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Article

Development and validation of a risk score to predict low birthweight using characteristics of the mother: Analysis from BUNMAP cohort in Ethiopia

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Abstract: At least one ultrasound is recommended to predict fetal growth restriction and low birthweight earlier in pregnancy. However, in low-income countries imaging equipment and trained manpower are scarce. Hence, we developed and validated a model and risk score to predict low birthweight using maternal characteristics during pregnancy, for use in resource limited settings. We conducted a prospective cohort study among 379 pregnant women in South Ethiopia. A step-wise multivariable analysis was done to develop the prediction model. To improve clinical utility, we developed a simplified risk score to classify pregnant women at high- or low-risk of low birthweight. The accuracy of the model was evaluated using the area under the receiver operating characteristics curve (AUC) and calibration plot. We evaluated the clinical impact of the model using a decision curve analysis across various threshold probabilities. Age at pregnancy, underweight, anemia, height, gravidity, and presence of comorbidity remained in the final multivariable prediction model. The area under the receiver operating characteristics curve (AUC) of the model was 0.83 (95% confidence interval: 0.78 to 0.88). The decision curve analysis shows the model provides a higher net benefit across ranges of threshold probabilities. In general, this study showed the possibility of predicting low birthweight using maternal characteristics during pregnancy. The model could help to identify those at higher risk of having a low birthweight baby. This feasible prediction model would offer an opportunity to reduce obstetric-related complications and thus improving the overall maternal and child healthcare in low- and middle-income countries.

Keywords: prediction; model; risk score; low birthweight; pregnant women; decision curve analysis

1. Introduction

Low birthweight (LBW), a weight at birth of less than 2,500 grams (5.5 lb), continues to be a significant public health problem globally. It is estimated that 15% to 20% of all births worldwide are LBW, accounting for more than 20 million in a year [1]. The rate of LBW vary considerably among regions and countries, with higher burden among low- and middle-income countries (LMIC). The prevalence in LMICs (16.5%) is twice higher than in high-income countries (7%) [2]. In Ethiopia, LBW rate varies across geographical areas, which ranges from 8% to 54% [3-6], showing a huge variation across geographical settings and time periods. A recent systematic review showed a pooled estimate of 17.3% in Ethiopia [7], which implies it still remains an important public health problem in the country.

LBW or being small for gestational age increases infant morbidity and mortality [8-12]. It is related to childhood health outcomes, such as susceptibility to infection, neurological deficits, and lower cognitive skills [13-15]. Later in life, it is associated with high blood pressure, diabetes, and coronary

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heart disease [16-20]. In 2016, the infant mortality rate in Ethiopia was 48 deaths per 1,000 live births, of which a significant proportion was attributed to LBW [21].

Demographic factors such as young maternal age, higher birth order, prim-gravida, low educational level, and poor maternal nutritional status before and during pregnancy are well recognized risk factors for LBW [7, 22-25]. Numerous other determinants have also been associated with intrauterine growth retardation, such as place of residence, poor diet, anemia, parity, and presence of chronic illness [25-27]. Socio-economic factors such as household income and level of education have also been suggested [26, 28].

LBW has a remarkable impact on the political, social, economic, and healthcare system in LMICs. Hence, by the end of 2025, the World Health Assembly set a policy target to reduce LBW by 30% [1]. Strategies have been implemented to reduce LBW with given emphasis on the packages of care provided at the prenatal, ante-natal, intra-natal, and post-natal period. As a result, the proportion of mothers attending ANC is improving. As part of the strategy, it is essential to diagnose or predict fetal growth restriction earlier in pregnancy to take appropriate measure for high risk groups. However, in LMICs imaging equipment and trained manpower are limited. It is assumed that a simple prediction tool could be an alternative in resource poor settings. However, no significant clinical attempt has been made to predict the probability of LBW. To our knowledge two studies [29, 30], tried to develop a prediction model, though, they have less practical implication due to the predictors used are not easily obtainable in primary healthcare settings. We developed and validated a model and risk score to predict LBW in primary care settings of LMICs. The risk scores developed could be used by clinicians and public health professionals working on maternal and child health unit to predict LBW earlier in pregnancy.

