect an odds ratio of 2·0 and with 10 % non-response rate we would require a sample size of 533 newborns. Thus, we enrolled 540 mothers and infants.

Data analysis

Data were double-entered into Epi Info™ 2002 software (CDC, Atlanta, GA, USA) and analysed using the Statistical Analysis Systems statistical software package version 9·1·3 (SAS Institute, Cary, NC, USA).

We computed proportions for categorical variables and mean, standard deviation and median for continuous variables. We compared continuous variables using the *t* test or ANOVA and categorical variables using the χ^2 test.

We computed the prevalence of LBW for each category of a potential risk factor as the number of infants with birth weight ≤2·5 kg divided by the total number of normal-weight plus LBW infants in each category. We computed the crude prevalence ratio (PR) for exposure variables as the prevalence of LBW among those in the high-risk category divided by the prevalence in the unexposed or presumed to be low-risk category. We used a log binomial regression model to estimate the adjusted prevalence ratios (adjPR) using PROC GENMOD in SAS.

We categorized sociodemographic variables as follows: mother's age as <20, 20–30 and ≥30 years; mother's and father's education as <5, 6–12 and >12 years; wealth index as low, medium and high; and monthly household income as below the median and greater than or equal to the median. MUAC and BSFT were dichotomized at the median. Vitamin C from diet was dichotomized into high (4th quartile) and low (1st–3rd quartile). Prenatal visits were categorized into ≥4, 2–3 and ≤1. Time of first visit was categorized into during first 16 weeks, 17–28 weeks and >28 weeks of gestation. An index of prenatal care adequacy was created as follows: sufficient, ≥3 visits and first visit before 16 weeks; fair, 2 visits or first visit between 17 and 24 weeks; and inadequate, no or 1 visit or first visit between 25 and 38 weeks. Overall health status was categorized into excellent, good, fair and poor.

Variables with $P < 0{\cdot}2$ in univariable analysis and umbilical cord BLL were considered for evaluation in multivariable analysis. We started with the most significant variable and added variables one by one while assessing their significance and change in effect estimate. Variables that were not significant or did not produce a change in effect estimate of >10 % were removed from the model. Variables significant at $P < 0{\cdot}05$ were kept in the final model. We tested interactions of variables in the model.

Ethical approval

The study was approved both by the Institutional Review Board of the University of Alabama at Birmingham and the Ethics Review Committee of the Aga Khan University in Karachi, Pakistan.

Results

Study participants

Of 807 mothers initially screened for eligibility, 565 were eligible. All subjects consented to participate in the study. Data on outcome or a major portion of the interview was missing for twenty-five participants. Thus 540 subjects were available for analysis, which was the planned target for enrolment (Fig. 1).

The gender distribution of infants was approximately equal (male, 54 %; female, 46 %). Mothers were relatively young with a median age of 25 years (Table 1). Fathers were more likely to have educational level greater than 12th grade compared with mothers (14 % *v*. 6·5 %). Only

