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Developing and Validating A Risk Score for Prediction of Preterm Birth at Felege Hiwot Comprehensive Specialized Hospital, Northwest Ethiopia: Retrospective Follow up Study

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BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

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DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS

DEVELOPING AND VALIDATING A RISK SCORE FOR PREDICTION OF PRETERM BIRTH AT FELEGE HIWOT COMPREHENSIVE SPECIALIZED HOSPITAL, NORTHWEST ETHIOPIA: RETROSPECTIVE FOLLOW UP STUDY

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A THESIS TO BE SUBMITTED TO DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS , SCHOOL OF PUBLIC HEALTH , COLLEGE OF MEDICINE AND HEALTH SCIENCES ,BAHIR DAR UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF PUBLIC HEALTH IN EPIDEMIOLOGY.

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DECLARATION SHEET

I, the under signed, declare that this is my original work, has never been presented in this or any other university, and that all the resource and materials used for the research have been fully acknowledged.

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Approval of internal examiner

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I hereby certify that I have examined this thesis entitled "DEVELOPING AND VALIDATING A RISK SCORE FOR PREDICTION OF PRETERM BIRTH AT FELEGE HIWOT COMPREHENSIVE SPECIALIZED HOSPITAL, NORTHWEST ETHIOPIA: RETROSPECTIVE FOLLOW UP STUDY," by Sefineh Fenta. We recommend and approve the thesis a degree of "Master of Public Health in Epidemiology".

Board of Examiners

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ABSTRACT

Background: Although there are available studies that determine the risk factors for preterm birth, they presently do not allow the prediction of risk in individual patients in daily practice. Thus, developing and validating the risk prediction score for preterm birth guide caregivers in promptly providing the treatment choice for individual patients and be more cost-effective by identifying high-risk patients who will benefit most from certain interventions.

Objective: To develop and validate a risk score for the prediction of preterm birth using maternal characteristics.

Method: A retrospective follow-up study was conducted on March (1- 30) 2021 at Felege Hiwot comprehensive specialized hospital. The sample size was determined by assuming 10 events per predictor, based on this assumption total sample size was1308. Data were collected using a semi-structured checklist through chart review. Data were coded and entered into Epidata, version 3.02, and was analyzed by using R statistical programming language version 4.0.4 for further processing and analysis. Bivariable logistic regression was done to identify the relationship between each predictor and preterm birth. Variables with ($p \leq 0.25$) from the bivariable analysis were entered into a backward stepwise multivariable logistic regression model, and significant variables ($p < 0.05$) were retained in the multivariable model. Model accuracy and goodness of fit were assessed by computing the area under the ROC curve (discrimination) and calibration plot (calibration) respectively.

Result: The incidence of preterm birth was 13.4%. Residence, gravidity, hemoglobin < 11 mg/dl, early rupture of membranes, antepartum hemorrhage, and pregnancy-induced hypertension were predictors of preterm birth. These predictors were all included in the model; the AUC was 0.786 with a sensitivity of 75.14 % and speci¦city of 67.46%. At the threshold scores of 3. The model calibration test had a p-value of 0.492.

Conclusion and recommendation: This study showed the possibility of predicting preterm birth using maternal characteristics during pregnancy. Thus, using this model could help to identify pregnant women at a higher risk of having a preterm birth to be linked to a center that has the necessary facilities for corticosteroid administration, antibiotic treatment in the event of infection, and other services.

Key words, Prediction Model, Preterm birth, Ethiopia

ACRONYMS AND ABBREVIATIONS

ANC	Antenatal Care
APH	Antepartum Hemorrhage
AUC	Area under Curve
CI	Confidence Interval
FFN	Fetal Fibronectin
FHCSRH	Felege Hiwot Comprehensive Specialized Referral Hospital
GA	Gestational Age
HGB	Hemoglobin
LMP	Last Menstrual Period
PIH	Pregnancy Induced Hypertension
PROM	Premature Rupture of Membrane
ROC	Receiver Operating Characteristic Curve
UTI	Urinary Tract Infection

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1. INTRODUCTION

1.1. Background

Preterm birth is described as babies that are born alive before the end of 37 weeks of pregnancy[1]. Preterm birth can be accidental (due to spontaneous preterm labor and/or preterm membrane rupture) or induced by the provider (by cesarean or labor induction)[2]. Most preterm births happen spontaneously[3].

Different programs work on the prevention and care of preterm birth. World Health Organization (WHO) has established guidelines to overcome preterm birth problems in 2016[4]. The Global Strategy for the Health of Mothers, Children and Adolescents and Sustainable Development Goals (SDGs) has designed and introduced a reduction in newborn and under-five mortality to 12 and 25 per 1,000 live births each year[5, 6]. Ethiopia also adopted a national strategy for newborn and child survival by incorporating the sustainable development goals to improve the care for newborns and preterm births[7].

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Preterm birth is a complex syndrome that arises from the interplay of risk factors for biology, climate, and lifestyle. Microbial-induced inflammation, decidual hemorrhage and vascular disease, decidual senescence, maternal-fetal tolerance disturbance, progesterone action decrease, uterine overdistension, stress, and others are associated with it[8]**.** Research so far has shown that due to the multifactorial etiology of preterm birth, accurate predictions of preterm birth, especially the use of a single biomarker to predict preterm birth, are still difficult[9]**.**

In most nations, predicting preterm birth is still largely based on subjective clinical experience. This approach may increase unnecessary hospital admissions and unnecessary but potentially harmful treatments, such as the use of steroids for the maturation of the fetal lung and tocolysis[10, 11]**.**

Given the tremendous personal, economic, and health effects of preterm birth, the predictive test for preterm birth is essential. This prediction may provide reassurance for women who are unlikely to deliver early, but they are also important for highlighting those women at higher risk of premature delivery to offer interventions[12].

1.2. Statement of the problem

An estimated 15 million babies worldwide are born too early per year. That's more than 1 in 10 infants. About 1 million newborns die per year because of preterm birth complications[13].

Across 184 countries, the rate of preterm birth ranges from 5% to 18% of babies born [14]. However, there are stark disparities in survival rates around the world. Half of the babies born at or below 32 weeks die in low-income settings due to a lack of practical, cost-effective, and critical care, such as comfort, breastfeeding assistance, basic infection care, and trouble Breathing[15].

In Ethiopia, every year, 320,000 babies are born too early and because of direct preterm complications, 24,400 children under five die [16]. According to the 2019 Mini Ethiopia Demographic and Health Survey, the neonatal mortality rate was 30 deaths per 1,000 live births and prematurity was the major cause of death[17]

Furthermore, the effect of preterm birth is also prolonged beyond the neonatal phase and throughout life[18]. Hence, the largest risk of severe health issues, including cerebral palsy, intellectual disability, chronic lung disease, and vision and hearing loss, is faced by babies born before maturity. This introduces a lifelong disability dimension. At some point in their lives, most people will face the struggles and potential disasters of preterm birth either directly in their families or indirectly through events for the nations[18, 19].

Factors associating with the underlying epidemiological or medical risk factors with preterm birth are poorly understood and the exact etiology is still not known. However, certain factors are known to increase the risk of a woman entering a preterm birth[20, 21]

Well-known risk factors for preterm birth are demographic factors such as young maternal age, rural residence, Short interval between pregnancies, < 4 antenatal care visits, antepartum hemorrhage, chronic illness, pregnancy-induced hypertension, multiple pregnancies, history of preterm birth, premature rupture of membrane, hemoglobin level less than 11g/dl, low educational level and poor maternal nutritional status before and during pregnancy[22-26]

Preterm childbirth, however, may be generally preventable. Three-quarters of preterm birth-related deaths may be prevented without an intensive care unit. Current cost-effective interventions include antenatal corticosteroids injections for pregnant women of 24-34 weeks of gestational age at risk of preterm delivery; kangaroo mother care, early initiation (initiated within the first hour of birth) and exclusive breastfeeding for the first six months of life and basic care for infections and breathing difficulties[27].

To alleviate this burden in the past few decades, numerous methods have been attempted internationally, including in Ethiopia, to prevent and enhance the treatment of preterm births [28-30].

The literature recommends treatment methods for improving preterm birth-related outcomes such as antenatal corticosteroid use, antibiotics, mother care for kangaroos, urgent intensive care, and diverse long-term health services. Through aligning policies with Sustainable Development Goals (SDGs) and investing in Every Woman and Every Child initiatives, the global community has dedicated itself to reducing preterm births[5, 31]. Collectively, pre-term birth prevention, diagnosis, and management are a wise approach to accelerate the achievement of the global goal of ending all preventable deaths of newborns and children by 2030. At the same time, this approach would decrease maternal deaths and stillbirths, and associated health system costs [32].

Although several efforts were undertaken to prevent and reduce preterm birth, its rate appears to have increased over time [19, 33]. Preterm birth prevention is a global research priority, but to date, limited progress has been achieved. Research is underway to recognize genomic, transcriptomic, proteomic, immunologic, and metabolomic preterm birth markers early in pregnancy and improve the assessment of gestational age[34]

There are clinical prediction models that attempt to predict the probability of preterm birth, however, all include laboratory tests that are generally not accessible in low-resource settings, like fetal fibronectin, insulin-like growth factor binding protein-1 (IGFBP-1), interleukin-6, and placental alpha-macroglobulin-1 to predict preterm birth[9, 35-39].

Hence, because of limited resources, the use of easily accessible data to forecast preterm birth seems to be appealing in low- and middle-income areas. Even though there are prediction models for preterm birth, variation in the occurrence of preterm birth globally is relevant, indicating variations in exposure to psychosocial, sociodemographic, and medical risk factors and genetic differences [40-42].

There is no prediction model for preterm birth in Ethiopia. Therefore, developing and validating a risk score for prediction of preterm birth using maternal(clinical and non-clinical) characteristics based on the available measurement is paramount to allow early preterm birth intervention such as utero transfer to tertiary care centers, appropriate corticosteroid administration while preventing excessive use, neuroprotective magnesium sulfate therapy, and antibiotic treatment in the event of infection[35, 43]

1.3. Significance of the study

Although there are available studies that determine the risk factors for preterm birth, they presently do not allow the prediction of risk in individual patients in daily practice. It is anticipated that our setting could use such a model to predict the risk of preterm birth and to refer patients early.