2. Methods and Materials

2.1. Study setting

The present study used data from the mother-child cohort (BUNMAP) project in Ethiopia, a population based cohort established in 2016. It is a cohort of pregnant women and their offspring living in selected clusters of Butajira Health and Demographic Surveillance Site (HDSS), South Ethiopia. Butajira HDSS is one of the oldest surveillance sites in Africa established in 1986. The livelihood of the residents is based on subsistent farming. Khat (Catha edulis Forsk) and chilli peppers are the main cash crops, while maize, banana, and Ensete (Enseteventricosun) are the main staples. Currently, the cohort enrolled 881 pregnant women and will follow the mother-child pair up to the third birthday of the child. Among those enrolled, 379 has given birth at the time of this analysis.

2.2. Ethical Statement

Ethical clearance was obtained from the Institutional Review Boards (IRB) of Addis Ababa University, College of Health Sciences (code: 099/17/SPH). Written informed consent and parental assent was obtained from study participants after explaining the possible risks, benefits, purposes of the study, issue of confidentiality and voluntarism. The study is in compliance with the principles of the declaration of Helsinki. All data were stored either in password-protected computers or, in the case of paper records, in locked files in the project's locked office in Addis Ababa.

2.3. Study design and participants

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The theoretical design of the present study was; the incidence of low birthweight (at time 1) as a function of multiple predictors during pregnancy (time 0). The source population for the cohort were all 15 to 49 years old women living in Butajira HDSS, who have the capacity to be pregnant. All pregnant women who were enrolled into the cohort and fulfilled the eligibility criteria were included to the analysis. To be included in this study, mothers must meet all of the following eligibility criteria; 1) women should have gave birth and 2) birthweight was taken within 72 hours of delivery. Whereas, women with fetuses having congenital malformations during ultrasonographic evaluation or 2) twins or above pregnancy were excluded.

2.4. Data collection

Outcome Assessment: after enrollment three ultrasound examinations of pregnant women were done, one during each trimester, to estimate gestational age, intrauterine fetal growth, and presence of any congenital anomaly. Birthweight was taken within 72 hours of post-delivery using digital scales. The main outcome, LBW, was defined as a weight of neonate below 2500 grams (5.51 pounds).

Predictor assessment: a questionnaire was adapted from the Ethiopian Demographic and Health Survey and other relevant literatures. A range of socio-demographic, obstetric, and clinical characteristics of the women including, morbidity, educational status, marital status, occupation, gravidity, parity, ante-natal care utilization, family planning, and the interval between pregnancies were collected. Nutritional status including height, and weight was taken for all women at baseline and during each trimester of pregnancy. The level of anemia was also assessed by measuring hemoglobin in red blood cells, using a Hemo-Cue (Hb-201) instrument.

2.5. Quality assurance mechanisms

Intensive training was given for data collectors and supervisors about the objective of the research, how they will collect the data, keep the collected data, and supervise the data collection process. Afterward, pilot study was done in order to assure that data collectors and supervisors are really competent enough to collect and supervise the data collection process. In case of paper form, questionnaires were controlled for completeness and logical errors, and where errors were found, the questionnaires were redone.

2.6. Data processing and analysis

The data were collected using Open Data Kit (ODK) platforms and were exported to R statistical programming language version 3.6.0 for further processing and analysis. There was 8 (2.1%), 7 (1.8%), and 6 (1.6%) missing values for hemoglobin level, weight, and height measurements. Moreover, marital status, alcohol consumption and presence of chronic morbidity each had 1 (0.3%) missing values (table 1). We assumed data were missing at random, and we therefore performed multivariate imputation by chained equations using "mice" package in R [31, 32]. Missing results were imputed for all variables evaluated for the prediction model but not for "low birthweight" as we analyzed only participants for whom birthweight was taken. Sensitivity analysis was performed to assess whether the assumption of missing at random (MAR) is valid, and the results were reasonably comparable (appendix A). Descriptive statistics including mean, standard deviations (SD), median, inter-quartile range (IQR), percentages, and rates were performed. Incidence and relative risk for low birthweight were also computed.