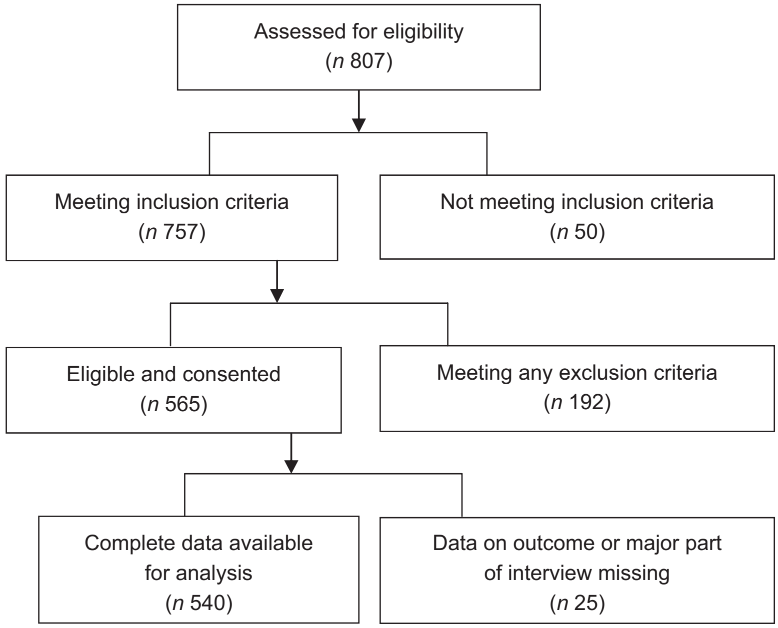

Fig. 1 Selection of participants in a study of umbilical cord blood lead levels and low birth weight in Karachi, Pakistan, 2005–2006

Table 1 Selected characteristics of 540 participants in a study of umbilical cord blood lead levels and low birth weight in Karachi, Pakistan, 2005–2006

Variable	*n* or Mean	% or SD
Child characteristics		
No. (%) of males	289	54
Mean (SD) birth weight (kg)	3·0	0·5
Mean (SD) crown–heel length (cm)	50·3	2·6
Mean (SD) head circumference (cm)	34·6	1·9
Geometric mean (SD) of cord BLL (μg/dl)	9·6	1·6
Arithmetic mean (SD) of cord BLL (μg/dl)	10·8	0·2
Parent characteristics		
Mean (SD) age of mother at delivery (years)	25·3	4·6
Mean (SD) years of mother's schooling	7·4	4·4
Mean (SD) years of fathers' schooling	8·5	4·4
No. (%) of mothers employed	12	2·2
No. (%) of fathers manual and minimal skilled labourers	320	59
No. (%) of households with income above Rs. 7000	251	46
No. (%) of households owning a car	23	4
No. (%) of mothers of Urdu (Mohajir)* ethnicity	368	68
Mean (SD) parity	1·2	1·3
Mean (SD) maternal BMI (kg/m^2)	24·6	4·4
Mean (SD) maternal MUAC (cm)	29·0	4·0
Mean (SD) maternal BSFT (mm)	9·7	3·5
No. (%) of mothers anaemic (Hb $<$ 11g/dl)†	307	70
Mean (SD) total Ca intake during pregnancy‡	974·0	370·9
Mean (SD) dietary Ca intake during pregnancy‡	747·1	298·2
No. (%) using Ca supplements during pregnancy	376	70
Mean (SD) Ca intake from supplements among supplement users‡	325·7	147·3
Mean (SD) total vitamin C intake during pregnancy‡	801·5	697·5
Mean (SD) dietary vitamin C intake during pregnancy‡	286·5	238·6
No. (%) using vitamin C supplements during pregnancy	406	75
Mean (SD) vitamin C intake from supplements among supplement users‡	685·0	649·0
Mean (SD) total Fe intake during pregnancy‡	70·0	83·1
Mean (SD) dietary Fe intake during pregnancy‡	23·1	9·3
No. (%) using Fe supplements during pregnancy	203	38
Mean (SD) Fe intake from supplements among supplement users‡	124·8	90·8

BLL, blood lead level; MUAC, mid upper-arm circumference; BSFT, biceps skinfold thickness.
*The Mohajirs are a group of people who migrated from parts of India not included in Pakistan at the time of creation of Pakistan, and they mostly speak Urdu.
†Data not available for all subjects.
‡Daily intake measured in mg.

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2 % of mothers were employed. About 59 % of fathers were manual or skilled labourers. Almost all homes (98 %) used natural gas as cooking fuel. The median monthly household income was Rs. 7000 (US$ 117). About 4 % of households owned a car. The mean maternal BMI was 24·5 kg/m^2, while 4 % had BMI below 18·5 kg/m^2 and 12 % had BMI ≥30·0 kg/m^2. The mean daily Ca, vitamin C and Fe intake was 974·0 mg, 801·5 mg and 70·0 mg, respectively (Table 1).

