DSpace Institution

DSpace Repository **http://dspace.org**

School of Public Health Thesis and Dissertations

2021-02

Development of Risk Prediction Model for Primary Postpartum Hemorrhage Among Mothers Delivered at Felegehiwot Comprehensive Specialized Hospital, Northwest Ethiopia: A Case-Control Study

Anteneh, Kassa

http://ir.bdu.edu.et/handle/123456789/13498

Downloaded from DSpace Repository, DSpace Institution's institutional repository

BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS

DEVELOPMENT OF RISK PREDICTION MODEL FOR PRIMARY POSTPARTUM HEMORRHAGE AMONG MOTHERS DELIVERED AT FELEGEHIWOT COMPREHENSIVE SPECIALIZED HOSPITAL, NORTHWEST ETHIOPIA: A CASE-CONTROL STUDY

BY: ANTENEH KASSA (Bsc, PUBLIC HEALTH)

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

FEBRUARY, 2021

BAHIR DAR, ETHIOPIA

BAHIR DAR UNIVERSITY
COLLEGE OF MEDICINE AND HEALTH SCIENCES
SCHOOL OF PUBLIC HEALTH
DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS

DEVELOPMENT OF RISK PREDICTION MODEL FOR PRIMARY POSTPARTUM HEMORRHAGE AMONG MOTHERS DELIVERED AT FELEGE HIWOT COMPREHENSSIVE SPECIALIZED HOSPITAL, NORTHWEST ETHIOPIA: A CASE-CONTROL STUDY

INVESTIGATOR: ANTENEH KASSA (BSC, PUBLIC HEALTH)
Email Adress: weproud16@gmail.com
ADVISORS: Mr. YIHUN MULUGETA. (BSC, MSC-IH, MPH IN EPIDEMIOLOGY AND BIOSTATISTICS, ASSOCIATE PROFESSOR OF EPIDEMIOLOGY AND GLOBAL HEALTH)
Email Adress: yihun.mulugeta@yahoo.com
Mr. ABEBAW GEDEF (Bsc, ASSISSTANT PROFESSOR OF BIOSTATISTICS)
Email Adress: abebaw2516@gmail.com

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

FEBRUARY, 2021

BAHIR DAR, ETHIOPIA

© 2021 anteneh kassa

Declaration

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

Principal investigator

Name: _____

Signature: _____

Date: _____

Advisors:

1. Name: _____

Signature: _____

Date:_____

2. Name: _____

Signature: _____

Date:_____

AKKNOWLEDGEMENTS

Firstly, my most sincere gratitude goes to my advisors; Mr. Yihun Mulugeta and Mr. Abebaw Gedef for their continuous support, encouragement and interest for the development of this research proposal. I also would like to extend my gratefulness and heartfelt thanks to all my colleagues, who gave me their unduly support and critical comments.

SUMMARY

Background: Postpartum hemorrhage is defined as loss of blood of more than 500 milliliters following a vaginal delivery or more than 1000 ml following caesarian section or blood loss that can cause hemodynamic derangement after delivery. The incidence of postpartum hemorrhage has increased in both high and low income countries. Worldwide, postpartum hemorrhage affects about 5% of all deliveries and more than 50% of deaths associated with it are preventable. Maternal mortality ratio an indicator in the sustainable development goal and Ethiopia set strategies to reduce it to less than 70 per 100,000 live births by 2030. Despite the sustained efforts to reduce postpartum hemorrhage, its magnitude is still at highest level and continues to remain the leading cause of maternal mortality. Therefore, for Ethiopia to achieve the SDG target focused on maternal mortality, individualized prediction model for primary postpartum hemorrhage could play additional role but, there are no studies that estimat the collective impact of different factors together on postpartum hemorrhage in Ethiopia as far as my search.

Objective: To develop and validate risk prediction model for primary postpartum hemorrhage using maternal characteristics.

Method: A hospital-based un-matched case–control study design will be conducted from 24th February 2021 to 30th April 2021. The sample size will be determined by double population proportion formula using r = 2 (ratio of control to case), 80% power and 95% confidence level and total sample size will be 810 mothers (270 cases and 540 controls). Systematic random sampling method will be used to select study units. Data will be coded and entered into Epi data version 3.2 and will be analyzed by STATA version 14 software. For model development simple binary logistic regression will be done to identify the relationship between each predictor and primary postpartum hemorrhage. Variables with p-value ≤ 0.2 from the univariate analysis will be entered into a backward stepwise multiple binary logistic regression model, and significant variables with p-value < 0.05 will be retained in the multivariate model.

The model accuracy will be checked by calculating calibration plot, the area under the ROC curve (AUC) (discrimination). To check for model goodness, Hosmer-Lemeshow goodness of fit statistics will be generated. Internal validation of the model will be calculated by bootstrapping method taking 2000 samples with replacement. The results of significant predictors will be reported as coefficients, odds ratios (AORs), with their 95% confidence intervals (CI).