2.6.1. Model development and validation

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We performed a univariable analysis using logistic regression to obtain insight into the association of each potential determinant with LBW and to select potential predictors for multivariable analysis. We fit all the variables with p-value < 0.25 in the univariable analysis to the multivariable model to be more liberal. Afterward, we used a stepwise backward elimination technique with p-value <0.10 for the likelihood ratio test to fit the reduced model. As the pregnant women came from different clusters, individual data were likely to be clustered within the different kebeles, which could affect the association of the predictors with the low birthweight. We accounted for such possible non-random differences within kebeles (clusters) using multilevel logistic regression techniques [33, 34]. We used a random intercept effect for the intercept (to adjust for differences in baseline rate of low birthweight per kebele) as well as for each candidate variable (to adjust for differences in the associations between variable and outcome per cluster). However, the multilevel analysis identified nearly the same intercept, coefficient, and confidence intervals as the standard multivariable logistic regression analysis.

To check for the model accuracy, we computed the area under the ROC curve (discrimination) and calibration plot (calibration) using '*classifierplots' and 'givitiR'* packages of R respectively [35]. AUC value of 0·5 indicates no predictive ability, 0·8 is considered as good, and 1 is perfect. The regression coefficients with their 95% confidence intervals, as well as the AUC, were internally validated using bootstrapping technique [36]. To this end, 2000 random bootstrap samples with replacement were drawn from the data set with complete data on all predictors. The model's predictive performance after bootstrapping is considered as the performance that can be expected when the model is applied to future similar populations.

To evaluate the clinical and public health impact of the model, we performed a decision curve analysis (DCA) [37], of standardized net benefit across a range of threshold probabilities (0 to 1). In the DCA, the model was compared against two extreme scenarios; 'intervention for all' and 'no intervention'. In our case, the intervention considered is referral of high risk pregnant mothers to facilities with ultrasound or other imaging services.

2.6.2. Risk score development

To construct an easily applicable low birthweight prediction score, we transformed each coefficient from the model to a rounded number by dividing to the lowest coefficient. The number of points was subsequently rounded to the nearest half integer. We determined the total score for each individual by assigning the points for each variable present and adding them up. The predicted probability of LBW was presented according to three categories of the risk score for reasons of statistical stability and practical applicability. The categories were arbitrarily chosen with a view to reasonable size of each category as well as public health sensibility. Later, the score was transformed to a dichotomous "prediction test," allowing each pregnant women to be classified as at high or low risk of LBW. We carried out a sensitivity analysis around different cutoff points of 3, 3.5, 4, 4.5, 5, and 5.5. The sensitivity, specificity, the positive and negative predictive value, and the likelihood ratios of categorized values of the score were calculated (appendix B).

This study was reported in accordance with the TRIPOD (transparent reporting of a multivariable prediction model for individual prognosis or diagnosis) statement [38], which included a 22-item checklist to give guidance for reporting the development and validation of a prediction model.

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3. Results

3.1. Baseline demographic, obstetric and clinical characteristics of pregnant women

We included a total of 379 women who gave birth at the time of this analysis. Table 1 shows the demographic, obstetric and clinical characteristics of pregnant women included in the analysis. The median age of the participants was 28 years (IQR: 22 - 35; and 51 (13.5%) of them were less than 20 years old. Most (92.6%) of the women were married and 221 (58.3%) of them never attended any formal education. Above one-third (37.2%) were primigravid, of which above two-third (71.0%) of them have attended at least one ANC visit in their previous pregnancy. A quarter (25.3%) of pregnancies was unplanned, and 127 (33.5%) of them used family planning before current pregnancy. One hundred four (28.0%) of them had body mass index (BMI) <18.5, and 156 (41.8%) were shorter than 155 cm height. Sixteen (4.2%) have history of chronic co-morbidity either cardiovascular, pulmonary, diabetes or chronic kidney diseases. The hemoglobin test result indicated, 132 (35.6%) of women have hemoglobin level less than 11gm/dL. Fifty three (14.0%) of women took alcohol at least once a week.

