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Prediction of low birth weight at term in low resource setting of Gulu city, Uganda: a prospective cohort study

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Abstract

Introduction: despite the widespread poverty in Northern Uganda resulting in undernutrition, not all mothers deliver low birth weight babies. Therefore, we developed and validated the risk prediction models for low birth weight at term in Northern Uganda from a prospective cohort study.

Methods: one thousand mothers were recruited from 16 - 24 weeks of gestation and followed up until delivery. Six hundred and eighty-seven mothers delivered at term. The others were either lost to follow-up or delivered preterm. Used proportions to compute incidence of low birth weight at term, build models for prediction of low birth weight at term in RStudio. Since there were few low birth weight at term, were generated synthetic data using ROSE-package in RStudio by over-sampling low birth weights and under-sampling normal birth weights, and evaluated the model performance against the synthetic data using K (10) - fold cross-validation. **Results:** mean age was 26.3 years with an average parity of 1.5. Their mean body mass index was 24.7 and 7.1% (49 of 687) had lateral placenta. The incidence of low birth weight was 5.7% (39 of 687). Predictors of low birth weight were gravidity, level of education, serum alanine aminotransferase (ALT), serum gamma-glutamyl transferase (GGT), lymphocyte count, placental location, and end-diastolic notch in the uterine arteries. This predicted low birth weight at term by 81.9% area under the curve (AUC), 76.1% accuracy, 72.9% specificity, and 79.1% sensitivity. **Conclusion:** a combination of gravidity, level of education, serum ALT, serum GGT, lymphocyte count, placental location, and end-diastolic notch in the uterine arteries can be used for screening for low birth weight in prenatal clinics for screening low birth weight at term.

Introduction

Low birth weight at term (≥ 37 weeks of gestation) is diagnosed when the baby weighs less than 2.5Kg at birth [1,2]. It affects 5 - 10% of babies born in

the global north [3], and slightly higher number in the global south [4-6]. The causes are multifactorial including prenatal undernutrition, maternal race, and low socioeconomic status [7-9]. There is a known black racial predisposition to low birth weight in multiracial communities [9]. However, inadequate maternal nutrition is the hallmark of sub-Saharan Africa [10]. In northern Uganda, over 60% of the population eats less than three meals a day [11]. This may worsen the pregnancy outcomes associated with nutritional problems [7].

Complications of low birth weight at term include low APGAR score at five minutes of birth, neonatal asphyxia, foetal distress, respiratory distress, neurodevelopmental deficits, impaired renal development, and neonatal death [12-15]. These may require advanced paediatric care available at tertiary level hospitals to manage neonates with low birth weight. Knowledge of the predictors of low birth weight may help prepare better to refer these mothers to tertiary health centers. Despite the widespread poverty and predominantly black population in Northern Uganda, not all mothers deliver low birth weight babies. Therefore, we set out to develop and validate the risk prediction models for low birth weight in Northern Uganda.

Methods

Study design and Study setting: this was a prospective cohort study at St. Mary's Hospital Lacor. It is a private, not-for-profit hospital, founded by the Catholic Church. It is located six kilometers west of Gulu city along Juba Road in Gulu district (Longitude 30 - 32 degrees East and Latitude 02 - 04 degrees North). St. Mary's Hospital Lacor is one of the teaching hospitals of Gulu University with a bed capacity of 482. It is staffed by specialists, medical officers, midwives, nurses, laboratory and radiology staff, as well as support and administrative staff. The hospital receives over nine thousand antenatal mothers and conducts about seven thousand deliveries per year [16].

Study population: we recruited 1,000 pregnant mothers 16 - 24 weeks from April 2019 to March 2020, gave them unique identifiers (study numbers). Excluded all participants with lethal congenital anomalies.

Sample size estimation: using Yamane 1967 formula [17] for calculating sample size for cohort studies using finite population size, St. Mary's hospital Lacor delivers approximately seven thousand mothers per year. Since my study duration is 12 months for recruitment of the mothers, the finite population I can access is about 7,000 mothers. Yamane 1967 formula: Sample size:

$$n = \frac{N}{1 + N(e)^2}$$

Where N is the finite population size= 7,000 mothers; margin of error (e)= 5%; therefore, $n = 7,000/1+7,000(0.05)^2$; $n = 379$. The required sample size was 379 mothers. We doubled the number (to >758) to cater for loss to follow up, preterm delivery and clients opting out of the study during the follow-up period. We expected over 50% loss to follow-up since rate of hospital delivery in this region is low [18], and some people may deliver from the free government hospitals nearby.

