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ORIGINAL ARTICLE

Prediction Model for Low Birth Weight and its Validation

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Abstract
Objective To evaluate the factors associated with low birth weight (LBW) and to formulate a scale to predict the probability of having a LBW infant.
Methods This hospital based case–control study was conducted in a tertiary care university hospital in North India. The study included 250 LBW neonates and 250 neonates with birth weight ≥2,500 g. Data were collected by interviewing mothers using pre-designed structured questionnaire and from hospital records.
Results Factors significantly associated with LBW were inadequate weight gain by the mother during pregnancy (<8.9 kg), inadequate proteins in diet (<47 g/d), previous preterm baby, previous LBW baby, anemic mother and passive smoking. The prediction model made on these six variables has a sensitivity of 71.6 %, specificity 67.0 %, positive LR 2.17 and negative LR of 0.42 for a cut-off score of ≥29.25. On validation, it has a sensitivity of 72 % and specificity of 64 %.
Conclusions It is possible to predict LBW using a prediction model based on significant risk factors associated with LBW.

Keywords Low birth weight · Prediction model · Risk factors · Validation

Introduction

According to World Health Organization (WHO), a newborn weighing less than 2,500 g at birth is termed as low birth weight (LBW) neonate. LBW in a newborn could either be due to intrauterine growth retardation or preterm birth, the former being the major cause in India. According to UNICEF's 2008 report, the incidence of LBW neonates is 30 % in India [1]. According to National Neonatal-Perinatal Database of the National Neonatology Forum, India; the incidence of LBW for intramural live-births in tertiary care centers is 31.3 % [2].

One of the goals of the Health and Family Welfare programs of the Government of India is to bring down the incidence of LBW from 30 % (prevalent since 1979) to 10 % by 2000 [3]. However, this seems unlikely even by the year 2013.

Many factors affect the duration of gestation and fetal growth, and thus, birth weight [4–14]. These may be related to the infant, the mother or the physical environment. LBW babies carry relatively higher risk of perinatal and neonatal mortality and morbidity. Their subsequent development and long-term growth is also lower. Barker's hypothesis establishes a link between intrauterine growth retardation and the occurrence of hypertension, insulin resistance, hypercholesterolemia, and hyperuricemia in adult life [13].

Despite the enormous role of LBW in neonatal mortality and morbidity as well as adolescent and adult morbidity, no significant clinical attempt has been made to predict the possibility of a LBW neonate. A study conducted in Cleveland, Ohio, U.S.A. proposed a four-factor scale [4]. The need for such a scale in Indian scenario was strongly felt and this study was undertaken with the objective of ensuing a prediction scale for LBW.

Material and Methods

This was a hospital based case–control study done in neonatal unit and post-natal wards in a tertiary care university hospital in North India during April-August 2011 after obtaining ethical clearance. 'Live' neonates with birth weight <2,500 g

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were included as cases (Low Birth Weight/LBW) and neonates with birth weight ≥2,500 g were included as controls (Normal Birth Weight/NBW).

The sample size was found to be 200 per group, calculated to the power 80, alpha 5 % for this unmatched case–control study by using the incidence of exposure of risk factors in cases (LBW) and controls (NBW) based on review of literature.

Each day, in the labor room, the first neonate born with birth weight <2,500 g was selected as a case. Following every case, the first neonate born with normal weight in the same labor room was selected as corresponding control. Next LBW neonate born was taken as next case and so on. 'Live' twins/triplets were included in the study as per weight of each neonate under respective group, considering the first-born twin first.

Informed consent was taken and mothers of these cases and controls were then interviewed in the post-natal wards (after they had been shifted from the labor room) using a pre-designed structured questionnaire devoting 10–15 min/mother. Additional relevant data were collected from obstetric and neonatal hospital records. Data were collected about demography, anthropometry, ANC care, routine investigations' records, obstetric history, medical and surgical history, environmental exposures (active or passive smoking) and dietary history (of diet prior to hospital admission) by 24 h recall method.