Table 1: Baseline demographic, obstetric and clinical characteristics of pregnant women who were enrolled to the BUNMAP project, south Ethiopia, 2016-2019

Characteristics	Missing	Frequency	Percent
Age	0 (0.0)		
<20 years		51	13.5
>=20 years		328	86.5
Marital status	1 (0.1)		
With partner		350	92.6
Alone		28	7.4
Formal education	0 (0.0)		
Yes		158	41.7
No		221	58.3
Gravidity	0 (0.0)		
Prim-gravida		141	37.2
Multigravida		238	62.8
Previous ANC (n=238)	0 (0.0)		
Yes		169	71.0
No		69	29.0
Intention to pregnancy	0 (0.0)		
Planned		283	74.7
Un-planned		96	25.3
Family planning before current pregnancy	0 (0.0)		
Yes		127	33.5
No		252	66.5
Birth interval (n=238)	0 (0.0)		
<24 months		98	41.2
>=24 months		140	58.8
Body Mass Index	7 (1.8)		
<18.5		104	28.0
>=18.5		268	72.0

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Height (in cm) <155 >=155	6 (1.6)	 156 217	 41.8 58.2
Hemoglobin (mg/dl) <11 >=11	8 (2.1)	 132 239	 35.6 64.4
Chronic morbidity Yes No	1 (0.1)	 16 362	 4.2 95.8
Alcohol (at least once/week) Yes No	1 (0.1)	 53 325	 14.0 86.0
Total		379	100

3.2. A prediction model for low birthweight

Out of 379 women who gave birth, 83 (21.9%) were low birthweight infants. The mean birthweight of was 2788.4 grams (SD: 611.4). After review of literature, 13 demographic, obstetric, and clinical characteristics of the mother were collected at baseline and considered to predict low birthweight at term. The univariable analysis found several factors were eligible to be included in the prediction model. Variables with P<0.25 in the univariable analysis were; age at current pregnancy, BMI, height, educational status, hemoglobin level, attending previous ANC, gravidity, and presence of comorbidity. Then, six predictors remained in the reduced multivariable regression analysis; younger age (<20 years), underweight (BMI<18.5), short stature (height<155cm), anemia (hemoglobin<11mg/dl), primi-gravidae, and presence of comorbidity. Using the results, a prediction model was developed and equation for the prediction model was obtained. (Table 2)

Table 2: Coefficients and risk-scores of each predictors included in the model to predict low birthweight (n= 379). Figures are numbers (percentages) unless mentioned otherwise.

Predictor variable	**Univariable analysis**		**Multivariable analysis**		**Simplified risk score ¶**
	β (95 % CI)	P-value	β (95 % CI)	P-value	
Age of the mother (<20)	1.596 (0.980, 2.222)	<0.01¥	1.593 (0.856, 2.344)	<0.01*	2.5
Marital status (single)	0.184 (-0.779, 1.033)	0.69	NA	-	-
Formal education (no)	0.431 (-0.072, 0.951)	0.098¥	0.479 (-0.382, 1.384)	0.284	
BMI (<18.5)	1.530 (1.015, 2.053)	<0.01¥	1.516 (0.915, 2.133)	<0.01*	2.5
Height (<155cm)	1.032 (0.535, 1.543)	<0.01¥	1.225 (0.637, 1.838)	<0.01*	2
Hemoglobin (<11.0 mg/dl)	1.270 (0.768, 1.783)	<0.01¥	1.213 (0.626, 1.815)	<0.01*	2
Gravidity (prim-gravida)	0.586 (0.091, 1.080)	0.02¥	0.606 (0.001, 1.215)	0.049*	1
Previous ANC (no)	-0.419 (-1.101, 0.288)	0.235¥	0.011 (-0.885, 0.949)	0.98	-
Birth interval (<24month)	-0.014 (-0.691, 0.647)	0.97	NA		-
Pregnancy (Unplanned)	0.079 (-0.491, 0.622)	0.78	NA		-
Family planning use (yes)	-0.127 (-0.661, 0.387)	0.63	NA		-
Comorbidity§ (yes)	1.627 (0.608, 2.686)	<0.01¥	1.475 (0.260, 2.744)	0.02*	2.5
Alcohol consumption	0.169 (-0.543, 0.826)	0.63	NA		-

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Variables retained in the reduced model using likelihood ratio test are; age, BMI, hemoglobin, height, gravidity, and comorbidity. Both backward and forward selection showed same results. β after internal validation with bootstrapping are shown.