Data collection: a questionnaire was filled with the help of a midwife (research assistant), blood samples taken for complete blood count, liver and renal function tests, and uterine artery Doppler sonography done. The laboratory and sonographers only used the study numbers to identify the participants. The mothers were followed up until September 2020 when the last one was delivered. The delivery team had no access to the questionnaire, laboratory and ultrasound results.

Outcomes: birth weight of the baby <2.5Kg at ≥37 weeks was taken as low birth weight.

Definitions: from maternal history, grouping was based on known classification e.g. level of education in Uganda is grouped as primary, secondary and tertiary education levels. Gravidity was grouped as prime gravida for first pregnancies, multigravida for 2-4 and grand multigravida >4. Laboratory tests were grouped according to the reference ranges given by the laboratory while ultrasound pulsatility and resistive indices were grouped using percentiles. End diastolic notch of the uterine arteries was either present or absent; if present it was either unilateral or bilateral. The participants with incomplete results were dropped from the final analysis.

Statistical analysis: six hundred eighty-seven (687) mothers delivered at term. Data were pre-processed using Stata® 15.0 and built models in RStudio (R version 4.1.1 (2021-08-10)). Used proportions to compute incidence of low birth weight at term. Univariable analysis was done, and all variables with p-values ≤0.20 or were known risk factors for low birth weight were included in a logistic regression model. Built models for prediction of low birth weight at term in RStudio. The predictors with p-value <0.05 in the logistic regression model were taken as independent risk factors for low birth weight. Since there were few low birth weight at term, we used all the participants for the development of the models. For the validation cohort, we generated synthetic data using ROSE-package in RStudio by over-sampling low birth weights and under-sampling normal birth weights to balance the data. We obtained 349 (51.2%) and 332 (48.8%) normal and low birth weights respectively. We evaluated (validated) the model performance against the synthetic data using K (10) - fold cross-validation. The original model was put into a confusion matrix against the ROSE-derived data to calculate the accuracy, sensitivity, and specificity of the model in RStudio.

Ethical consideration: the study was approved by Makerere University School of Medicine Research and Ethics Committee (Reference number 2018-

105), Uganda National Council for Science and Technology (Reference number HS258ES), and administrative clearance to conduct the research at St. Mary's Hospital Lacor was also obtained (Reference number LHIREC Adm 009/11/18). The participants were informed about the study during the morning health education by the midwives when they arrived in the hospital. Those who satisfied the inclusion criteria were approached and requested to join the study. Written informed consent was sought from every participant in either English or Acholi language.

Results

One thousand pregnant mothers were recruited. Six hundred and eighty-seven (687) mothers delivered at term. Three hundred and thirteen (313) mothers were lost to follow-up or delivered preterm, dropped and not used in the data analysis. The prevalence of birth weight < 2.5Kg at term was 5.7% (39 out of 687) (Figure 1).

General characteristics of the study population: mean maternal age was about 26 years, with majority being informally employed. Only one in five of the mothers had a tertiary level of education (Table 1). Average body mass index was 24.7Kg² while prevalence of prenatal hypertension was 0.7%. About 7.1% had lateral placental location and 10.2% had bilateral end diastolic notch [19] (Table 2). Average maternal haemoglobin level was 10.8g/dL with a haematocrit of 32.5%. Mean serum alkaline phosphatase (ALP), GGT, aspartate aminotransferase (AST) and ALT were 154.3IU, 21.7IU, 20.2IU and 30.7IU respectively (Table 2). The mothers were followed up for an average of 19.1 weeks over one and half years (April 3rd 2019 to September 30th 2020)

Unadjusted estimates of the variables against low birth weight: all continuous variables were categorized using the laboratory reference ranges and interquartile ranges for the participants. Both ranges were analyzed and the best-fitted range for the models was chosen by the researcher. All

variables with unadjusted p-value of ≤ 0.20 at univariable analysis were taken for multivariable level to build the models (Table 3, Table 4). A model was chosen based on one with fewer variables producing higher accuracy, sensitivity, specificity and AUC.