In addition, it guides caregivers in promptly providing the treatment choice for individual patients and be more cost-effective by identifying high-risk patients who could benefit most from certain interventions. Hence, the finding of the study might be used by clinicians and public health professionals working on maternal and child health units to predict preterm birth earlier in pregnancy. It may also be used as a resource for future researchers.

The study would also be important for policymakers and program designers that work on the prevention and care of preterm birth. The findings of this study might help different stakeholders of federal and regional health officers and hospitals to see important ways to improve the prevention and care of preterm birth.

Furthermore, it also provides information for the mothers and clients visiting health facilities during service.

2. LITERATURE REVIEW

2.1. Overview of preterm birth

Premature birth is when a baby is born too early before the completion of 37 weeks of pregnancy[44]. When a preterm baby is born, the risk of death and permanent injury is greater. Prematurity is the highest risk factor for infant morbidity and mortality at the immediate neonatal time and has even impacts in infancy, adolescence, and even adulthood. This influences the victims' physical health, cognitive and behavioral dimensions make it one of the most critical issues for modern public health [45, 46].

In every country, preterm childbirth affects families. Though Asia and sub-Saharan Africa account for more than 80 percent of preterm births, the issue is universal. The U.S. and Brazil are actually among the top 10 countries with the largest number of preterm birth[44].

Out of 135 million live births, about 15 million babies were born prematurely last year in 184 countries, according to the born too soon study[19]. The prevalence of preterm birth rates in high-income countries is 5–10% varying widely from country to country[46]. Each year around 9.1 million preterm births occurred in South Asia and sub-Saharan Africa[19]. The pooled prevalence of preterm birth in Ethiopia is 10.48%[22].

2.2. Predictors of preterm birth

2.2.1. Sociodemographic characteristics

Studies showed that socio-demographic factors have an association with preterm birth. Mothers who are younger and older maternal age (<20 and ≥ 35), being unmarried, being male, living in a rural area, low economic status, and illiteracy have a higher risk to deliver preterm birth[17, 47]. A cross-sectional study conducted in eight hospitals of Tehran, Iran reported that advanced maternal age was a risk factor for preterm birth[48].

Another study conducted at Kenyatta National Hospital, Nairobi, Kenya determined that advanced maternal age (≥31 years) were a significant risk factor for a preterm birth and preterm birth was higher among male babies of 73% males and 27% females[49] and in contrast to this a cross-sectional study done in Addis Ababa public hospitals, Ethiopia showed that mothers who were younger than 25 years were at higher risk to give preterm birth[50].

A study which is also conducted in Central Zone hospitals of Tigray, Northern Ethiopia shows that being unmarried was the risk of preterm birth by four times than the married[51].

2.2.2. The maternal obstetric complication and Pre-existing maternal illness

Different studies have shown that preterm birth depends on various maternal obstetric such as preterm birth history, abortion history, birth interval, number of prenatal care visits, parity, anemia, and medical pregnancy conditions risk factors such as UTI, hypertension, diabetes mellitus, being Anemic, HIV, and Obstetrical complications like premature rupture of membrane(PROM), pregnancy-induced hypertension(PIH), antepartum hemorrhage (APH), GDM, Hyperemesis gravidarum, Oligohydramnios, and, and polyhydramnios are significantly associated with preterm delivery[22, 47, 52, 53].

2.2.3. Maternal nutritional factors

Maternal nutritional status is significantly associated with preterm birth, where mothers with low nutritional status (MUAC 26cm) during their pregnancy period[54].

A cross-sectional study done at Baluchistan, Pakistan showed that overweight and obese mothers were at a higher risk of delivering preterm babies as compared to the underweight and normal mothers [55]. Another study done in a secondary health care facility of Cairo, Egypt showed that low maternal weight (<50kg) was highly associated with preterm birth[56]. Similarly, in a study done in Malawi preterm birth was increased by three-fold for those who were underweight (BMI <18.5)[57].

Newborns whose mothers had not used iron/folic acid supplementation during current pregnancy were at increased risk to be born preterm[58].

2.3. Predicting models for preterm birth

Using a model incorporating(quantitative fetal fibronectin) qfFN and past spontaneous preterm birth/PPROMn, spontaneous preterm birth in symptomatic women can be reliably predicted[59]**.** Targeted intervention should allow for the prediction of preterm births in women at risk. In asymptomatic women, particularly in those with a short cervix, both cerclage and progesterone have shown promise in reducing spontaneous preterm birth [60-62].

For spontaneous preterm delivery within 7 days after admission, four predictors were identified: cervical length at admission, gestational age, amniotic fluid glucose, and (Interleukin)IL-6. The diagnostic performance of the model was assessed in the validation cohort using the receiver operating characteristic curve and showed an area under the curve (AUROC) of 0.86 (95%(CI) 0.77-0.95[63].

A model incorporating qfFN (quantitative fetal fibronectin) and CL, which replaces the single-threshold fFN test, demographic details, and obstetric history, can be reliably predicted for spontaneous preterm birth in high-risk asymptomatic women[59]. A weak indicator of spontaneous preterm birth is the uterocervical angle, measured at mid-trimester[64]. However, another study showed that an increased risk for spontaneous preterm birth < 37 weeks was associated with a wide uterocervical angle > 95 degrees observed during the second trimester[65].

An umbrella of the systematic review showed that cervical fetal fibronectin, alpha-fetoprotein, C-reactive protein, and interleukin 6 may have good overall diagnostic accuracy in the detection of spontaneous preterm birth-risk pregnancies[36]. The model can effectively predict preterm delivery in pregnant women after cervical conization, based on age and cervical duration during mid-pregnancy[66].

A research carried out in the UK found that data on maternal characteristics and obstetric history were predictive of spontaneous early preterm deliveries at 11-13 weeks of gestation; this model had an AUC of 0.67[67].

A study conducted in China showed that significant predictors of increased risk of preterm birth with a model output of c statistics(95% CI) of 0.60 (0.57–0.63) were advanced maternal age, lower maternal height, history of preterm delivery, amount of vaginal bleeding during pregnancy, and lack of folic acid intake before pregnancy for the prediction of overall preterm birth[68].

In addition, Gravidity, educational status, residency, previous history of preterm birth, twin pregnancy, pre-gestational diabetes mellitus (type I or II), chronic hypertension, placenta previa, gestational hypertension were significant predictors of potential preterm birth with the AUC 0.746 and 61.4 percent sensitivity (95% CI: 61.4-66.7 %) and 86.6% specificity[69]. In another study revealed that maternal features and history will substantially predict the frequency of spontaneous delivery before 34 weeks of gestation in the first trimester[70].

A nested case-control study indicated that maternal blood EBF1-based transcripts of miRNA may be useful in 3rd-trimester screening for spontaneous preterm birth risk, along with other biomarkers[71]. Cervicovaginal fluid cytokines, especially IL-6 and IL17af, may be better predictors of preterm birth than fFN in symptomatic women diagnosed with PTL and/or pPROM[72].

Gestational age at admission, vaginal bleeding at admission, membrane rupture, daily physical activity, multiple pregnancy, and WBC were the six most powerful predictors, which were calculated through univariable logistic regression analysis and multivariable logistic regression analysis regression with a concordance index of the prediction model for preterm birth between 32 and 37 weeks of gestation was 0.717 (95% CI: 0.675-0.759)[73].

Similarly, the combination of biophysical, biochemical, immunological, microbiological, fetal cell, exosomal, or cell-free RNA at different gestational ages, integrated as part of a multivariable predictor model may be necessary to advance our attempts to predict sPTL and preterm birth. In the prediction of spontaneous preterm birth within 48 hours, a prognostic model including qfFN and clinical risk factors showed excellent results, which is likely to be of clinical benefit [74, 75].

3. Conceptual framework

Below are the abstract frameworks of the study which shows the relationships of different variables with outcome variables are socio-demographic, obstetric, nutritional, and maternal medical condition This is adapted in different researches and slightly modified.