¥ Variables included in the multivariable analysis (P<0.25 in univariable analysis)

§ Comorbidity include pulmonary: history of asthma or COPD (chronic obstructive pulmonary disease); cardiac: history of heart failure or ischemic heart disease; renal diseases

NA - not included to the multivariable analysis (P>0.25 in the univariate analysis)

¶ Simplified risk score: we divided the coefficient of predictors included in the reduced model by the smallest (0.606)

The area under the receiver operating characteristics curve (AUC) of the final reduced model was 0.83 (95% confidence interval: 0.78 - 0.88) (Figure 1). The calibration test had a p-value of 0.89, indicating that the model does not misrepresent the data (Figure 2). Validation of the model with the bootstrap technique showed hardly any indication of undue influence by particular observations, with optimism coefficient of 0.0092, resulting AUC of 0.82 (corrected 95% CI: 0.76 - 0.89).

a) b)

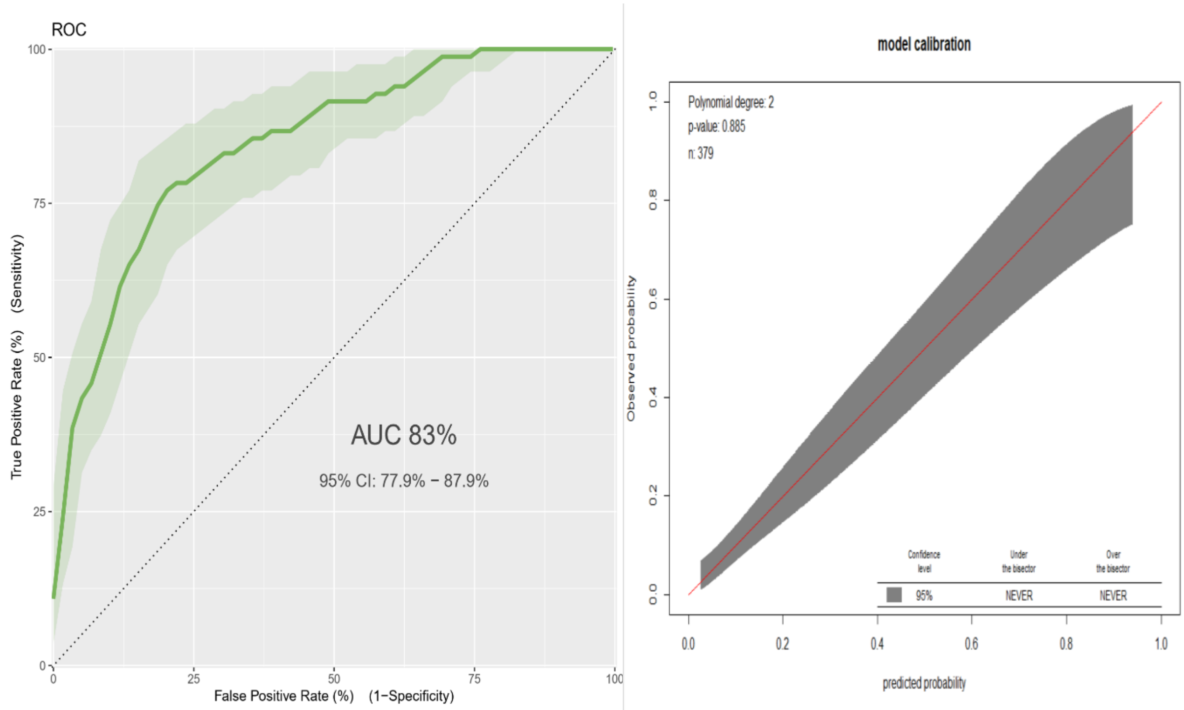

Figure 1: a) Area under the ROC curve for the prediction model, and b) Predicted versus observed low birthweight probability in the sample. This analysis includes neonates born at term (n=379). The calibration plot created using "*givitiCalibrationBelt*" in R programming.
Linear predictors for estimated risk of low birthweight = 1/(1+exp-(-2.54+1.593×age(<20) + 1.516×BMI (<18.5) + 1.213xhemoglobin (<11) + 1.225*height(<155)+ 0.606xprim-gravid + 1.475xcomorbidity.
ROC=receiver operating characteristic**s**

Using the coefficients (β) the predicted risk cutoff point has a probability of >0.2631, with sensitivity of 71% [95%CI: 60-81], specificity 82% [95%CI: 77-86], positive predictive value 52%

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[95%CI: 43-62], and negative predictive value of 91% [95%CI: 87-94]. The positive and negative likelihood ratio was 3.9 [95%CI: 2.95-5.14] and 0.35 [95%CI: 0.25-0.50], respectively.