Risk prediction models for low birth weight: six risk prediction models were built from maternal history and physical examination, obstetric ultrasound parameters and uterine artery Doppler indices, maternal laboratory lab tests and the combinations of maternal history with either laboratory tests or ultrasound parameters or all the variables (Table 5, Table 6). In model 6, (combination of all the variables) (details in Table 6), the predictors of low birth weight were gravidity, level of education, serum ALT, serum GGT, lymphocyte count, placental location and end-diastolic notch in the uterine arteries. Being a prime gravida (aOR = 5.89, 95% CI 1.42 - 41.94, p=0.032), having a laterally (one-sided) located placenta (aOR = 3.42, 95% CI 1.23 - 9.45, p=0.018) and presence of end-diastolic notch (aOR = 2.59, 95% CI 1.07 - 6.28, p=0.035) were independent risk factors, while having a tertiary level of education (aOR = 0.16, 95% CI 0.04 - 0.69, p=0.013), normal lymphocyte count (aOR = 0.30, 95% CI 0.10 - 0.91, p=0.033) and serum ALT (aOR = 0.22, 95% CI 0.09 - 0.56, p=0.001) were protective against low birth weight.

Evaluation of the performance of the models 1-6 for the prediction of low birth weight: the models' performance was evaluated using K (10) - fold cross validation against synthetic data derived from the ROSE package in RStudio, and listed in (Table 2). Model accuracies ranged from 59.3% - 76.1%, while AUC from 62.6% - 81.9%. In the absence of ultrasound scan and laboratory tests, model 1 can predict low birth weight with 62.3% accuracy, 37.3% sensitivity, 88.3% specificity and 65.3% AUC.

Discussion

We developed and validated risk prediction models for low birth weight at term in Northern Uganda from a prospective cohort study. From maternal history, the predictors of low birth weight were education level and gravidity. This predicted low birth weight at term by 65.3% AUC, 62.3% accuracy, 88.3% specificity, and 37.3% sensitivity. In Ethiopia, similar demographic characteristics were used to predict low birth weight. At a 26% false positive rate, they predicted low birth weight with 83%, AUC with 82% specificity and 71% sensitivity [20]. While in India, Singh *et al.* [21] found the prediction model AUC of 79% with 72% sensitivity and 56% specificity. In the USA, maternal history predicted low birth weight with 75.3% accuracy [22]. Considering the uterine artery Doppler indices, the predictors of low birth weight were placental location and end-diastolic notch in the uterine arteries. This predicted low birth weight at term by 62.6% AUC, 59.3% accuracy, 42.5% specificity, and 75.4% sensitivity. In Denmark, uterine artery pulsatility index predicted low birth weight with 74% AUC [23], while in Saudi Arabia, placental thickness of <2cm and diameter of <18cm predicted low birth weight with 88.6% AUC [24]. This probably outline the differences in population and techniques used in the data analysis. When the maternal history is combined with uterine artery Doppler indices, the predictors of low birth weight were education level, gravidity, placental location, and end-diastolic notch. This predicted low birth weight at term by 71.6% AUC, 62.3% accuracy, 64.8% specificity and 61.8% sensitivity. In India, a combination of uterine artery Doppler indices and maternal history predicted low birth weight with 65.9% AUC, 45.4% sensitivity and 84.6% specificity [25].

While we found the predictors of low birth weight to be serum GGT, serum ALT and lymphocyte count to have predicted low birth weight at term by 66.9% AUC, 59.3% accuracy, 35.8% specificity and 81.7% sensitivity, there is limited data on the

prediction of low birth weight using maternal full haemogram, liver and renal function tests. There is no evidence that maternal blood levels of alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), or pregnancy-associated plasma protein A (PAPP-A) used as a single predictor are useful to predict low-birth-weight newborns [26]. When the laboratory blood tests were combined with maternal history, the predictors of low birth weight were gravidity, level of education, serum ALT, serum GGT and lymphocyte count. This predicted low birth weight at term by 66.9% AUC, 66.7% accuracy, 59.6% specificity and 73.4% sensitivity. The addition of blood glucose levels to maternal history in Mexico predicted low birth weight with 72% AUC [27]. After combining all the variables from maternal history, laboratory tests, and uterine artery Doppler indices, the predictors of low birth weight were gravidity, level of education, serum ALT, serum GGT, lymphocyte count, placental location, and end-diastolic notch in the uterine arteries. These predicted low birth weight at term by 81.9% AUC, 76.1% accuracy, 72.9% specificity and 79.1% sensitivity. Considering the few predictors, this model can be used for screening low birth weights in prenatal clinics. This makes our model favorably compared to the other models. This is a baseline study in Northern Uganda. We hope it will open doors to a wide range of research in sub-Saharan Africa. There were many losses to follow-up or preterm birth. This could have skewed the models in other ways. Future research should be done in several other locations for external validation of these models to ensure generalizability.