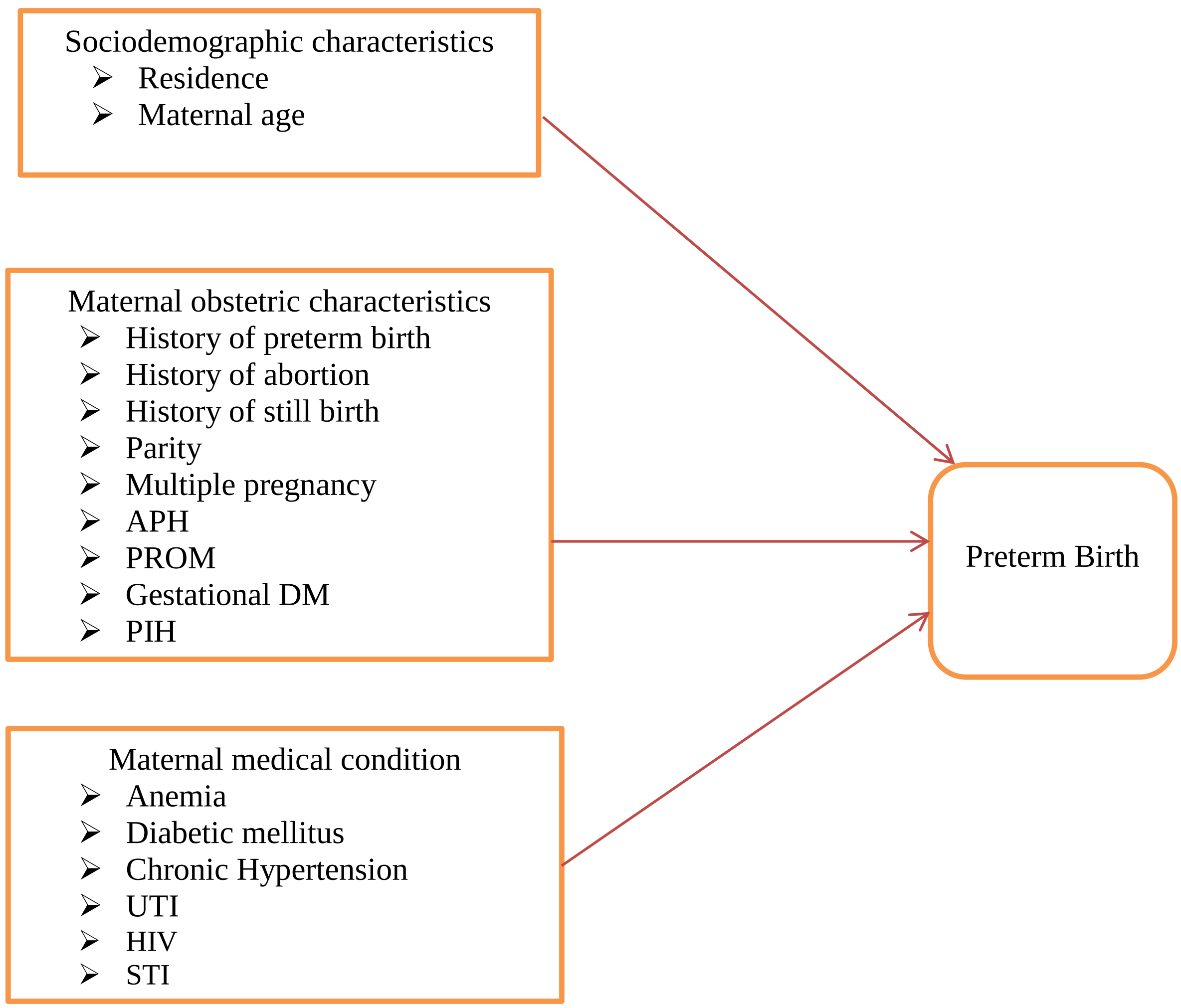

Figure 1.Conceptual framework for developing and validating a risk score for prediction of preterm birth using maternal characteristics in Felege Hiwot Comprehensive Specialized Referral Hospital, Northwest Ethiopia, 2021.

4. OBJECTIVE

4.1. General objective

To develop and validate a risk score for the prediction of preterm birth using maternal characteristics among mothers who gave birth in FHCSH, 2021.

4.2. Specific objectives

- To determine the incidence of preterm birth among mothers who gave birth in FHCSH.
- To identify predictors of preterm birth among mothers who gave birth in FHCSH.
- To develop a risk score to predict preterm birth using maternal characteristics.

5. METHODS AND MATERIALS

5.1. Study Design

A retrospective follow-up study was employed**.**

The theoretical design of the present study was; the incidence of preterm birth as a function of multiple predictors during pregnancy.

5.2. Study setting and study period

The study was conducted from March (1- 30) in 2021 among women delivered at Felege Hiwot comprehensive specialized hospital (FHCSH) which is found in Bahir Dar city. Bahir Dar is the capital city of Amhara national regional state and is found 575kms northwest of Addis Ababa. Felege Hiwot comprehensive specialized hospital was established with the German State government during the regime of Emperor H/ Selassie I in April 1963 G.C and is one of the oldest public hospitals in the Northwestern part of the country and located at the northern end of the city near Lake Tana and aspires to see a healthy, productive and prosperous society and become a center of medical service Excellency by 2029. During its establishment, it was planned to serve 25,000 people. Currently, it serves more than 10 million people coming from Bahir Dar city, west Gojjam zone, east Gojjam zone, Awi zone, North and South Wollo zones, South& North Gondar zones, and some parts of Benishangul Gumuz and Oromia regions. The hospital has currently a total of 1431 manpower (5 obstetricians and gynecologists and 63 midwives among others) in different disciplines. It has a total of 500 formal beds, 11 wards (emergency ward and Inpatient wards such as Gynecological &Obstetric, Surgical, orthopedics, Medical, Pediatric, L&D, Eye unit, NICU, psychiatric, oncology, and 22 OPDS), 39 clinical and non-clinical departments /service units / providing laboratory, Diagnostic, curative & Rehabilitation service at outpatient & inpatient bases as well as disease prevention & health promotion services[76].

5.3. The population of the study

5.3.1. Source population

The domain of the study was all pregnant mothers who gave birth at FHCSH.

5.3.2. Study population

Mothers who gave birth at FHCSH from January 30/2019 to January 30/2021 at FHCSH

5.3.3. Study unit

Selected cards of those Mothers who gave birth at FHCSH from January 30/2019 to January 30/20201

5.4. Eligibility criteria

5.4.1. Inclusion

All medical records of mothers who gave birth and had at least one ANC follow-up in FHCSH from January 30/2019 to January 30/2021

5.4.2. Exclusion

Maternal card with unknown last normal menstrual period (LNMP) and had no first-trimester ultrasound was the exclusion criteria for this study. Mothers whose records were lost during the study were excluded.

5.5. Variables

5.5.1. Outcome variable

Preterm birth (Yes/No)

5.5.2. Predictor variables

Socio-demographic characteristics: Residence, Maternal age,

Maternal obstetric characteristics: History of preterm birth, History of abortion, gravidity, parity, history of stillbirth, multiple pregnancy, APH, PROM, Gestational DM, and PIH

Maternal medical condition: HGB, Diabetic Mellitus, Chronic Hypertension, UTI, and HIV

Maternal nutritional: iron/folic acid intake

5.6 Term and operational definitions

Last Menstrual Period: The date of the starting of last menstruation the women had to the index pregnancy.

Anemia: According to WHO, pregnancy anemia defined as an HGB level below 11 gm/dl (HCT<33%)

Pregnancy-induced hypertension (PIH): Is systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg after gestation age of twenty weeks on the previously normal hypertensive woman.

Gravidity: The total number of pregnancies, including abortion, ectopic pregnancy, and any other pregnancies documented on the chart.

Parity: The number of deliveries after 28 weeks of gestation including IUFD and stillbirth documented in the chart.

5.6. Sample size determination

The sample size required for model development was determined based on the minimum standard of 10 events per candidate predictor considered, according to the formula N = (n × 10)/I where

N is the sample size, n is the number of candidate predictor variables and I is the estimated event rate in the population[77]. Since there were 17 candidate predictors considered and 10 events per candidate predictor, the estimated number of events for the study was 170. Based on a study done on the prevalence of preterm birth in Debre Tabor hospital was 13%[78], so taking into account this the required sample size was calculated as follow, n= 170*100/13= 1308

5.7. Sampling method and procedures

A simple random sampling technique was employed to select participants using the medical registration number of a delivered mother from the delivery registration book. First, all mother delivered at FHCSH from January 30/2019 to January 30/20201 was identified from the delivery registration book. After that records of mothers who meet the inclusion criteria were included in the study. Subsequently, a sampling frame was prepared. Finally, the study unit was selected by using a computer-generated random number.

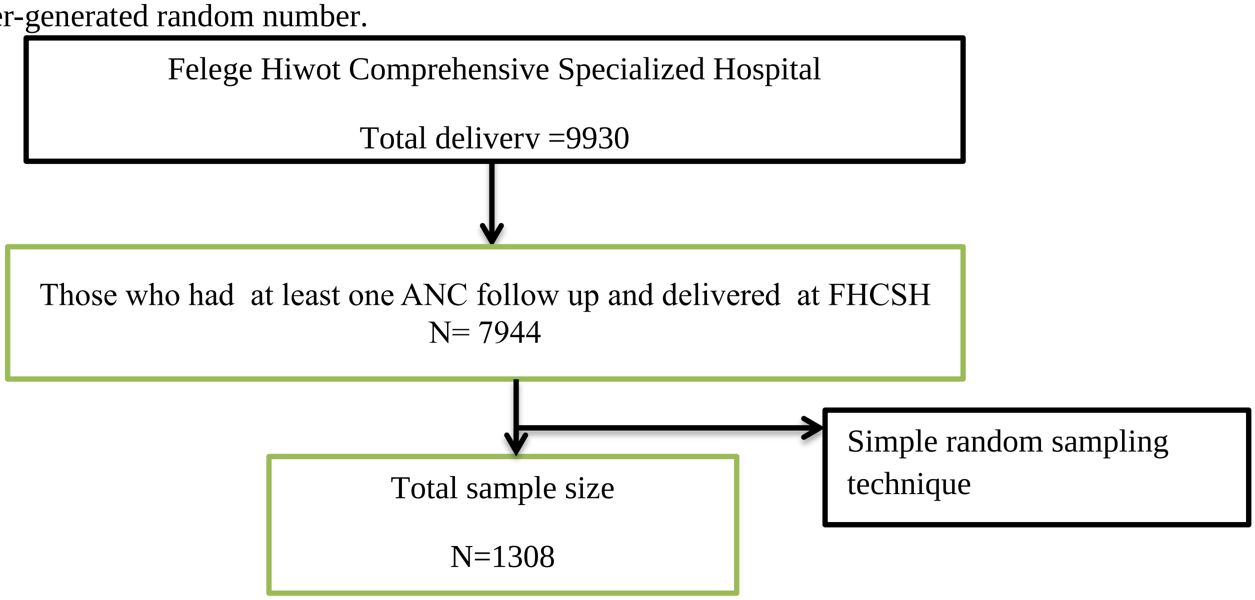

Figure 2: Diagram of sampling techniques at Felege Hiwot Comprehensive Specialized Hospital, Northeast Ethiopia, in 2021

5.8. Data collection tool and procedures

Data was collected using a structured checklist through chart review. Checklists were developed after reviewing various relevant literatures [22, 24-26, 79]. It consists of socio-demographic (Maternal age, Residence), Maternal obstetric characteristics : (History of preterm birth, History of abortion, history of stillbirth gravidity, Parity, Multiple pregnancy, APH, PROM, Gestational DM, and PIH), Maternal medical condition : (HGB level, Diabetic Mellitus, Chronic Hypertension, UTI and HIV))

The outcome variable was attributed to women whose medical records indicated a physician or midwife diagnosis of preterm birth and delivery between 28 and 36 completed weeks of gestation. The gestational age (GA) was measured using either LNMP, which is found to be a more reliable measure of GA in a low-resource setting[80, 81], or an early ultrasound result.