As shown in figure 3, the model has the highest net benefit across the entire range of threshold probabilities, which clearly indicates that the model has highest clinical and public health value. Hence, referral decision made using the model has higher net benefit than not referring at all or referring all regardless of their risk threshold.

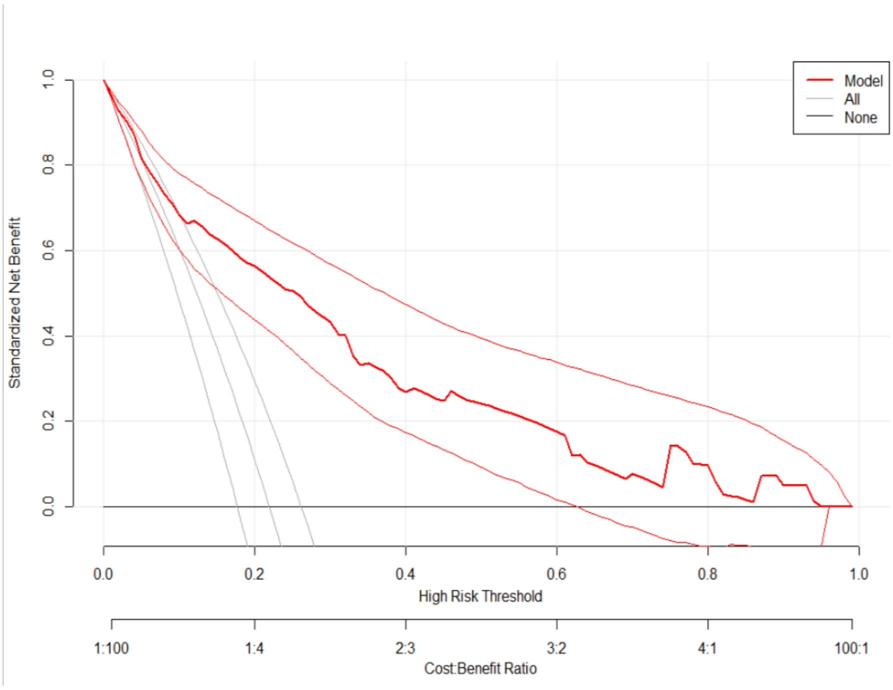

Figure 3: A decision curve plotting net benefit of the model against threshold probability and corresponding cost-benefit ratio.

3.3. Risk classification using a simplified risk score

For practical utility, we developed a simplified risk score from the model. Rounding of all regression coefficients in the reduced model to 1 point resulted in a simplified prediction score presented in table 2. The simplified score had a considerably comparable prediction accuracy with the original β coefficients, with AUC of 0.82 [95%CI: 0.76-0.89]. The possible minimum and maximum score a women can have is 0 and 12.5 respectively. The proportion of LBW were 7.7%, 36.3%, and 73.8%, respectively, in the estimated low (score <4), intermediate (4 to 6), and high-risk group (>=6). (Table 3)

Table 3: Risk classification of low birthweight using simplified prediction score in 379 pregnant women

Score* (risk category)	**Prediction model based on maternal characteristics**	
	Number of women	Incidence of LBW
Low (<4)	246 (64.9%)	19 (7.7%)
Intermediate (4 to 6)	91 (24.0%)	96 (36.3%)
High (>=6)	42 (11.1%)	46 (73.8%)
Total	379 (100%)	175 (21.9%)
**Score = (age<20 *2.5) + (BMI<18.5*2.5) + (hemoglobin<11mg/dl*2) + (height<155cm*2) + (prim-gravid*1) + (presence of chronic morbidity*2.5).*		