Conclusion

In places with no laboratory tests and ultrasound scan, the predictors of low birth weight from maternal history alone are level of education and number of pregnancies (gravidity). These predicted low birth weight by 65.3% AUC with 62.3% accuracy.

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What is known about this topic

- *Black women are more at risk of low birth weight in multiracial communities;*
- *Malnutrition is a predictor of low birth weight;*
- *Low birth weight is known to be associated with increased risks of early neonatal death.*

What this study adds

- *Being a prime gravida, and having laterally located placenta are risk factors for low birth weight while tertiary level of education is protective;*
- *The prevalence of low birth weight in Gulu city, Northern Uganda is comparable to those in multiracial communities.*

Competing interests

The authors declare no competing interests.

Authors' contributions

Silvia Awor, wrote the proposal, collected data and drafted the manuscript. Benard Abola built the models and cross-validated the models. Rosemary Byanyima, Paul Kiondo and Christopher Garimoi-Orach are doctoral committee members who provided expert opinion and guided to write the manuscript. Jaspar Ogwal-Okeng, Annette Nakimuli and Dan Kabonge Kaye are doctoral supervisors who guided through the concept and writing of the manuscript. All the authors have read and agreed to the final manuscript.

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Tables and figure

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Table 6: model 5 - 6 for the prediction of low birth weight

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Figure 1: participant flow through the study

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Table 1: social demographic characteristics of the mothers delivered at term

Characteristics (n=687)	Mean (SD) or proportions (%)	Median (IQR)
Maternal age (years)	26.3 (5.4)	26 (22 - 30)
Age at menarche (years)	14.4 (1.5)	14 (14 - 15)
Parity	1.5 (1.5)	1 (0 - 2)
Marital status (single)	11 (1.6)	
Marital status (married/cohabiting)	676 (98.4)	
Primary level of education	244 (35.5)	
Secondary level of education	317 (46.1)	
Tertiary level of education	126 (18.4)	
Unemployed	214 (31.2)	
Informal (non-salaried) employment	416 (60.5)	
Formal (salaried) employment	57 (8.3)	
Personal history of preeclampsia present	4 (0.6)	
No personal history of preeclampsia	683 (99.4)	
No history of miscarriage	557 (81.1)	
History of miscarriage	130 (18.9)	
No family history of preeclampsia	656 (95.5)	
Family history of preeclampsia	31 (4.5)	
No chronic illness	625 (91.0)	
Presence of a chronic illness	62 (9.0)	
Not living with a smoker	604 (87.9)	
Living with a smoker in one house	83 (12.1)	
No Alcohol use in pregnancy	642 (93.4)	
Alcohol use in pregnancy	45 (6.6)	

Table 2: clinical and laboratory characteristics of mothers who delivered at term