The median birth weight was 3·0 kg, and median head circumference was 34·5 cm. Of 540 infants, 100 (18·5 %) infants were born with weight ≤2·5 kg. In the univariable analyses, factors statistically significantly associated with LBW included MUAC, BSFT, dietary vitamin C intake, cooking frequency, hours of rest during the third trimester, number of prenatal visits, feeling of depressive symptoms and perception about health status (Table 2).

Multivariable log binomial regression modelling indicated that perceived health status, number of prenatal visits, parity and interaction of MUAC and dietary vitamin C intake during pregnancy were significantly associated with LBW. High umbilical cord BLL was not associated with LBW. Mothers who perceived that their health status was poor were more likely to give birth to an LBW infant than mothers who reported good health status (adjPR = 1·83; 95 % CI 1·09, 3·07). Mothers who had one or no prenatal care visits during pregnancy were twice as likely to give birth to an LBW infant than mothers who had four or more visits (adjPR = 2·18; 95 % CI 1·39, 3·43). There was a significant interaction of MUAC and dietary vitamin C intake. Those mothers who had MUAC ≤ 28·9 cm (equal to or below median) and vitamin C intake >208·7 mg/d (4th quartile) were eleven times more likely to give birth to an LBW infant (adjPR = 10·80; 95 % CI 1·46, 79·76). Mothers who had MUAC > 28·9 cm and vitamin C intake ≤208·7 mg/d were also eleven times more likely to give birth to an LBW infant (adjPR = 10·67; 95 % CI 1·50, 76·02), and those who had MUAC ≤ 28·9 cm and vitamin C intake ≤208·7 mg/d were thirteen times more likely to give birth to an LBW infant (adjPR = 13·19; 95 % CI 1·85, 93·79), as compared with those who had MUAC > 28·9 cm and vitamin C intake >208·7 mg/d. Women who were pregnant for the first time or had given birth five or more times were more likely to give birth to an LBW infant (adjPR = 1·53; 95 % CI 1·08, 3·43). We also developed a model with maternal BSFT replacing maternal MUAC and the results were similar (Table 3).

Discussion

In the present study of mother–infant pairs recruited from tertiary-care hospitals of Karachi, low vitamin C intake and MUAC below the median, poor perceived health status, and low prenatal care were associated with LBW. These results suggest that nutritional factors, prenatal care and perceived health status are important determinants of birth weight in a population where nutritional deficiencies are common and prenatal care is not adequate. Thus, improving overall nutritional status and access to prenatal care will be critical steps in reducing LBW.

Our study found that nutritional status of the mothers modified the effect of dietary vitamin C intake during pregnancy on LBW. Mothers who had low dietary intake of vitamin C and poor nutritional status as measured by below-median MUAC and BSFT were more likely to give birth to an LBW infant. Many studies from other parts of the world have reported the association of indices of maternal nutritional status (MUAC, BSFT, weight, BMI) with infant birth weight[19–21]. For example, a recent study in Zimbabwe reported that maternal MUAC was strongly related with LBW[20]; another in Sao Paulo, Brazil, reported an association between LBW and MUAC[19].

Previous studies have also reported the association of low vitamin C intake during pregnancy with LBW. In a follow-up study of women in rural India, intake of green leafy vegetables and fruits – both rich sources of vitamin C – was significantly associated with higher birth weight. Investigators reported that the effect was strongest in lighter and thinner women[22]. Another study in the UK also found a positive association of dietary vitamin C intake during pregnancy and birth weight[23]. A Korean study reported that higher serum vitamin C and vitamin E during pregnancy are associated with higher birth weight[24]. Recent evidence indicates a role of oxidative stress in the pathophysiology of LBW[25,26]. Vitamins C and E are antioxidants and counteract oxidative stress. Our findings of an association of vitamin C and birth weight are consistent with the aforementioned studies. Taken together, both our results and these previous findings have important public health implications for providing vitamin C during pregnancy. Our results also highlight that supplements will be more effective in reducing LBW among women with poor nutritional status to start with. Thus, below-median MUAC and BSFT can be used as an indicator to screen women presenting for prenatal care for more rigorous efforts for supplementation to reduce LBW. MUAC and BSFT at delivery have been reported to be strongly correlated with MUAC and BSFT during early pregnancy[16].