A total of five health personnel were involved in the data collection process. four health personnel, who have a diploma in Midwifery, as data collectors and one personnel, who owns a Bachelor of Science (BSc) Degree in Midwifery, as supervisors.

5.9. Data management and analysis

Data were entered into a software application (EPI DATA, version 3.02) and was analyzed by using R statistical programming language version 4.0.4 for further processing and analysis. There were 13(1%), 2(0.2 %), 11 (0.9 %),15 (2.5%), 21 (1.7%) ,29(2.3%),20(1.6%) and 20 (1.6%) missing values for premature rupture of membranes , residence, chronic hypertension, multiple pregnancy gestational diabetes Mellitus, pregnancy-induced hypertension ,antepartum hemorrhage and hemoglobin respectively.(Annex 3)

We assumed data were missing at random, and we, therefore, performed a multivariate imputation by chained equations for all variables evaluated in the prediction model [82]. Sensitivity analysis was performed to assess whether the assumption of missing at random (MAR) is valid or not, and the results were reasonably comparable (Annex 4). Descriptive statistics including median, inter-quartile range (IQR), and percentages, were carried out.

5.9.1. Model Development and Validation

For model development, bivariable logistic regression was done to obtain insight into the association of each potential predictor and preterm birth. Variables with ($p \leq 0.25$) from the bivariable analysis were entered into a backward stepwise multivariable logistic regression model, and significant variables ($p < 0.05$) were retained in the multivariable model.

The results of significant predictors were reported as coefficients with 95% confidence intervals (CI).

To check for the model accuracy and goodness of fit, we computed the area under the ROC curve (discrimination) and calibration plot (calibration) using "classifierplots" and "givitiR" packages of R respectively. The AUC ranged from 0.5 (no predictive ability) to 1 (perfect discrimination)[83].

The regression coefficients and their 95% confidence levels, and the AUC were adjusted for over fitting or over-optimism using bootstrapping technique.

To make internal validation, we computed 1000 random bootstrap[84] samples with the replacement on all predictors in the data. 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)**[85]**, 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 the referral of high-risk pregnant women to facilities where appropriate corticosteroid administration, antibiotic treatment in the event of infection, and other services take place.

5.9.2. Risk Score Development

To construct an easily applicable preterm birth prediction score, we transformed each coefficient from the model to a rounded number by dividing it by the lowest coefficient. The number of points was subsequently rounded to the nearest integer. We determined the total score for each individual by assigning the points for each variable present and adding them up. The score was transformed to a dichotomous, allowing each pregnant woman to be classified as a high or low risk of preterm birth.

The receiver operating characteristic curve (ROC) was plotted and the area under the curve (AUC) was calculated to measure the discriminatory power of the scoring system.

5.10. Data quality assurance

To maintain the quality of data, the data collectors and supervisors were trained for a day on the objective of the study, the content of the checklists, how to fill the checklists. Afterward, reviewing 15 charts on medical records of mothers who gave birth at Felege Hiwot Comprehensive Specialized Hospital which is found in Northwest Ethiopia were done. After that, some adjustments were done accordingly. The checklist was developed in English.

5.11. Ethical considerations

The ethical clearance was obtained from the ethical review board of Bahir Dar University, college of medicine, and health sciences institutional review board. The chief executive officer at Felege Hiwot Comprehensive Specialized Hospital offered permission to conduct the study. Confidentiality was maintained by omitting the personal identifier of the participant during the data collection procedure and information was used only for research purposes.

6. RESULT

6.1. Socio-demographic characteristics

A total of 1260 study cards were reviewed from a sample of 1308, about 48 cards were not reviewed due to the outcome of intrauterine fetal death, abortion.

The median age of the study participants was 26years with IQR (24-30years); the majority of the participants 1086 (86.2%) were in the age group of 20-34 years. More than three fourth of the participants 926 (73.49%) were urban residents.

Table 1: Socio-demographic characteristics of mothers who gave birth at FHCSH from January 30/2019 to January 30/2021

Variable	Category	Frequency	Percent (N=1260)
Age	<20 yrs.	79	6.3
	20-34 yrs.	1086	86.2
	>=35 yrs.	95	7.5
Residence	Urban	926	73.49
	Rural	334	26.51

6.2. Maternal Obstetric Related Factors

From the total of mothers who delivered at FHCSH, more than two-third 841 (66.7%) were multigravida.

About parity, above half of them713 (56.6%) were multipara. Concerning past obstetric history, 55 (6.5%) of them had a history of previous preterm birth, 76 (9%) of them had a previous history of stillbirth and 162 (19.3%) of them had a previous history of abortion.

Regarding current obstetric characteristics, more than half of participants 681(54%) gave birth by spontaneous vaginal birth, and the onset of labor was spontaneous 841 (66.1%).

The majority of the participants are RH positive 1137 (90.2%) and 195 (15.5%) of the participants had a history of premature rupture of membrane.

Table 2: Obstetric related factors of mothers who gave birth at FHCSH from January 30/2019 to January 30/2021

Variables	Category	Frequency	Percent
Gravidity	Primigravida	419	33.3
	Multigravida	841	66.7
History of preterm birth (N=841)	Yes	55	6.5
	No	787	93.6
History of still birth (N=841)	Yes	76	9
	No	765	91
History of abortion(N=841)	Yes	162	19.3
	No	679	80.7
Mode of delivery	SVD	681	54
	Instrumental	81	6.1
	C/S	498	39.5
Blood RH factor	Positive	1137	90.2
	Negative	123	9.8
PROM	Yes	195	15.5
	No	1065	84.5
PIH	Yes	110	8.73
	No	1150	91.27
Type of PIH (n=110)	Preeclampsia/eclampsia	100	90.9
	Gestational hypertension	8	7.3
	Superimposed preeclampsia	2	1.8
Gestational diabetus mellitus	Yes	44	3.5
	No	1216	96.5
Antepartum hemorrhage	Yes	84	6.7
	No	1176	93.3
Type of APH (n=84)	Abruption placenta	67	79.8
	Placenta previa	17	20.2

6.3. Maternal Infection and Chronic Disease-Related Factors

Regarding the HIV status of mothers, 109 (8.7%) mothers were positive. Hemoglobin level, 236 (18.7%) mothers had a hemoglobin level of <11g/dl.

Only 12 (1%) mothers had urinary tract infections. Similarly, 21(1.7%) mothers have chronic hypertension and 11(0.8%) mothers have diabetes mellitus. About VDRL, only 4 (0.3%) mothers were VDRL reactive. Almost all mothers 1253 (99.4%) had iron/folate acid intake.

Table 3: Infection and Chronic Disease-Related Factors of mothers who gave birth at FHCSH from January 30/2019 to January 30/2021.

Variable	Category	Frequency	Percent
HIV status	Positive	109	8.7
	Negative	1151	91.3
VDRL	Reactive	4	0.3
	Nonreactive	1256	99.7
HGB	<11g/dl	236	18.7
	>=11g/dl	1024	81.3
Urinary tract infection	Yes	12	1
	No	1248	99
Diabetes mellitus	Yes	11	0.8
	No	1249	99.2
Chronic hypertension	Yes	21	1.7
	No	1239	98.3

HIV (human immune virus), VDRL (Venereal disease research laboratory), HGB (hemoglobin)

6.4. Development of prediction model for preterm birth

Out of 1260 delivered neonates, 169 (13.4%) (95%, CI (11.6%, 15.4%) was preterm infants. (Figure 3). The bivariable logistic regression analysis found several factors were eligible to be included in the prediction model. Variables with $P \leq 0.25$ in the bivariable logistic regression analysis were, hemoglobin level, Gravidity, residence, gestational diabetes mellitus, APH, PIH, chronic hypertension, PROM, and multiple pregnancies.

Table 4: Bivariable logistic regression analysis for development of preterm birth prediction model

Variables	Category	Preterm birth		β	95 % CI	P- value
		Yes	No			
Gravidity	Primigravida	72	347	0.464	(0.131, 0.793)	0.001*
	Multigravida	97	744	1		
Residence	Urban	89	837	1		
	Rural	80	254	1.1436	(0.683 , 1.796)	<0.001*
GDM	Yes	14	30	1.160	(0.50, 1.818)	0.001*
	No	155	1061	1		
APH	Yes	36	48	1.771	(1.302, 2.23)	<0.001*
	No	133	1043	1		
PIH	Yes	44	66	1.697	(1.272, 2.12)	<0.001*
	No	125	1025	1		
HIV status	Yes	11	98	-0.35	(-1.07, 0.22)	0.28
	No	158	993	1		
Age of mother	>20 yrs.	18	61	1		
	20-30 yrs.	143	943	-0.67	(-1.23, 0.12)	0.27
	>=35 yrs.	18	77	-0.23	(-0.96 ,0.50)	0.53
HGB level	<11d/dl	42	194	0.42	(0.04 , 0.87)	0.027*
	>=11g/dl	127	897	1		
Chronic	Yes	5	16	0.71	(-0.31, 1.73)	0.16*

hypertension	No	164	1075	1		
UTI	Yes	2	10	0.25	(-1.27, 1.78)	0.80
	No	167	1081	1		
DM	Yes	2	9	0.36	(-1.17, 1.90)	0.64
	No	167	1082	1		
PROM	Yes	74	121	1.83	(1.47, 2.18)	<0.001*
	No	95	970	1		
Multiple pregnancy	Yes	20	70	0.67	(0.14, 1.19)	0.019*
	No	149	1021	1		

*Variables included in the multivariable analysis (P < 0.25 in univariable analysis):PROM(premature rupture of membrane),APH(antepartum hemorrhage),chronic hypertension, HGB(hemoglobin level),residence, gravidity ,PIH (pregnancy induced hypertension),GDM (gestational diabetus mellitus),multiple pregnancy