Characteristics (n=687)	Mean (SD) or proportions (%)	Median (IQR)
Body mass index	24.7 (3.9)	23.9 (22.0 - 27.0)
Systolic blood pressure	105.8 (12.4)	104 (97 - 103)
Diastolic blood pressure	63.7 (10.4)	63 (57 - 70)
Gestation age at recruitment (weeks)	20.4 (2.6)	20.3 (18.5 - 22.1)
Gestation age at delivery (weeks)	39.5 (1.6)	39.6 (38.0 - 40.6)
Average duration for follow up (weeks)	19.1	
No hypertension	682 (99.3)	
Prenatal hypertension	5 (0.7)	
Multiple pregnancy	7 (1.0)	
Singleton	680 (99.0)	
Lateral placental location	49 (7.1)	
Central placenta location	638 (92.9)	
No end-diastolic notch	501 (72.9)	
Unilateral end-diastolic notch	116 (16.9)	
Bilateral end diastolic notch	70 (10.2)	
Average pulsatility index	0.80 (0.29)	0.75 (0.61 - 0.95)
Average resistive index	0.51 (0.11)	0.50 (0.44 - 0.58)
Serum ALT	30.7 (27.5)	25 (18 - 35)
Serum AST	20.2 (23.3)	14 (7 - 26)
Serum GGT	21.7 (8.6)	20 (15-29)
Serum ALP	154.3 (50.1)	149 (115 - 180)
Serum bicarbonate	35.2 (2.3)	25 (24 - 27)
Serum albumin	4.1 (3.0)	3.9 (3.5 - 4.1)
Serum urea	25.6 (27.0)	18 (14 - 25)
Serum sodium	137.6 (4.0)	137.4 (135.2 - 139.4)
Serum potassium	4.2 (1.3)	4.2 (3.9 - 4.5)
Serum chloride	106.4 (4.3)	105.8 (103.6 - 108.9)
Serum phosphorus	1.3 (0.8)	1.1 (0.9 - 1.4)
Serum calcium	2.4 (1.1)	2.2 (2.1 - 2.4)
Serum creatinine	1.0 (0.6)	0.9 (0.8 - 1.2)
Neutrophil count	3.7 (2.2)	3.5 (2.6 - 4.5)
Lymphocyte count	1.8 (0.9)	1.6 (1.3 - 2.1)
Total white blood cell count	6.3 (3.0)	6.0 (4.9 - 7.6)
Platelet count	233.8 (69.4)	220 (179 - 267)
Haemoglobin level	10.8 (2.0)	10.9 (9.5 - 12.1)
Haematocrit	32.5 (6.6)	32.8 (28.7 - 36.0)
Mean corpuscular volume	82.4 (7.8)	82.3 (79.7 - 89.1)
Mean corpuscular haemoglobin concentration	32.9 (2.6)	32.9 (31.4 - 34.5)
ALT: Alanine transaminase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: gamma glutamyl transferase		

Table 3: unadjusted risk ratio of social demographic characteristics and low birth weight

Variable	IRR (95% CI)	P-value
Age at menarche ≤15 (years)	1	
Age at menarche >15 (years)	0.75 (0.34 - 1.66)	0.477
Prime gravida	4.82 (1.13 - 20.49)	0.033
Gravida 2-4	2.91 (0.69 - 12.19)	0.144
Gravida >4	1	
Nullipara	2.71 (1.04 - 7.12)	0.042
Para 1 - 2	1.67 (0.63 - 4.45)	0.303
Para >2	1	
Marital status (single)	1	
Marital status (married / cohabiting)	0.65 (0.10 - 4.32)	0.657
Primary level of education	1	
Secondary level of education	1.01 (0.54 - 1.90)	0.975
Tertiary level of education	0.48 (0.17 - 1.42)	0.186
Unemployed	1	
Informal (non-salaried) employment	1.22 (0.61 - 2.41)	0.576
Formal (salaried) employment	1.37 (0.45 - 4.13)	0.582
No history of miscarriage	1	
History of miscarriage	1.04 (0.49 - 2.20)	0.921
No chronic illness	1	
Presence of a chronic illness	1.40 (0.57 - 3.44)	0.463
Not living with a smoker	1	
Living with a smoker in one house	1.50 (0.69 - 3.27)	0.310
No alcohol use in pregnancy	1	
Alcohol use in pregnancy	0.73 (0.18 - 2.94)	0.659

Table 4: unadjusted risk ratio of clinical and laboratory characteristics with low birth weight