Inadequate prenatal care has been reported to be associated with LBW from many settings across the world like the USA, France, Finland, Brazil, Saudi Arabia, Bangladesh, Nepal and India[27–29]. Furthermore, it is well reported that provision of prenatal care is associated with improvement in LBW[30]. However, other studies have reported no association of no or low prenatal care with poor birth outcomes[31]. Many indices are used to assess the adequacy of prenatal care, incorporating the date of the first visit, total number of visits and length of pregnancy. However, inconsistencies in the definition of adequacy have led to controversies about the effectiveness of the current model

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Table 2 Crude prevalence ratios and their 95 % confidence interval for factors associated with low birth weight in Karachi, Pakistan, 2005–2006

	Total *n*	Low birth weight		PR	95 % CI	*P*
		n	%			
Child gender						
Female	251	51	20	1·19	0·84, 1·70	0·316
Male	289	49	17	1·00	–	
Parent characteristics						
Mother's age at delivery (years)						
<20	38	6	16	0·80	0·35, 1·83	0·594
21–30	401	74	18	0·93	0·60, 1·45	0·755
>30	101	20	20	1·00	–	
Mother's education (years of schooling)						
<5	177	33	19	1·31	0·55, 3·11	0·548
6–12	328	62	19	1·32	0·57, 3·07	0·515
>12	35	5	14	1·00	–	
Father's education (years of schooling)						
<5	125	26	21	1·54	0·79, 3·01	0·207
6–12	341	64	19	1·39	0·75, 2·57	0·297
>12	74	10	14	1·00	–	
Wealth index*						
Low	64	13	20	1·11	0·62, 1·98	0·731
Medium	307	56	18	0·99	0·67, 1·48	0·978
High	169	31	18	1·00	–	
Monthly household income						
Median and less (≤Rs. 7000)	289	51	18	0·90	0·63, 1·29	0·576
Above median (>Rs. 7000)	251	49	20	1·00	–	
Mother's ethnicity†						
Sindhi	26	5	19	0·96	0·42, 2·16	0·914
Punjabi	73	12	16	0·82	0·47, 1·43	0·477
Pakhtoon	30	4	13	0·66	0·26, 1·69	0·389
Baloch	43	5	12	0·58	0·25, 1·35	0·206
Urdu (Mohajir)	368	74	20	1·00	–	
Maternal nutrient intake and nutritional status						
BMI						
Low (<18·5 kg/m^2)	22	4	18	0·86	0·34, 2·14	0·741
Normal (18·5–24·9 kg/m^2)	297	63	21	1·00	–	
High (25·0–29·9 kg/m^2)	158	23	15	0·69	0·44, 1·06	0·091
Obese (≥30·0 kg/m^2)	63	10	16	0·75	0·41, 1·38	0·351
MUAC						
1st & 2nd quartiles (≤28·9 cm)	270	61	23	1·56	1·09, 2·25	0·016
3rd & 4th quartiles (>28·9 cm)	270	39	14	1·00	–	
BSFT						
1st & 2nd quartiles (≤9·0 mm)	272	61	22	1·54	1·07, 2·22	0·018
3rd & 4th quartiles (>9·0 mm)	268	39	15	1·00	–	
Daily Fe supplement intake during pregnancy						
Non-users	299	31	15	1·34	0·91, 1·97	0·127
Users	241	69	20	1·00	–	
Daily total Fe intake during pregnancy						
1st quartile (<20·4 mg)	134	24	18	1·10	0·65, 1·86	0·725
2nd quartile (20·5–29·7 mg)	135	30	22	1·36	0·83, 2·24	0·220
3rd quartile (29·8–77·28 mg)	136	24	18	1·08	0·64, 1·83	0·767
4th quartile (>77·28 mg)	135	22	16	1·00	–	
Daily Ca supplement intake during pregnancy						
Non-users	202	69	18	1·03	0·70. 1·51	0·879
Users	338	31	19	1·00	–	
Daily total Ca intake during pregnancy						
1st quartile (≤724·9 mg)	135	28	21	1·17	0·71, 1·90	0·538
2nd quartile (725·0–965·6 mg)	135	22	16	0·92	0·54, 1·55	0·746
3rd quartile (965·7–1181·1 mg)	135	26	19	1·08	0·66, 1·79	0·754
4th quartile (>1181·1 mg)	135	24	18	1·00	–	
Daily vitamin C supplement intake during pregnancy						
Non-users	134	29	22	1·24	0·84, 1·82	0·290
Users	406	71	17	1·00	–	
Daily total vitamin C intake during pregnancy						
1st quartile (≤297·9 mg)	135	36	27	1·80	1·10, 2·94	0·019
2nd quartile (298·0–662·3 mg)	135	18	13	0·90	0·50, 1·62	0·727
3rd quartile (662·4–979·6 mg)	135	26	19	1.30	0·76, 2·21	0·334
4th quartile (>979·6 mg)	135	20	15	1·00	–	