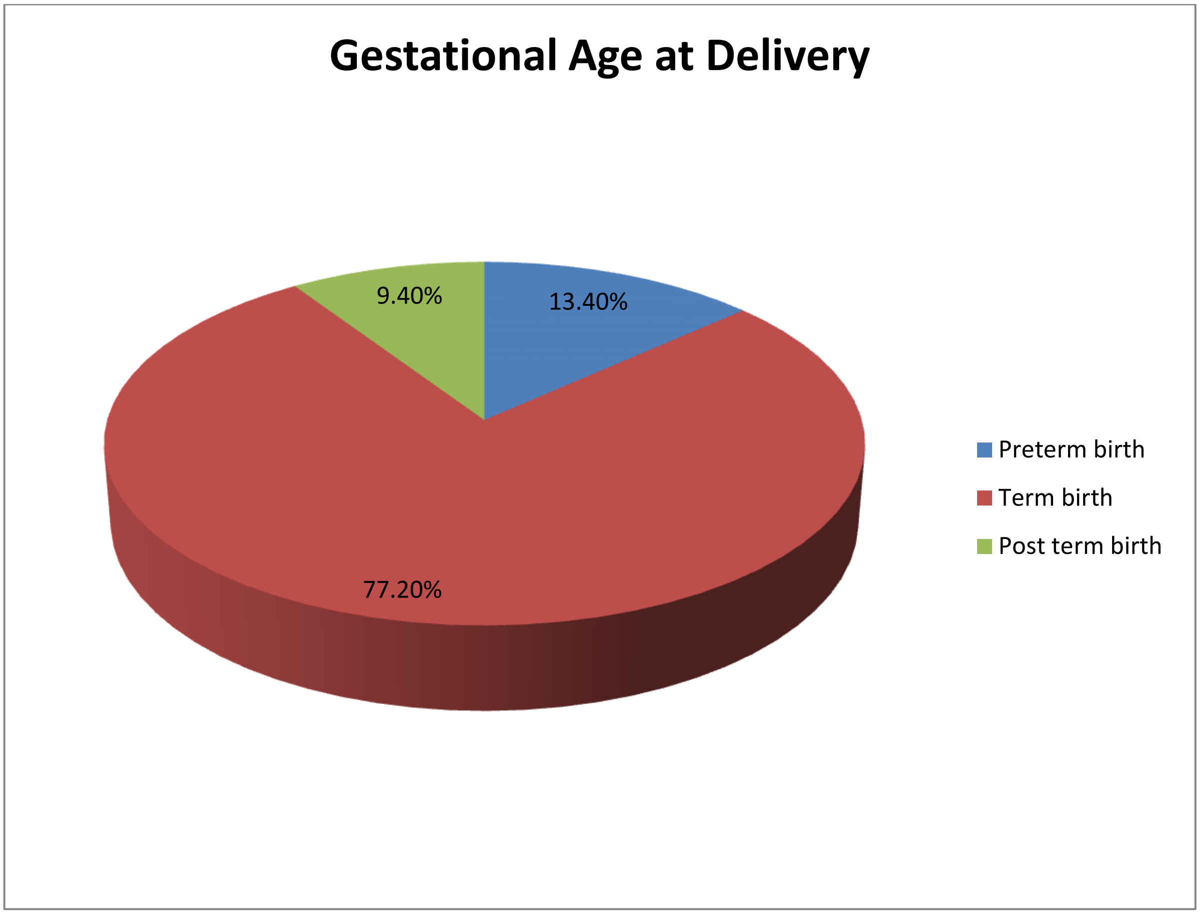

Figure 3: The proportion of preterm birth among mothers who gave birth at FHCSH from January 30/2019 to January 30/2021.

Results of the multivariable analysis are shown in table (5). Residence, Gravidity, PROM, APH, PIH, and HGB were retained in the final model. The discriminatory power of the model has an AUC of 0.816 (95% confidence interval: 0.779 – 0.856) as shown in figure (4).

In figure (4), classifiers that give curves closer to the top-left corner indicate better performance. As a baseline, a random classifier is expected to give points lying along the diagonal (FPR = TPR). A perfect result would be the point (0, 1) indicating 0% false positives and 100% true positives.

Using a default threshold of 0.5, meaning that a probability in [0.0, 0.49] is a negative outcome (0) and a probability in [0.5, 1.0] is a positive outcome (1). The model has a sensitivity of 22.5 %, specificity of 97.8 %, a positive predictive value of 62.3 %, and a negative predictive value of 89 %.

Using the coefficients (β) the predicted risk cutoff point was a probability of (SpEqualSe > 0.1320), the model has a sensitivity of 75.74%, specificity of 72.87%, a positive predictive value of 30.2%, and a negative predictive value of 95.1%.

The calibration test had a p-value of 0.6228, indicating that the model does not misrepresent the data or calibration of the model was visually accurate since observed and predicted probabilities were similar, as shown in Figure (b).

Validation of the model with the bootstrap technique showed hardly any indication of undue influence by particular observations, with an optimism coefficient of 0.085, resulting AUC of 0.789 (corrected 95% CI: 0.748–0.83) as showed in figure (5).

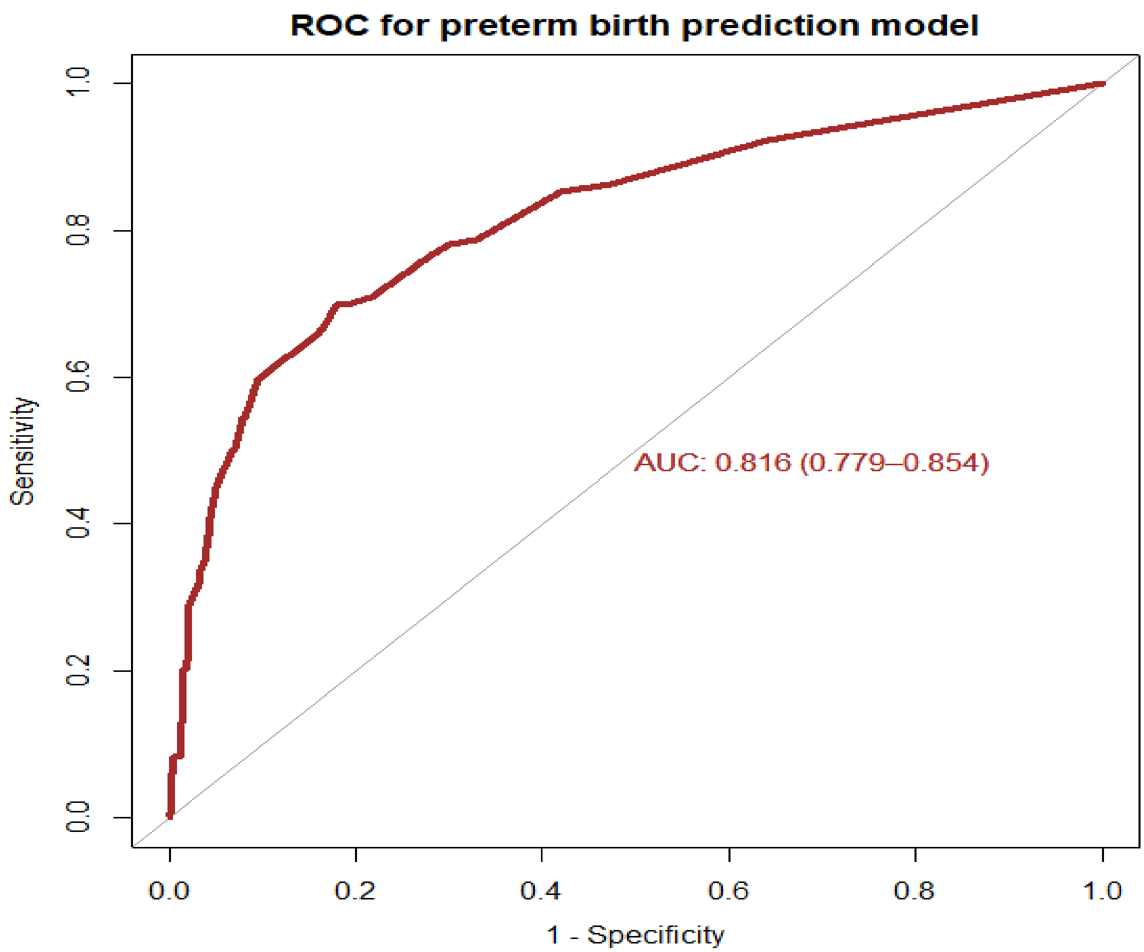

Figure 4: ROC (AUC) of the original risk prediction model for preterm birth among mothers who gave birth at FHCSH from January 30/2019 to January 30/2021. AUC (area under the curve), ROC (Receiver operating characteristic curve).