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When dichotomized to high risk (>4) and low risk (<=4) based on the risk score, 114 (30.1%) were categorized as high risk and 265 (69.9%) as low risk for LBW. Using "*Youden index*", the suggested cut-off to predict LBW using risk scores is > 4 with sensitivity of 72.3% [95%CI: 61-82], specificity of 81.8% [95%CI: 77-86], positive predictive value of 52.6% [95%CI: 43-62], negative predictive value of 91.3% [95%CI: 87-94], positive likelihood ratio of 3.96 [95%CI: 3.01-5.22], and negative likelihood ratio of 0.34 [95%CI: 0.24-0.48]. Detailed information on the risk score performance at different possible cutoff points is available in annex 2.

4. Discussion

The present study shows an incidence of low birthweight was 21.9%. The optimal combination of symptoms and signs to predict LBW are age <20, BMI <18.5, hemoglobin <11 mg/dl, height <155 cm, prim-gravida, and presence of comorbidity. This study quantified the predictive performance of a model using maternal characteristics during pregnancy without any advanced laboratory or imaging tests.

Predicting the probability of LBW in pregnant women is essential to take appropriate measures accordingly. The WHO recommends one ultrasound for every pregnant women before 24 weeks of gestation to estimate gestational age, fetal weight and any fetal anomalies.[39] Nevertheless, in LMICs imaging equipment and trained professionals are merely available in low level healthcare system. Previously the focus of research was to explain the maternal and fetal determinants of LBW. In recent years, the focus shifted to predicting low birthweight optimally using a combined set of characteristics. In our study, a combination of 6 maternal characteristics results in AUC of 0.83, which is good accuracy according to diagnostic accuracy classification.[40] A study by Singh and his colleagues developed a model using; 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 with a AUC of 0.79.[29] However, some of the predictors they used such as, inadequate weight gain during pregnancy and inadequate proteins in diet, are not easily obtainable information in routine clinical and public health practice that make the model less practical. On the other hand, Rejali and his associates performed a decision curve analysis involving 15 predictor variables and found a net benefit (NB) of 0.311.[30] Nevertheless, 4 of the variables included to the prediction model were obtained from factor analysis, reduced from other several variables. Despite its good accuracy, since it demands advanced statistical skill by end users it is unlikely to be used by health care professionals in routine clinical practice. However, our prediction model constitutes variables that are easily obtainable and have reasonable accuracy to be used by both mid- and lower-level health professionals in the primary care settings. Among the maternal characteristics included in our mode, 3 can be easily found from history taking, 2 by physical measurements, and 1 test for hemoglobin using field Hemo-Cue instrument.

In our model, using 4 as cutoff point has acceptable level of specificity, sensitivity, PPV and NPV to predict LBW. It is also possible to shift the cutoff point to increase either of the parameters depending on the program aim and availability of resources. Although the ultrasonographic evaluation of pregnant women gives a better indicator of fetal growth and prediction of birthweight, maternal characteristics during pregnancy alone enabled to predict the risk of low birthweight in advance. Our prediction model is not a replacement for the ultrasonographic assessment of pregnant mothers, however, it will be a screening tool in resource-poor settings for further diagnostic workup and management options. The simplified score derived from the regression models is easier to use in routine clinical and public health practice than the regression models, and has comparable discrimination and calibration.

This study has several strengths. Firstly, we used an adequate number of participants with the outcome, i.e. LBW which helped us to construct the model using a sufficient number of predictor variables. Secondly, we internally validated our model using bootstrapping technique and resulted small optimism coefficient, indicating our model is less sample dependent. Thirdly, our prediction model is constructed from easily obtainable maternal characteristics that make it applicable in primary care settings. However, the findings from this study should be interpreted with the perspective of the following limitations. As a single site study, it is confined to a single area, which needs external validation before using it in another context. Due to small sample size, we did not validate the model in separate dataset. However, the bootstrapping showed minimal optimism, indicating a stable predictive capability of the model.