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Table 2 *Continued*

	Total *n*	Low birth weight *n*	Low birth weight %	PR	95 % CI	*P*
Environmental exposures						
Location of house with respect to road						
On the main road	94	16	17	0·66	0·39, 1·11	0·122
In the street near road	286	43	15	0·57	0·40, 0·86	0·006
In the street far from road	160	41	26	1·00	–	
Exposure to tobacco smoke at home or work						
Yes	144	32	22	1·29	0·89, 1·88	0·177
No	396	68	17	1·00	–	
Lived during pregnancy in house where insecticide was used						
Yes	396	66	17	0·71	0·49, 1·02	0·063
No	144	34	24	1·00	–	
Lived during pregnancy in house where DDT was used						
Yes	253	39	15	0·73	0·50, 1·04	0·084
No	287	61	21	1·00	–	
Mosquito coils were used during pregnancy						
Yes	241	46	19	1·06	0·74, 1·51	0·760
No	299	54	18	1·00	–	
Type of kitchen						
Indoor kitchen with no partition	71	10	14	0·47	0·22, 1·01	0·054
Indoor kitchen with partition	320	57	18	0·60	0·35, 1·04	0·067
Enclosed kitchen outside house	112	22	20	0·66	0·36, 1·23	0·191
Outdoor kitchen	37	11	30	1·00	–	
Doing all household work during pregnancy						
Yes	345	70	20	1·32	0·89, 1·95	0·164
No	195	30	15	1·00	–	
Cooking frequency						
Same or more often than before	374	78	21	1·57	1·02, 2·43	0·042
Less than before	166	22	13	1·00	–	
Total hours of rest per day in third trimester of pregnancy						
1st & 2nd quartiles ($\leq$6 h)	127	52	19	1·01	0·71, 1·44	0·940
3rd & 4th quartiles ($>$6 h)	413	48	18	1·00	–	
Maternal obstetric/pregnancy-related medical factors						
Parity						
0 or $\geq$5 births	219	47	22	1·62	1·03, 2·53	0·030
2–4 births	327	53	16	1·00	–	
Physician diagnosed anaemia during pregnancy						
Yes	240	51	21	1·30	0·91, 1·85	0·145
No	300	49	16	1·00	–	
Number of prenatal visits						
$\leq$1	41	13	32	1·88	1·13, 3·12	0·015
2–3	155	29	19	1·11	0·74, 1·66	0·613
$\geq$4	344	58	17	1·00	–	
Timing of first prenatal visit						
$>$28 weeks or no visit	135	31	23	1·96	0·99, 3·91	0·054
17–28 weeks	328	60	18	1·57	0·81, 3·01	0·180
$\leq$16 weeks	77	9	12	1·00	–	
Adequacy of prenatal care utilization						
No or 1 visit or first visit between 25 and 38 weeks	247	45	18	1·53	0·76, 3·08	0·238
2 visits or first visit between 17 and 24 weeks	226	47	21	1·74	0·87, 3·50	0·119
$\geq$3 visits and first visit before 16 weeks	67	8	12	1·00	–	
Feeling of depression						
Very much to extreme	72	21	29	1·66	1·10, 2·51	0·017
Quite a bit to some, enough to bother me	47	5	11	0·61	0·26, 1·42	0·249
Little to none	421	74	18	1·00	–	
Perception about health status						
Poor	136	39	29	2·39	1·27, 4·50	0·007
Fair	286	44	15	1·08	0·59, 1·98	0·803
Good	118	17	14	1·00	–	
History of trauma or injury						
Yes	53	13	25	1·37	0·83, 2·28	0·251
No	487	87	18	1·00	–	
Vaginal discharge during pregnancy						
Yes	130	19	15	0·74	0·47, 1·17	0·179
No	410	81	20	1·00	–	
High blood pressure						
Yes	74	13	18	0·94	0·55, 1·60	0·822
No	466	87	19	1·00	–	