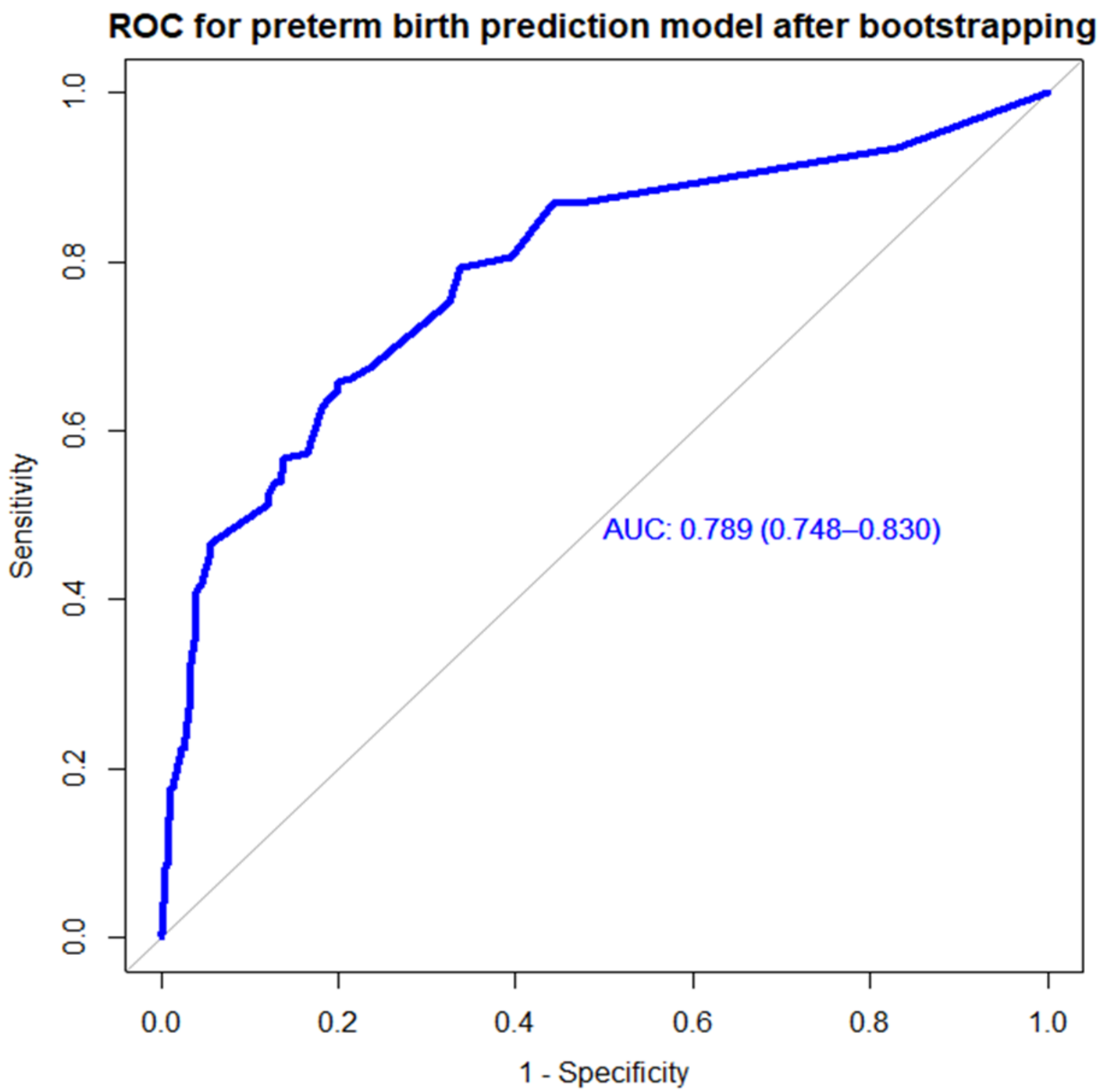

Figure 5: ROC (AUC) of risk prediction model after bootstrapping for preterm birth among mothers who gave birth at FHCSH from January 30/2019 to January 30/2021. AUC (area under the curve), ROC (Receiver operating characteristic curve).

Simplified risk score: we divided the coefficient of predictors included in the reduced model by the smallest.

Table 5: Coefficients and risk-scores of each predictor included in the model to predict preterm birth (*n* = 1260)

Predictors Variables	Multivariable analysis			
	Original β (95 % CI)	Bootstrap β	P-value	Risk score
Residence (rural)	1.161 (0.780, 1.545)	1.148	<0.001	2
Gravidity (primigravida)	0.675 (0.291, 1.061)	0.666	0.01	1
PROM (yes)	2.081 (1.669 , 2.50)	2.051	<0.001	3
APH (yes)	1.364 (0.806 , 1.915)	1.348	<0.001	2
PIH (yes)	1.387 (0.887 , 1.879)	1.368	<0.001	2
HGB <11g/dl	0.676 (0.255 , 1.09)	0.677	<0.001	1

The probability or risk of preterm birth = 1/ (1 + exp – (-3.517+ 1.148 * Residence (rural) + 0.666 *gravidity (primigravida) + 2.051*PROM (yes) + 1.348 * APH (yes) + 1.387*PIH +0.677*HGB (<11g/dl)

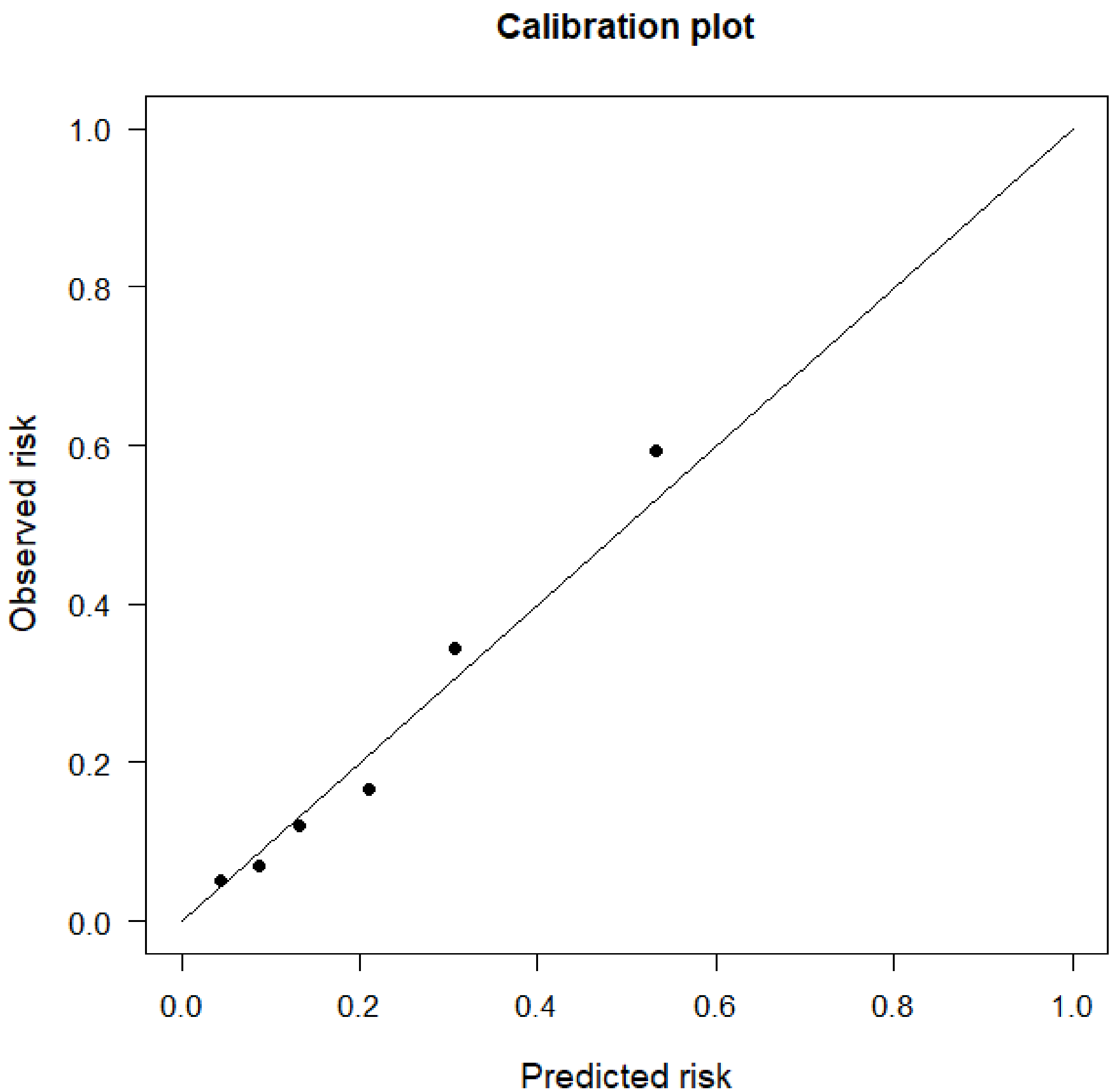

Figure 6: Predicted versus observed preterm birth probability in the sample. This analysis includes mothers who gave birth at FHCSH from January 30/2019 to January 30/2021(n = 1260). Calibration plot created using "plot Calibration" in R programming.

Besides model performance was assessed by AUC, sensitivity, specificity and accuracy, clinical and public health utility of the model was also assessed by decision curve analysis (DCA).

When applying DCA, we first evaluate whether our model understudy has a higher net benefit than the default strategies (referring all and none). This model outperforms the default strategies across the relevant threshold range. The model has the highest net benefit across the entire range of threshold probabilities, which indicates that the model has the highest clinical and public health value. Hence, referral decision made using the model has a higher net benefit than not referring at all or referring all regardless of their risk thresholds as shown in figure 7.