Weight of the neonates was accessed from labor room registers recorded by pediatricians/trained nurses within an hour of birth in gram using a beam balance to the nearest 20 g. The infant's gestational age was calculated as the number of weeks passed between the first day of mother's last menstrual period (LMP) and her date of delivery. If the mother was not sure of her LMP, Ballard score was used. Preterm neonates were defined as those with period of gestation <37 completed weeks. Small for gestational age (SGA) babies were identified using intrauterine growth curves for weight [15]. For Ante-natal Clinic visits, a criterion of 'less than 4 visits' was used to define inadequate ANC care based on WHO recommendations [16, 17].

Pre-pregnancy weight was defined as weight before conception or earliest first trimester weight measurement. Since negligible weight gain is seen till 12 wk of gestation [18, 19], weight gain from end of first trimester to term gestation or delivery (whichever is earlier) was taken to represent the total weight gain during pregnancy.

Maternal anemia was defined as hemoglobin <11 g/dL as per WHO definition considering the earliest reading taken during the first or second trimester.

Socioeconomic status was determined using Kuppuswamy's Socioeconomic Status Scale modified for the year 2007 [20]. Low socio-economic status was defined as 'Lower' and 'Lower Middle' on Kuppuswamy's Scale.

Mother's dietary history was taken by 24 h recall method for the diet that she ate before hospital admission and calculation of calories and proteins was done using ICMR food charts [21]. Smoking habits of mothers and their husbands were enquired. Among smokers, the number of cigarettes/beedis smoked per week was recorded. Smoking ≥5 cigarettes/beedis per week was classified as significant smoking habit [22]. Passive smoking was defined as smoking of ≥5 cigarettes/beedis per week by the father.

Data for 250 cases and 250 controls were collected and entered periodically into spread sheet using Microsoft Access 2010.

Statistical analysis was done using Stata SE 11 software. Using a table of random numbers, 50 cases from the total pool of 250 cases were selected. Using a separate table of random numbers, 50 controls out of a total pool of 250 controls were selected. These 50 cases and 50 controls were set aside for validation of the prediction model.

The remaining 200 cases and 200 controls were analyzed through logistic regression model in Stata SE 11 software. Continuous data was analysed using Student's t-test/Wilcoxon rank-sum test, while Chi-Square/Fisher's Exact Test was used for categorical data. Unadjusted odds ratio (95 % CI) for each factor with the outcome (Univariate Logistic Regression analysis) and adjusted OR (95 % CI) for important factors considered simultaneously (by Multivariable Logistic Regression analysis) were obtained. Various risk factors mentioned in Table 1 were found significant on univariate analysis. Out of these, a total of seven variables were found significant by multivariate logistic regression. One of the variable among these was 'sex of the newborn' which was dropped since it cannot be used in a prediction model to be used in antenatal period. Using the other six variables, a weighted prediction score was formulated based on their coefficients derived from logistic regression. Equation for prediction and ROC curve were obtained. The discriminatory power of the model was evaluated by Receiver-operator characteristic (ROC) analysis.

The remaining 50 cases and 50 controls (set aside by selection *via* table of random numbers) were then utilized to validate the prediction model.

Results

Demographics of the study population: mean weight of 200 study cases (LBW) was 2.0±0.4 kg and that of 200 controls (NBW) was 3.2±0.4 kg ($P<0.001$). Among the cases, 47 % were males and 60 % controls were males (P 0.0653). Among the cases, 43 % were preterm and 56 % were term SGA and 22 % were both preterm as well as SGA. Thus approximately 78 % of the babies were SGA. Mean gestational age of the cases was 36.3±3.1 wk and that of the controls was 39.1±1.4 wk.