Variable	IRR (95% CI)	P-value
Body mass index <25 Kg	1	
Body mass index ≥25 Kg	0.57 (0.29 - 1.11)	0.098
Normal diastolic blood pressure <90mmHg	1	
Diastolic hypertension ≥90mmHg	2.15 (0.57 - 8.15)	0.260
Uterine artery Doppler indices		
Lateral placental location	3.66 (1.85 - 7.23)	0.000
Central placenta location	1	
No end-diastolic notch	1	
Unilateral end-diastolic notch	2.47 (1.25 - 4.87)	0.009
Bilateral end diastolic notch	2.73 (1.26 - 5.92)	0.011
Average pulsatility index ≤1.235	1	
Average pulsatility index >1.235	2.00 (0.93 - 4.34)	0.078
Average resistive index ≤0.655	1	
Average resistive index >0.655	2.00 (0.93 - 4.34)	0.078
Serum GGT ≤30IU	3.07 (0.96 - 9.82)	0.059
Serum GGT >30IU	1	
Serum bicarbonate <24 mEq/L	1	
Serum bicarbonate 24 - 27 mEq/L	1.98 (0.71 - 5.56)	0.194
Serum bicarbonate >27 mEq/L	2.39 (0.77 - 7.42)	0.133
Serum calcium <2.09mg/dL	1	
Serum calcium 2.09 - 2.41mg/dL	1.66 (0.77 - 3.59)	0.199
Serum calcium >2.41mg/dL	0.89 (0.33 - 2.39)	0.810
Neutrophil count of < 2630 cells/μl	1	
Neutrophil count of 2630 - 4540 cells/μl	0.66 (0.35 - 1.27)	0.214
Neutrophil count >4540 cells/μl	0.39 (0.15 - 0.97)	0.044
Lymphocyte count of 900 cells/μl	1	
Lymphocyte count of 900 - 3900 cells/μl	0.38 (0.16 - 0.93)	0.033
Lymphocyte count >3900 cells/μl	2.17 (0.68 - 6.96)	0.192
Platelet count of <178 cells/μl	1	
Platelet count of 178 - 266 cells/μl	1.02 (0.51 - 2.04)	0.951
Platelet count > 266 cells/μl	0.34 (0.11 - 1.06)	0.063
Mean corpuscular haemoglobin concentration <31.5g/dL	1	
Mean corpuscular haemoglobin concentration 31.5 - 34.4g/dL	0.60 (0.30 - 1.20)	0.150
Mean corpuscular haemoglobin concentration >34.4g/dL	0.80 (0.38 - 1.72)	0.574

ALT: Alanine transaminase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: gamma glutamyl transferase

Table 5: model 1 - 4 for the prediction of low birth weight		
Variable	OR (95% CI)	p-value
Model 1: maternal history and physical examination		
Secondary education	0.92 (0.46 - 1.88)	0.819
Tertiary level education	0.31 (0.07 - 0.97)	0.070
Gravida 2 - 4	3.30 (0.93 - 21.02)	0.113
Prime gravida	5.58 (1.51 - 36.10)	0.025
Intercept	0.02 (0.003 - 0.07)	0.000
Model 2: obstetric ultrasound and uterine artery Doppler indices		
Lateral placental location	2.86 (1.10 - 6.95)	0.025
Unilateral end-diastolic notch	1.79 (0.75 - 4.00)	0.171
Bilateral end-diastolic	2.20 (0.82 - 5.26)	0.093
Intercept	0.04 (0.03 - 0.06)	0.000
Model 3: combination of maternal history, ultrasound and uterine artery Doppler indices		
Secondary education	0.97 (0.48 - 2.00)	0.931
Tertiary level education	0.23 (0.05 - 0.75)	0.028
Gravida 2 - 4	3.56 (0.99 - 22.87)	0.095
Prime gravida	4.97 (1.32 - 32.53)	0.039
Lateral placental location	3.29 (1.20 - 8.35)	0.015
Unilateral end-diastolic notch	1.98 (0.83 - 4.46)	0.101
Bilateral end-diastolic	2.01 (0.73 - 4.88)	0.141
Intercept	0.01 (0.002 - 0.05)	0.000
Model 4: maternal laboratory tests		
Serum GGT of 0.0 - 30.0 IU	2.91 (1.01 - 12.27)	0.082
Lymphocyte count of 900 - 3900 cells/ μ l (normal)	0.30 (0.12 - 0.95)	0.024
Lymphocyte count > 3900 cells/ μ l (high)	2.28 (0.46 - 10.88)	0.295
Serum ALT of 12 - 49 IU	0.33 (0.15 - 0.84)	0.013
Serum ALT <12 IU	0.60 (0.17 - 1.98)	0.408
Intercept	0.16 (0.03 - 0.71)	0.026
ALT: Alanine transaminase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: gamma glutamyl transferase		