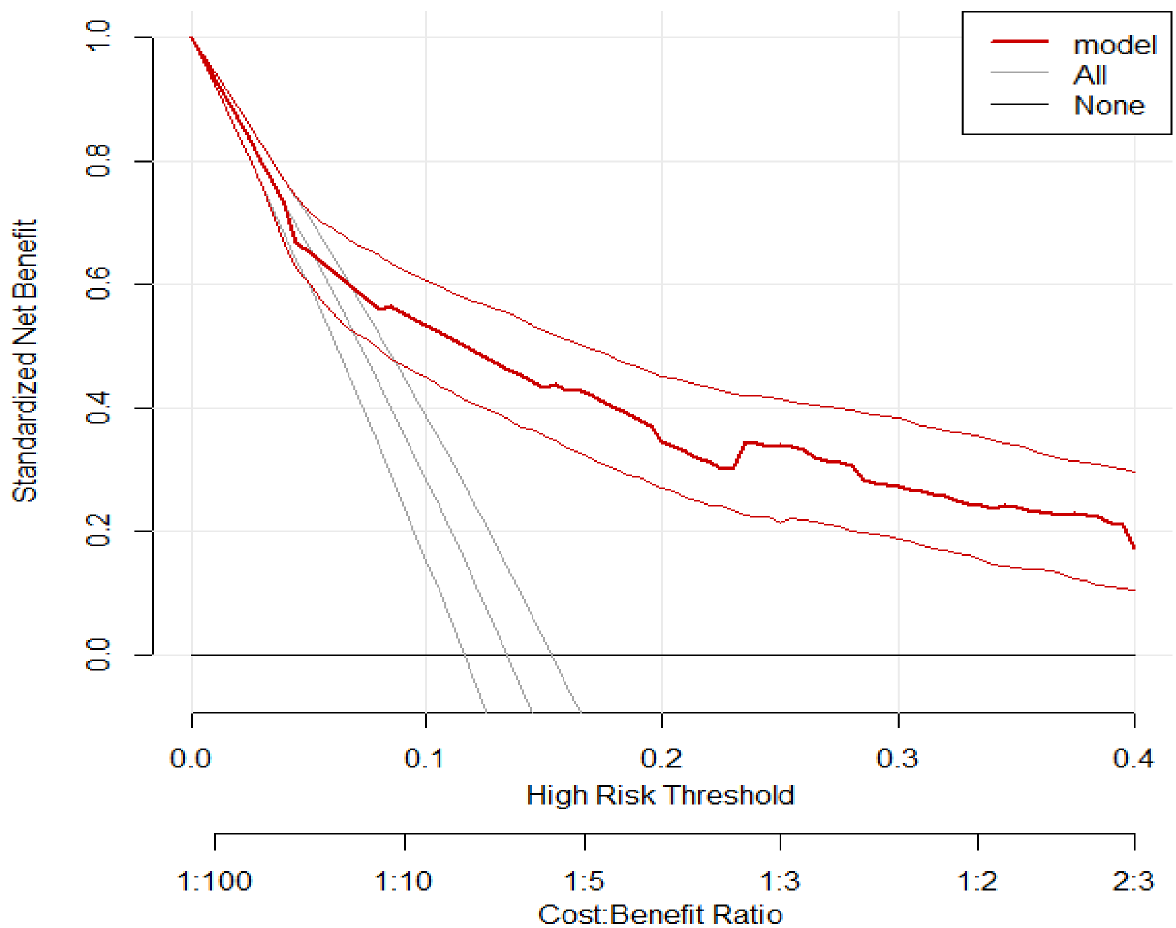

Figure 7: A decision curve plotting the net benefit of the model against threshold probability.

6.5. Risk Classification Using a Simplified Risk Score

We created a simplified risk score from the model for practical use. The reduced model's prediction score was simplified by rounding all regression coefficients.

The simplified score had a considerably comparable prediction accuracy with the original β coefficients, with an AUC of 0.786 (95%CI: 0.729–0.827) (figure 8). Indicating a 78.6% the probability that a randomly selected mother with preterm birth will receive a higher risk score than a randomly selected mother without preterm birth.

The possible minimum and maximum scores a mother can have are 0 and 11, respectively.

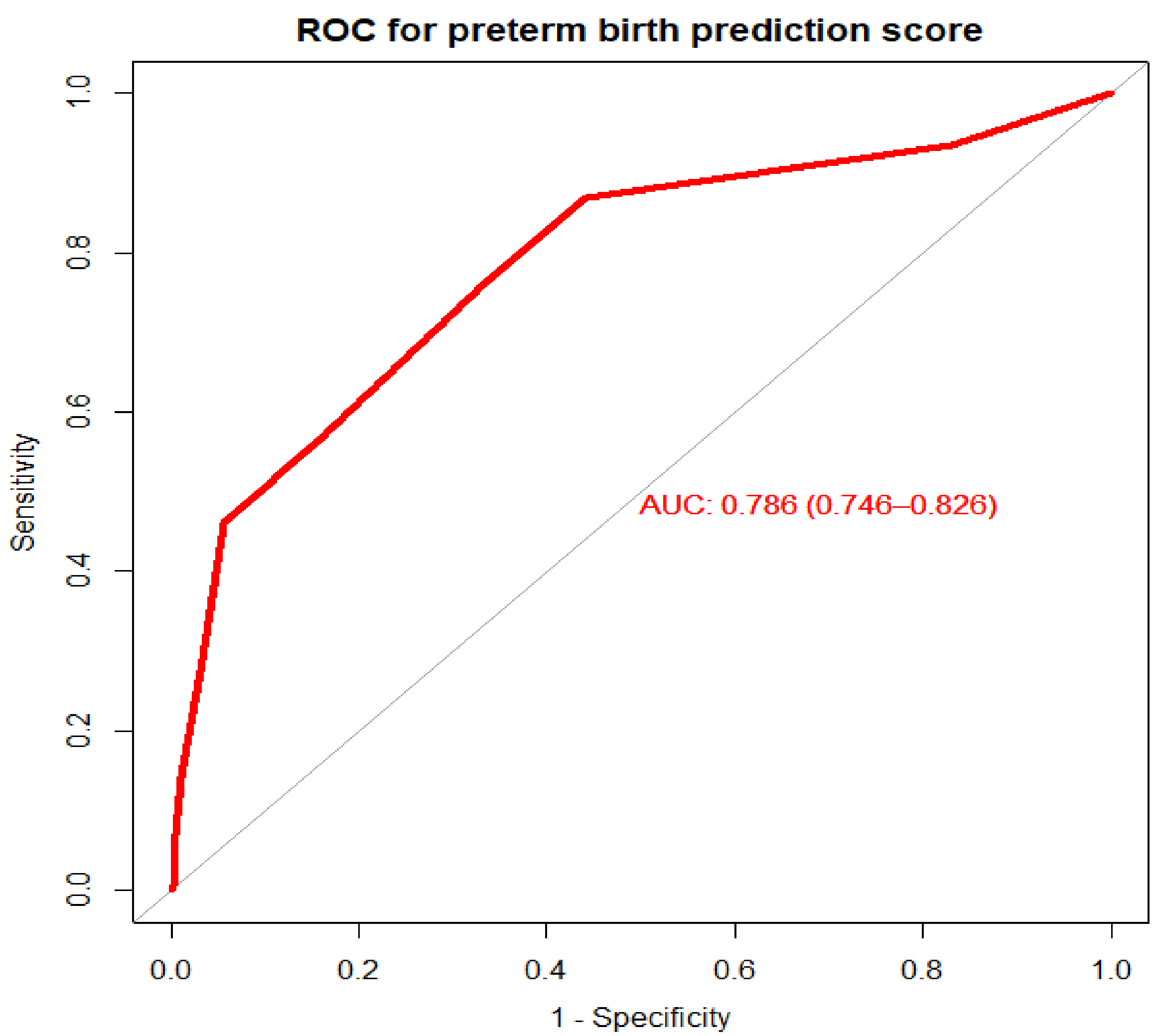

Figure 8: Area under the ROC curve for the simplified risk score to predict the risk of preterm birth among mothers who gave birth at FHCSH from January 30/2019 to January 30/2021.

Table 6. Risk classification of preterm birth using simplified prediction score (n = 1260)

Score*(risk category)	Prediction Model Based on Maternal Characteristics	
	Number of mothers	Incidence of preterm birth
<3 (Low)	982 (77.9%)	72 (7.9%)
>=3 (High)	278 (14.36%)	97 (53.59%)
Total	1260 (100%)	169 (13.4%)

**** Score = (2*PIH) + (3*PROM) + (hemoglobin < 11 mg/dl) + 2*residence + (2*APH) + gravidity***.

When dichotomized to low risk (<3) and high risk (≥3) based on the risk score, 278 (14.36%) were categorized as high risk and 982 (77.9%) as low risk for preterm birth. Using "SpEqualSe", the suggested threshold score to predict preterm birth using risk scores is ≥3with a sensitivity of 75.14 % and specificity of 67.46%.

7. DISCUSSION

The present study was designed to develop and validate risk scores to predict preterm birth using maternal characteristics among mothers who gave birth in FHCSH.

Thus, predicting the probability of preterm birth in pregnant women is essential to take appropriate measures accordingly. Identifying women at risk of preterm birth is an important task for clinical care providers. However, in low and middle-income countries, there are only a few methods available for reliably predicting actual preterm labor in women. Previously, the focus of the research was to explain the maternal and fetal determinants of preterm birth. In recent years, the focus shifted to predicting preterm birth optimally using a combined set of characteristics.

Maternal characteristics were identified in this retrospective study to build a preterm birth prediction risk score. The optimal combination of maternal factors to predict preterm birth include residency, gravidity, hemoglobin < 11 mg/dl, early rupture of membranes, antepartum hemorrhage, and pregnancy-induced hypertension, according to the prediction model. The model has an AUC of 0.816 (95%CI: 0.776 – 0.856).

Without any advanced laboratory or imaging testing, this study measured the predicted performance of a model based on maternal features during pregnancy. Furthermore, we discovered that utilizing SpEqualSe as an optimal cut point, the sensitivity and specificity of this prediction model achieved 75.14 percent and 67.46 percent, respectively, at the score threshold of 3.

In our study, a combination (residency, gravidity, hemoglobin < 11 mg/dl, early rupture of membranes, antepartum hemorrhage, and pregnancy-induced hypertension) of maternal characteristics results in an AUC of 0.816 (95%CI: 0.776 – 0.856), has an excellent accuracy according to diagnostic accuracy classification[86].

A study conducted in China showed that a model developed using advanced maternal age, lower maternal height, history of preterm delivery, amount of vaginal bleeding during pregnancy, and lack of folic acid intake before pregnancy for the prediction of overall preterm birth with AUC of (0.6)**[68]**.

This difference may be due to some of the predictors they used such as lower maternal height, lack of folic acid intake before pregnancy, and advanced maternal age. However predictors they used such as lack of folic acid intake before pregnancy not easily obtainable information in routine clinical practice, which makes their model less practical. This 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 model, five can be easily found from history taking and one by test for hemoglobin.

The model's accuracy is consistent with a retrospective study done in China that established a preterm birth prediction model based on maternal characteristics, including demographics and clinical characteristics, and a model with predictors (gravidity, educational status, residency, previous history of preterm birth, twin pregnancy, pre-gestational diabetes mellitus (type I or II), chronic hypertension, and place of birth) with AUC of 0.749 (95%CI: 0.732–0.767) **[69]**.