Table 1 Logistic regression analysis of the variables related to low birth weight

Variable	Unadjusted OR [95 % CI]	*p* value for Unadjusted OR	Adjusted OR [95 % CI]	*p* value for Adjusted OR
Weight gain by the mother during pregnancy <8.9 kg	4.6 [2.7, 7.7]	**<0.001**	6.1 [1.3, 27.8]	**0.019**
Mother's height <1.53 m	2.5 [1.6, 3.9]	**<0.001**	.7 [0.1, 3.3]	0.642
Pre-pregnancy BMI <20.621	2.2 [1.3, 3.7]	**0.003**	5.6 [0.8, 40.6]	0.089
Female sex of the baby	1.6 [1.1, 2.4]	**0.016**	4.2 [1.1, 16.5]	**0.039**
Primigravida	1.8 [1.2, 2.7]	**0.003**	–	–
Primipara	1.8 [1.2, 2.6]	**0.005**	–	–
Educational status (Less than or equal to intermediate)	1.6 [1.0, 2.4]	**0.046**	.7 [0.1, 3.3]	0.633
ANC visits <4	1.7 [1.1, 2.7]	**0.047**	1.2 [0.1, 23.9]	0.924
Pre-pregnancy weight <45 kg	2.6 [1.6, 4.2]	**<0.001**	2.1 [0.3, 15.5]	0.450
Anemic mother	2.9 [1.8, 4.8]	**<0.001**	20.0 [1.6, 246.5]	**0.020**
Multiple births (Twins)	8.1 [2.4, 27.6]	**0.001**	–	–
Hypertension (Chronic/ Gestational)	2.4 [1.1, 5.6]	**0.048**	4.2 [0.1, 171.3]	0.444
Proteinuria	6.9 [1.5, 31.1]	**0.012**	6.2 [0.1, 558.8]	0.428
Inadequate spacing (<24 mo)	3.5 [1.9, 6.4]	**<0.001**	1.0 [0.2, 4.2]	0.972
Passive smoking	2.6 [1.5, 4.2]	**<0.001**	5.6 [1.1, 29.4]	**0.043**
Previous preterm baby	4.1 [2.2, 7.6]	**<0.001**	6.9 [1.4, 33.8]	**0.017**
Previous LBW baby	5.2 [3.0, 8.9]	**<0.001**	6.2 [1.7, 23.3]	**0.006**
Inadequate calories in mother's diet (<1667.1 kcal/d)	2.3 [1.5, 3.5]	**<0.001**	2.0 [0.3, 12.0]	0.451
Inadequate proteins in mother's diet (<47 g/d)	2.3 [1.5, 3.4]	**<0.001**	6.1 [1.1, 36.2]	**0.044**
Low socio-economic status	1.4 [0.9, 2.2]	0.092	–	–

Data in bold represents significant *p* values ($p<0.05$)

Table 1 shows unadjusted and adjusted odds ratio, *p* value and 95 % CI obtained for the risk factors associated with LBW. Several factors were found significant by univariate analysis and have been mentioned in Table 1. Factors found significant by multivariate analysis were inadequate weight gain by the mother during pregnancy (OR, 6.1 [95 % CI 1.3, 27.8]; *p* 0.019), inadequate proteins in diet (OR, 6.1 [95 % CI 1.1, 36.2]; *p* 0.044), previous preterm baby (OR, 6.9 [95 % CI 1.4, 33.8]; *p* 0.017), previous LBW baby (OR, 6.2 [95 % CI 1.7, 23.3]; *p* 0.006), anemic mother (OR, 20.0 [95 % CI, 1.6, 246.5]; *p* 0.020), passive smoking (OR, 5.6 [95 % CI 1.1, 29.4]; *p* 0.043) and female sex of the baby (OR, 4.2 [95 % CI 1.1, 16.5]; *p* 0.039).

Using these results, a prediction model was made and equation for the prediction model was obtained (Table 2). Also, ROC curve was obtained to evaluate the model and area under the curve (AUC) was found to be 0.79 (Fig. 1).