Table 6: model 5 - 6 for the prediction of low birth weight

Model 5: maternal history and laboratory tests		
Secondary education	0.91 (0.44 - 1.92)	0.798
Tertiary level education	0.26 (0.06 - 0.86)	0.045
Gravida 2 - 4	3.34 (0.90 - 21.87)	0.119
Prime gravida	6.35 (1.63 - 42.51)	0.020
Serum GGT of 0.0 - 30.0 IU	3.22 (1.11 - 13.74)	0.059
Lymphocyte count of 900 - 3900 cells/ μ l (normal)	0.37 (0.14 - 1.21)	0.070
Lymphocyte count > 3900 cells/ μ l (high)	3.59 (0.67 - 19.04)	0.128
Serum ALT of 12 - 49 IU	0.31 (0.13 - 0.80)	0.010
Serum ALT <12 IU	0.60 (0.16 - 2.06)	0.427
Intercept	0.04 (0.004 - 0.32)	0.005
Model 6: combination of maternal history, laboratory tests, ultrasound and uterine artery Doppler indices		
Gravida 2 - 4	3.91 (0.99 - 27.09)	0.091
Prime gravida	5.89 (1.42 - 41.94)	0.032
Secondary education	1.06 (0.51 - 2.29)	0.876
Tertiary level education	0.16 (0.03 - 0.60)	0.013
Serum GGT of 0.0 - 30.0 IU	3.25 (1.11 - 13.96)	0.059
Lymphocyte count of 900 - 3900 cells/ μ l (normal)	0.30 (0.11 - 1.00)	0.033
Lymphocyte count > 3900 cells/ μ l (high)	2.40 (0.43 - 13.22)	0.310
Serum ALT of 12 - 49 IU	0.22 (0.09 - 0.58)	0.001
Serum ALT <12 IU	0.45 (0.12 - 1.59)	0.224
Lateral placental location	3.42 (1.18 - 9.19)	0.018
Unilateral end-diastolic notch	2.59 (1.03 - 6.18)	0.035
Bilateral end-diastolic	2.58 (0.91 - 6.60)	0.057
Intercept	0.04 (0.003 - 0.31)	0.005

ALT: Alanine transaminase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: gamma glutamyl transferase

Table 7: model performance evaluation using K-fold cross-validation

Model	Accuracy (%)	Sensitivity (%)	Specificity (%)	AUC (%)
Model 1 (history and physical exam)	62.3	37.3	88.3	65.3
Model 2 (uterine artery Doppler indices)	59.3	75.4	42.5	62.6
Model 3 (combination of model 1 and 2)	62.3	61.8	64.8	71.6
Model 4 (maternal blood tests)	59.3	81.7	35.8	66.9
Model 5 (combination of model 1 and 4)	66.7	73.4	59.6	66.9
Model 6 (combination of models 3 and 4)	76.1	79.1	72.9	81.9

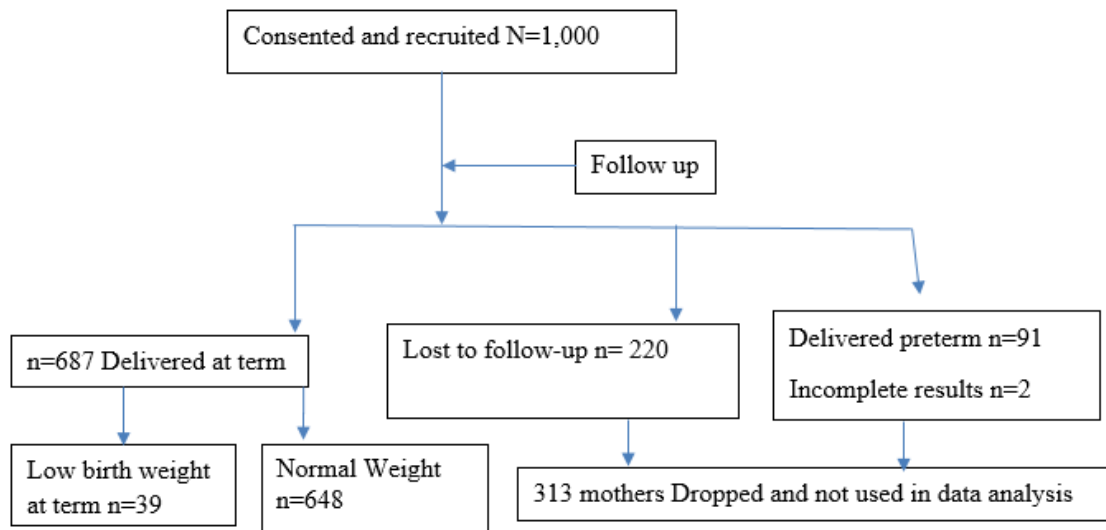


Figure 1: participant flow through the study