5. Implications for practice and Conclusions

This study shows the possibility of predicting LBW using a simple prediction model constructed from maternal characteristics. This model will help to do a risk stratification of pregnant women and to identify those at higher risk of having a LBW baby. Subsequently, high-risk groups can be linked to a center which is equipped with ultrasound facilities for further assessment and better management during pregnancy, delivery and post-natal period. Hence, this feasible prediction score would offer the opportunity to reduce neonatal complications related with low birthweight and thus improving the overall maternal and child health care. We strongly recommend validating the prediction tool in another context before introducing to the clinical and public health practices.

Author Contributions: HYH conceived the study. HYH, SHG, BSE and JV contributed to the study design. HYH and JV developed the analysis plan. HYH, MAR, BSE, and SHG were involved in curation of data from the BUNMAP project. BSE, MAR and SHG supervised the data collection. HYH analyzed the data and wrote the manuscript. HYH, BSE, MAR, SHG, and JV interpreted the data. All authors participated in manuscript revision for intellectual content and approval of the final version.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

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Sensitivity analysis of the model to predict low birthweight: comparison of the regression coefficients, standard errors (SE), and p-values for complete case analysis (CCA), and multiple imputation (MI) for generalized linear mixed model fit by maximum likelihood. (Number of cluster=10, Standard deviation = 0.06308)

Predictor variable*	**Complete case analysis**			**Multiple imputation**		
	B	SE	P-value	β	SE	P-value
Age (<20)	1.610	0.3770	1.66e-05	1.593	0.3700	1.66e-05
formal education (no)	0.478	0.4469	0.2863	0.479	0.3246	0.2841
BMI (<18.5)	1.533	0.3100	2.65e-07	1.516	0.3076	2.64e-07
Height (<155cm)	1.235	0.3110	2.46e-05	1.225	0.3038	2.45e-05
Hemoglobin (<12.0 mg/dl)	1.206	0.3024	5.82e-05	1.213	0.2998	5.78e-05
Gravidity (prim-gravida)	0.577	0.3168	0.0600	0.606	0.3068	0.0490
Previous ANC (no)	0.011	0.4644	0.9814	0.011	0.3818	0.9801
Comorbidity§ (yes)	1.471	0.6221	0.0248	1.475	0.6043	0.0246

**Variables retained in the reduced model using likelihood ratio test are; age, BMI, hemoglobin, education, gravidity, comorbidity, unplanned pregnancy, and alcohol use.*

§ Comorbidity include pulmonary: history of asthma or COPD (chronic obstructive pulmonary disease); cardiac: history of heart failure or ischemic heart disease; renal diseases

Appendix B: Performance of the risk scores at different cutoff points

Cutoff point*	**high risk n(%)**	**Sensitivity (95%CI)**	**Specificity (95%CI)**	**PPV (95%CI)**	**NPV (95%CI)**	**LR+ (95%CI)**	**LR- (95%CI)**
3	152 (40.1)	0.81 (0.71-0.89)	0.71 (0.66-0.76)	0.44 (0.36-0.52)	0.93 (0.89-0.96)	2.81 (2.28-3.46)	0.27 (0.17-0.42)
>3.5	133 (35.1)	0.77 (0.67-0.86)	0.77 (0.71-0.81)	0.48 (0.39-0.57)	0.92 (0.88-0.95)	3.31 (2.61-4.19)	0.30 (0.20-0.45)
>4	114 (30.1)	0.72 (0.61-0.82)	0.82 (77-86)	0.53 (43-62)	0.91 (87-94)	3.96 (3.01-5.22)	0.34 (0.24-0.48)
>4.5	76 (20.1)	0.53 (0.42-0.64)	0.89 (0.85-0.92)	0.58 (0.46-0.69)	0.87 (0.83-0.91)	4.90 (3.34-7.21)	0.53 (0.42-0.66)
>5	66 (17.4)	0.49 (0.38-0.61)	0.92 (0.88-0.94)	0.62 (0.49-0.74)	0.87 (0.82-0.90)	5.85 (3.79-9.02)	0.55 (0.45-0.69)
>5.5	42 (11.1)	0.37 (0.27-0.49)	0.96 (0.93-0.98)	0.74 (0.58-0.86)	0.85 (0.80-0.88)	10.05 (5.28-19.12)	0.65 (0.55-0.77)

**Sum of the risk score*

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