Equation for the Prediction model:

$$\text{Final weighted score} = 10\ (\text{Weight gain} < 8.9\ \text{kg}) + 14.75\ (\text{Proteins} < 47\ \text{g/d}) + 14.75\ (\text{Previous preterm baby}) + 15\ (\text{Previous LBW baby}) + 14.5\ (\text{Hb} < 11.0\ \text{g/dL in mother}) + 10.2\ (\text{Passive smoking})$$

With each variable being assigned a value of '1' if present and '0' if absent.

Sensitivity and specificity at various cut-offs were analyzed. The suggested cut-off score to predict LBW using this model is ≥29.25 with a sensitivity of 71.6 %, specificity 67.0 %, correctly classified 69.15 %, positive likelihood ratio 2.17 and negative likelihood ratio of 0.42. For a score of ≥24.75 the model has a sensitivity of 73.7 %, specificity of 61.3 %, correctly classified 67.16 %, positive likelihood ratio of 1.90 and negative likelihood ratio of 0.43.

The remaining 50 cases and 50 controls were then utilized to validate the model. On validation, the model was found to have 72 % sensitivity and 64 % specificity for prediction of LBW using a cut-off score ≥29.25. For cut off score of ≥24.75, it had 72 % sensitivity and 56 % specificity.

Discussion

Like various studies from both developing and developed countries [4–13], the present study has found that risk of having a LBW baby is multifactorial in origin [14]. Many

Table 2 Prediction model for low birth weight

Variable	Estimated regression coefficient (SE)	Weights[a] (Points)	*p* value
Inadequate weight gain by the mother	1.20 (0.53)	10	**0.025**
Inadequate proteins in mother's diet	1.77 (0.54)	14.75	**0.001**
Previous preterm baby	1.77 (0.65)	14.75	**0.007**
Previous LBW baby	1.80 (0.54)	15	**0.001**
Anemic mother	1.74 (0.72)	14.5	**0.016**
Passive smoking	1.22 (0.68)	10.2	0.074

Data in bold represents significant *p* values ($p<0.05$)

Final weighted score: 10 (Inadequate weight gain) + 14.75 (Inadequate dietary proteins) + 14.75 (Previous preterm baby) + 15 (Previous LBW baby) + 14.5 (Anemic mother) + 10.2 (Passive smoking) with each variable being assigned a value of '1' if present and '0' if absent

[a] Obtained by multiplying the regression coefficient by 10 and dividing by 1.20 (the least regression coefficient)

maternal, biosocial, medical and obstetric factors contribute to the occurrence of LBW.

Sharma, et al. found that low literacy level, low per capita income, birth order ≥2 and maternal age >30 y were significant maternal risk factors of LBW in Chandigarh, India [5].

A study from Pakistan by Khan, et al. shows that the maternal factors like malnutrition, young age, poverty, close birth spacing, hypertension and antenatal per vaginum bleeding during pregnancy have independent effect in causing LBW [6]. In another study from Pakistan by Badshah, et al. the main risk factors for SGA identified were: maternal age, nationality, consanguinity, anemia and history of previous abortion/miscarriage [7].

Ullah, et al. identified these as risk factors for LBW in the rural community of Rajshahi district in Bangladesh: maternal weight <50 kg at 3rd trimester, birth interval <2 y and female sex of newborn [8]. In a study by Vega, et al. multivariate logistic regression analysis showed that eight variables: number of pregnancies, previous adverse outcome, previous LBW, pregnancy maternal weight, number of prenatal visits, month of first prenatal visit, maternal smoking and intrahepatic cholestasis of pregnancy were significantly associated with LBW [9].