On the other hand, a model incorporating four predictors (cervical length at admission, gestational age, amniotic fluid glucose, and IL-6). The diagnostic performance of the model was assessed in the validation cohort using the receiver operating characteristic curve and showed an area under the curve (AUROC) of 0.86**[63]** and similarly, the combination of biophysical, biochemical, immunological, microbiological, fetal cell, exosomal, or cell-free RNA at different gestational ages, integrated as part of a multivariable predictor model may be necessary to advance our attempts to predict sPTL and preterm birth. In the prediction of spontaneous preterm birth within 48 hours, a prognostic model including qfFN and clinical risk factors showed excellent results**[74, 75]**. Both models have higher discriminatory performance. The reason for the lower discriminatory performance in our study as compared to the studies described above could be because we used secondary data available from the register and as this dataset is limited and some variables that require advanced laboratory tests were not included in the model.

Hence, predictors necessitate laboratory testing, which is often unavailable in low-resource settings. As a result, such predictors are difficult to come by in ordinary clinical and public health practice, making the model less useful.

In our prediction score, using 3 as a cutoff point has an acceptable level of specificity, sensitivity, PPV, and NPV to predict preterm birth. It is also possible to shift the cutoff point to increase either of the accuracy measures depending on the program aim and availability of resources

The simplified risk 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

This prediction model helps to identify the high preterm birth risk group or individual during pregnancy.

In this study, the incidence of preterm birth was found to be 13.4% with 95% CI (11.6%, 15.4%). This finding was higher than the findings conducted in Gondar town health institutions 4.4%[87]. This might be due to the difference in study time and setting. In addition, this discrepancy may be due to a difference in exclusion criteria for multiple pregnancies. In our study mothers with multiple pregnancies were included, whereas these mothers were excluded from the mentioned study. Therefore lower rate is expected in their study as over distention of the uterus in multiple pregnancies is a causative factor for preterm labor. This finding was in line with studies [22, 26, 78].

8. STRENGTH AND LIMITATION

This study has several strengths. Firstly, we used an adequate number of participants with the outcome, which helped us to construct the model using a sufficient number of predictor variables.

Secondly, 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.

Furthermore, data were collected from each mother’s card; due to this, some important variables were missed, such as previously highlighted factors with preterm birth in different studies.

9. CONCLUSIONS

Incidence of preterm birth relatively high in Felege Hiwot referral comprehensive specialized hospital. This study shows the possibility of predicting preterm birth using a simple prediction model constructed from maternal characteristics.

Thus, the optimal combination of maternal characteristics such as residence, gravidity, hemoglobin < 11 mg/dl, and premature rupture of membrane, antepartum hemorrhage, and pregnancy-induced hypertension shows the possibility of predicting preterm birth using a simple prediction model constructed from maternal characteristics.

In addition, risk score calculations based on a combination of predictors was effective and had comparable accuracy with the model-based approach of original β coefficients.

The prediction score was used to risk-stratify pregnant women and identify those who were more likely to have a preterm birth. Following that, high-risk groups might be linked to a center that has the necessary facilities for corticosteroid administration, antibiotic treatment in the event of infection, and other services.

10. RECOMMENDATIONS

For clinicians

This score may assist for clinical decision-making. In addition, using this score may also be useful to counsel and educate patients by calculating the overall probability of preterm birth for the individual patient and considering specific risk factors present during the gestational period.

For healthcare policy makers

To incorporate this convenient and easily applicable score in health care system to be used by clinicians to inform pregnant mothers about future course of their outcome.

For scholars

Doing further research is needed to validating the prediction tool using prospective follow-up studies in another context before introducing it to the clinical and public health practices.

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ANNEXES

Annexes 1: Information Sheet

Title of the Research Project: Developing and validating a risk score for prediction of preterm birth at Felege Hiwot comprehensive specialized hospital, Northwest Ethiopia: retrospective follow up study, 2021.

Name of Investigator: Sefineh Fenta (BSc in Public Health)

Name of the Organization: Bahir Dar University, College of Health Science and Medicine, School of Public Health, Department of Epidemiology and Biostatistics.

Name of the Sponsor: Bahir Dar University.

Introduction: This information sheet is prepared for FHCSH. The form aims to make the above-concerned office clear about the purpose of the research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: Developing and validating a risk score for prediction of preterm birth at Felege Hiwot comprehensive specialized hospital, Northwest Ethiopia, 2021.

Procedure: To achieve the above objective, information that is necessary for the study was taken from selected medical records of delivery register and ANC chart.

Risk and /or Discomfort: Since the study was conducted by taking appropriate information from the medical chart, it did not inflict any harm on the patients. The name or any other identifying information will not be recorded on the data extraction tool and all information taken from the chart will be kept strictly confidential and in a safe place. The information retrieved will only be used for the study purpose.

Benefits: The research has no direct benefit for one whose document/ record was included in this research. But the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing predicted plans there is a benefit for clients in the program of getting appropriate care and treatment services. The research work had a paramount direct benefit for clinicians to stratify patients as high risk or low risk, thus to provide appropriate management.

Confidentiality: To assure confidentiality the data on the chart was collected without the name of the clients and the information was collected from this research project was kept confidential. Besides, it was not revealed to anyone except the investigator.

Person to contact: This research project was reviewed and approved by the institutional review board of College of Health Science, school of public health, Bahir Dar University. If you have any questions you can contact any of the following individuals (Investigator and Advisors) and you may ask at any time you want.

Sefineh Fenta , Bahir Dar University, College of Health Science and Medicine, School of Public Health, Department of Biostatistics and Epidemiology, principal investigator

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Zelalem Alamrew (MPH & MSC Epidemiology, Assistant professor of Epidemiology), Bahir Dar University, College of Health Science and Medicine, School of Public Health, Department of Biostatistics and Epidemiology, principal advisor; Email Address: kzolam@gmail.com

Gizachew Tadesse (MPH / EPIDEMIOLOGY), Bahir Dar University, College of Health Science and Medicine, School of Public Health, Department of Biostatistics and Epidemiology, co-advisor;

Email Address: leulgzat@mail.com

Annexes 2: Data extraction checklist

Code: ………………………

Name of data collector …………………………………signature……………………..

Name of supervisor……………………………………..signature………………………

Date ……………………………………………………..

Data extraction checklist (for developing and validation of risk score for prediction model for PTB)

Part I: Socio demographic characteristics			
S.no	Variables	Category	Skip
100	Age	……………………..	
101	Residence	1. Urban 2. Rural	
Part II: Current and past obstetrics characteristics			
201	Gravidity	……………………….	
202	Parity	……………………	
203	History of the previous preterm birth	1. Yes 2. No	
204	History of previous still birth	1. Yes 2. No	
205	History of previous abortion	1. Yes 2. No	
206	Mode of delivery	1. SVD 2. Instrumental 3. C/S	
207	Onset of labour	1. Spontaneously 2. Induced	
208	History of premature rapture of membrane	1. Yes 2. No	
209	Gestational age at delivery	……………….in weeks	
210	Status of delivery	1. Preterm birth 2. Term birth 3. Post term birth	
211	Blood RH factor	1. Positive 2. Negative	
212	History of gestational diabetus mellitus	1. Yes 2. No	
213	History of antepartum hemorrhage	1. Yes 2. No	Skip to 216
214	If yes for Q#214, what was the DDx?	1. Placenta previa 2. Abruption placenta	

		3. Others specify……..	
215	History of pregnancy induced hypertension	1. Yes 2. No	Skip to 218
216	If yes for Question #216, what was the diagnosis?	..………………….	
217	History of multiple pregnancy	1. Yes 2. No	
Part III: Current and past medical characteristics			
301	HIV status	1. Positive (reactive) 2. Negative(non-reactive)	
302	Baseline HGB level	……………………………….…..	
303	History of chronic hypertension	1. Yes 2. No	
304	History of urinary tract infection	1. Yes 2. No	
305	History of Diabetus mellitus	1. Yes 2. No	
306	History of sexually transmitted disease or VDRL reactive?	1. Reactive 2. Non-reactive	
Part IV: **Nutritional assessment during current pregnancy**			
401	History of Iron /folic acid intake	1. Yes 2. No	
402	If yes number ≠ 402 number of tabs taken	1. 30 tabs 2. 60tabs 3. >=90 tabs	

Annexes 3: Table 7: Socio-demographic characteristics, obstetric and Chronic Disease Related Factors of mothers who gave birth at FHCSH from January 30/2019 to January 30/2021.

Variables	Missing (frequency)	Percent
Residence	2	0.2
Gravidity	0	0
PROM	13	1
Chronic hypertension	11	0.9
Multiple pregnancy	15	1.2
Gestational diabetus mellitus	21	1.7
Pregnancy induced hypertension	29	2.3
Antepartum hemorrhage	20	1.6
Hemoglobin level	20	1.6

Annexes 4

Table 8. Sensitivity analysis of the model to predict preterm birth: Comparison of the regression coefficients, standard errors (SE), and p-values for complete case analysis (CCA) and multiple imputated data (MI).

Predicator variables	Complete case analysis			Multiple imputation		
	B	SE	P value	B	SE	P value
Chronic hypertension (yes)	0.7313	0.6297	0.24	0.581	0.6285	0.92
Residence (rural)	0.815	0.1946	<0.001	1.154	0.1958	<0.001
GDM(yes)	0.709	0.4028	0.07	0.472	0.4236	0.26
HGB(<11g/dl)	0.497	0.2185	0.02	0.642	0.2153	0.001
PROM (yes)	1.898	0.2080	<0.001	2.097	0.2129	<0.001
APH (yes)	1.194	0.2858	<0.001	1.298	0.2874	<0.001
PIH (yes)	1.353	0.2600	<0.001	1.368	0.2523	<0.001
Multiple pregnancy (yes)	0.539	0.3173	0.08	0.446	0.3257	0.17
Gravidity(primigravida)	0.426	0.1944	0.02	0.711	0.1976	<0.001