Table 2 *Continued*

	Total *n*	Low birth weight *n*	%	PR	95 % CI	*P*
Gestational diabetes						
Yes	29	6	21	1·12	0·54, 2·35	0·754
No	511	94	18	1·00	–	
Umbilical cord BLL (μg/dl)						
<10	281	57	20	1·00	–	
≥10	259	43	17	0·82	0·57, 1·17	0·273

PR, prevalence ratio (computed using log binomial regression); MUAC, mid upper-arm circumference; BSFT, biceps skinfold thickness; DDT, dichlorodiphenyltrichloroethane; BLL, blood lead level.
*Wealth index was based on proportionate weighted sum of household assets, categorized on the basis of tertiles.
†The Mohajirs are group of people who migrated from parts of India not included in Pakistan at the time of creation of Pakistan, and they mostly speak Urdu.

Table 3 Multivariable log binomial regression models for factors associated with low birth weight in Karachi, Pakistan, 2005–2006

Risk factor	Model with MUAC* adjPR	95 % CI	*P*	Model with BSFT† adjPR	95 % CI	*P*
Perceived health status						
Good	1.00	–		1.00	–	
Fair	0.99	0.59, 1.65	0.970	0.97	0.58, 1.62	0.910
Poor	1.83	1.09, 3.07	0.021	1.90	1.14, 3.16	0.014
MUAC/BSFT and dietary vitamin C intake (mg/d)‡						
MUAC/BSFT > median & vitamin C > 208·7	1.00	–		1.00	–	
MUAC/BSFT ≤ median & vitamin C > 208·7	10.80	1.46, 79.76	0.020	5.10	1.20, 21.63	0.027
MUAC/BSFT > median & vitamin C ≤ 208·7	10.67	1.50, 76.02	0.018	5.21	1.29, 20.95	0.020
MUAC/BSFT ≤ median & vitamin C ≤ 208·7	13.19	1.85, 93.79	0.010	6.78	1.70, 27.09	0.007
Number of prenatal visits						
≥4	1.00	–		1.00	–	
2–3	1.27	0.86, 1.89	0.233	1.29	0.87, 1.92	0.213
≤1	2.18	1.39, 3.43	0.001	2.10	1.32, 3.32	0.001
Parity						
1–4 births	1.00	–		1.00	–	
0 or ≥5 births	1.53	1.08, 2.16	0.016	1.55	1.09, 2.19	0.013
Umbilical cord BLL						
Low (<10 μg/dl)	1.00	–		1.00	–	
High (≥10 μg/dl)	0.86	0.61, 1.21	0.380	0.84	0.59, 1.18	0.316

adjPR, adjusted prevalence ratio, MUAC, mid upper-arm circumference; BSFT, biceps skinfold thickness.
*Model with MUAC as measure of nutritional status.
†Model with BSFT as measure of nutritional status.
‡Interaction of MUAC/BSFT and vitamin C intake. Median MUAC = 28·9 cm; median BSFT = 9·0 mm; vitamin C of >208·7 mg = 4th quartile.

of prenatal care[32]. To address the issue of adequate number of visits, timing and content, many trials were conducted in developed and developing countries. A recent WHO-sponsored review of trials testing a new model with fewer number of visits and a goal-oriented approach found that LBW incidence was the same even after reduced number of visits, although at substantially reduced cost[33]. In our study, one or no prenatal visit was significantly associated with LBW in comparison with four or more visits. Another study in Pakistan also reported an association of low prenatal visits (less than three) with LBW[34]. Thus, in our setting improving access to prenatal care could reduce LBW further.