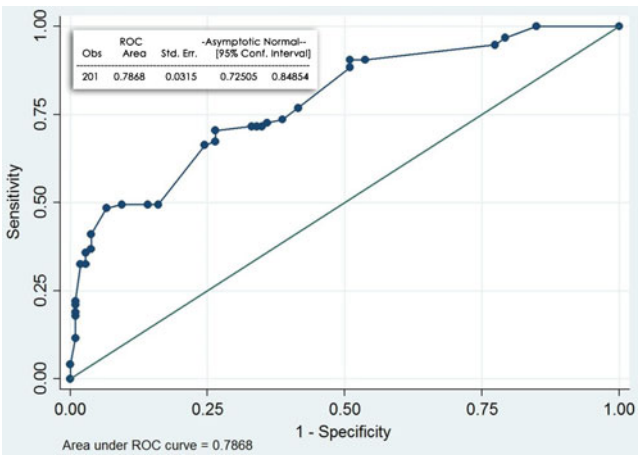

Fig. 1 ROC curve for LBW prediction model. Cut off score for prediction of LBW: ≥29.25

M.S. Kramer from Canada did a meta-analysis of English and French medical literature published from 1970 to 1984 on determinants of LBW which revealed that for developing countries, male neonates have a higher birth weight than female neonates and lesser risk of IUGR [14]. Similarly, the present study found that male neonates have a lesser risk of LBW than females (*p* 0.039). Among populations where short stature is prevalent, low maternal height accounts for a significant number of IUGR infants with a relative risk of 1.27 for maternal height <157.5–158 cm [14]. This trend is consistent with the index study (unadjusted OR of 2.5 for maternal height <1.53 m). He also observed a relative risk of 1.84 for pre-pregnancy weight <49.5 kg. The authors found an unadjusted odds ratio of 2.6 for weight <45 kg.

Kramer's meta-analysis as well as index study inferred that socio-economic status has no independent effect on intrauterine growth. It was seen that as parity increases, the mean birth weight increases and primiparity has a risk ratio of 1.23 for LBW [14]. Indeed, the index study found that primipara mothers have a higher risk for delivering a LBW baby with an unadjusted odds ratio of 1.8 ($p<0.05$).

The meta-analysis found a RR of 3.08 for prior premature birth; the authors found an adjusted OR of 6.9 for previous preterm birth. Also, he observed a relative risk of 2.75 for ≥1 prior LBW, the authors found an adjusted OR of 6.2. The present study found that having a previous abortion (spontaneous or induced considered together) did not increase the risk for LBW. Kramer found no significant effect of prior spontaneous abortion on birth weight and of prior induced abortion on intrauterine growth [14].

The authors found an adjusted odds ratio of 6.1 for weight gain by the mother during pregnancy <8.9 kg. Dr. Kramer found a RR of 1.98 for total gestational weight gain <7 kg in well-nourished women. He also states that since a large proportion of pregnant women are undernourished in developing

countries, the RR and etiological fraction may actually be much higher [14].

Despite significant impact of LBW on neonatal mortality and morbidity, little work has been done to predict its possibility. Only one study conducted in Ohio, U.S.A. proposed a four-factor scale (low family functioning, stressful events, Quetelet's Index and cigarette smoking) which predicted LBW with 65 % sensitivity, 84 % specificity and 42 % PPV [4]. Using the results of index study the authors formulated a prediction model or scale to predict LBW in Indian scenario with a sensitivity of 71.58 % and specificity of 66.98 %. Additionally, the authors also validated their prediction model on a total of 100 neonates (50 % of whom were LBW).

A limitation of this study is that the samples were taken from hospital deliveries, and this was a single-site study. Additional limitations pertain to any case–control study—*i.e.,* inability to calculate relative risk, unforeseeable risk factor incidence, and memory/recall bias.

Conclusions

It is possible to predict LBW using a prediction model. Most of the risk factors for LBW are preventable. This model will help to do risk stratification of mothers and to identify those at risk of having a low birth weight baby. Subsequently, these mothers can be referred during early pregnancy to a center which is equipped with facilities for management of high risk pregnancy and low birth weight babies.

Contributions AS, SA, HC and KA: Conception and design, analysis and interpretation of data, drafting the manuscript, critical revision of the manuscript for intellectual content and final approval of the version to be published; RP: Statistical analysis.

Conflict of Interest None.

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