Poor self-rated health status is a determinant of adverse health outcomes and mortality[35]. It has been suggested that improvement or decline in self-rated health reflects primarily ongoing changes in the amount of distress or limitation associated with physical symptoms, mainly chronic ill health[36]. A previous study of the self-rated health status of women in Pakistan reported them to have poor overall self-reported health[37]. These findings are consistent with the findings of studies on South Asian immigrants in the UK[38]. Distress also leads to more negative health perceptions and negative health perception promotes distress[39]. Stress during pregnancy has been found to be associated with low social support[40]. Studies have reported an association of low or lack of social support with LBW[41]. In our study, poor self-rated health status was associated with LBW. Taken together with the previous findings that poor self-rated health reflects chronic ill health, pregnant women in our study are experiencing chronic ill health and lack of well-being and social support that is affecting their own health as well birth outcomes. Overall well-being and chronic ill health need further investigation in the context of pregnancy and birth outcomes in a developing country

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setting. There have been studies about stress and social support, but more work is needed to replicate our findings by directly measuring self-rated health status, its association with birth outcomes and its implications in the reduction of LBW.

Various studies from different parts of the world using maternal blood and bone Pb levels and umbilical cord BLL as a marker of prenatal Pb exposure have reported inconsistent results for an association between Pb and LBW[11–13]. Such inconsistencies in results may be due to different populations with different background risks, different biomarkers used for measuring Pb exposure, or differences in control for important covariates. Findings from the current study are consistent with many other studies from different parts of the world which did not find an association of Pb levels and LBW[13,42–44].

Studies have also reported the association of outdoor air pollution, exposure to biomass fuel and ETS with LBW[6,8,9]. However, none of these factors was significant in our study.

Limitations

The major strengths of the present study include the large sample size and measurement and control for important confounders. An FFQ was employed for estimation of dietary intakes of Ca, Fe and vitamin C that has been used previously but not formally validated. Many of the exposure measurement methods were based on self-report with the possibility of imperfect recall and misclassification. However, since all procedures were standardized and performed consistently, only non-differential misclassification is likely, which may have attenuated measures of effect. The study enrolled women who gave birth in study hospitals. In urban areas of Pakistan, a substantial proportion ($\sim 30\,\%$) of women deliver at home[45]. Hence, those delivering at hospital may be different from women delivering at home in their cultural beliefs, medical conditions forcing them to deliver in hospital, or may be more health-conscious. Therefore, caution should be used about the generalizability of these findings. Another potential limitation is the possibility of selection bias. However, selection bias is not likely in our case, because selection bias occurs when the comparison group (non-LBW infants) does not provide an estimate of the exposure distribution in the source population from which the LBW cases originate. The non-LBW infants originated from the same hospitals as the LBW infants, representing the same secondary bases of LBW, thus reducing the risk of selection bias.

Conclusion

In Pakistan, mothers with low intake of vitamin C during pregnancy and poor nutritional status were more likely to give birth to an LBW infant. These results highlight the importance of supplementation of vitamin C, which will be more effective in reducing LBW among women with poor nutritional status, although there remains a need to evaluate the effectiveness of vitamin C in reducing LBW through randomized trials. There is also a need to evaluate and replicate our finding that women with MUAC or BSFT below the median can benefit more from supplements. Very few prenatal care visits also the increased risk for LBW; thus access to prenatal care services should be improved. Moreover, future work should examine the reasons for under-utilization of already available services, including quality of care and the population's perceptions about the usefulness of these services. Environmental factors including umbilical cord BLL were not significantly associated with LBW.

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