Keywords: Primary post partum hemorrhage, risk prediction model, risk score,FHCSH, Ethiopia

ACRONYMS AND ABBREVIATIONS

ANC- Antenatal Care

AOR- Adjusted Odds Ratio

AUC- Area Under the Receiver Operating Characteristic Curve

CI- Confidence Interval

CS- Cesarean Section

EDHS- Ethiopian Demographic and Health Survey

FHCSH- Felege Hiwot Comprehensive Specialized Hospital

Hgb- Hemoglobin

MMR- Maternal Mortality Ratio

PIH- Pregnancy Induced Hypertension

PPH- Postpartum Hemorrhage

ROC- Receiver Operating Characteristic Curve

SDG- Sustainable Development Goals

WHO- World Health Organization

TABLE OF CONTENTS

AKKNOWLEDGEMENTS i
SUMMARY ii
ACRONYMS AND ABBREVIATIONS iii
TABLE OF CONTENTS iv
LIST OF TABLES vi
LIST OF FIGURES vii
LIST OF ANNEXES viii
1. INTRODUCTION 1
1.1. Background 1
1.2. Statement of the problem 3
1.3. Significance of the study 5
2. LITERATURE REVIEW 6
2.1. Overview of Postpartum Hemorrhage 6
2.2. Predictors of Postpartum Hemorrhage 6
2.3. Predictive models of postpartum hemorrhage 9
3. Conceptual framework 10
4. OBJECTIVES OF THE STUDY 11
4.1. General objective 11
4.2. Specific Objectives 11
5. Methods and Materials 12
5.1. Study design 12
5.2. Study setting and period 12
5.3. Population of the Study 12
5.3.1. Source population 12
5.3.2. Study population 12
5.3.3. Study Unit 12
5.4. Eligibility criteria (inclusion, exclusion) 13
5.4.1. Inclusion Criteria 13
5.4.2. Exclusion Criteria 13
5.5. Variables of the Study 13
5.5.1. Dependent variable 13

5.5.2. Independent Variables 13
5.6. Operational definition 13
5.7. Sample size and sampling methods 14
5.7.1. Sample size Determination 14
5.7.2. Sampling methods and procedure 15
5.8. Survey instruments and procedures 16
5.9. Data management and analysis 17
5.10. Data quality assurance 17
5.11. Ethical considerations 18
6. WORK PLAN AND BUDGET BREAKDOWN 19
6.1. Work plan 19
6.2. Budget breakdown 21
7. REFERENCES 22
ANNEXES 32
Annex 1: Information Sheet 32
Annex 2: Data extraction Checklist 34

LIST OF TABLES

Table 1. Sample size determination for the development and validation of risk prediction model for primary PPH among mothers delivered at FHCSH, Northwest Ethiopia, 2021. 15
Table 2. Timeline for the study of development and validation of risk prediction model for primary postpartum hemorrhage among mothers delivered at FHCSH, Northwest Ethiopia, 2021 19
Table 3: budget breakdown for development an d validation of risk prediction model for PPH, FHCSH, Northwest Ethiopia, 2021 21

LIST OF FIGURES

Figure 1. Conceptual framework for development and validation of a risk prediction model for primary PPH among mothers delivered at FHCSH, NW Ethiopia, 2021 adapted from literatures(7, 37, 42, 82, 88, 97). 10

Figure 2: Schematic presentation of sampling procedure among women delivered at FHCSH, Bahir Dar city, North West Ethiopia, 2021..... 16

LIST OF ANNEXES

Annex 1: Information Sheet 32
Annex 2: Data extraction Checklist 34

1. INTRODUCTION

1.1. Background

The world health organization (WHO) defines postpartum hemorrhage (PPH) as loss of blood of more than 500 milliliters following a vaginal delivery or more than 1000 ml following caesarian section (1). It also can be defined as any amount of vaginal bleeding that causes hemodynamic instability or that causes 10% drop in maternal hemoglobin from the baseline within 24 hours of delivery (2). Post-partum haemorrhage (PPH) that occurs within 24 hours of delivery is classified as early (primary) postpartum haemorrhage and haemorrhage which occurs after 24 hours of delivery is termed as secondary (late) postpartum haemorrhage (3). Primary postpartum hemorrhage may occur before delivery of the placenta and up to 24 hours after delivery of the fetus (4). Postpartum hemorrhage (PPH) is the most common type of obstetric hemorrhage and accounts for the majority of the 14 million cases that occur each year (5).

Postpartum hemorrhage (PPH) is the leading cause of global maternal death and accounts for approximately one-quarter of all maternal deaths worldwide (6). Subsequently, PPH has received increasing attention as a quality indicator for obstetric care (7).

Primary postpartum hemorrhage rates and PPH related deaths are increasing through time as a result of advancing maternal age, increasing rates of cesarean section, more induction and augmentation of labor, multiple births (8, 9) and maternal obesity (9, 10).

The four major causes of primary PPH were/are atony uterus (about 83%), retained products of conceptions (RPOCs) , trauma, coagulation problem, and uterine rupture (11, 12).

Postpartum hemorrhage predisposes women to a number of complications such as postpartum depression and anxiety (13), need for blood transfusion, anemia, hepatic failure, Acute Respiratory Distress Syndrome, open surgery, care in intensive care units, coagulopathy, hysterectomy and cardiac ischemia/arrest (13, 14).

Postpartum hemorrhage is a preventable condition and early, timely intervention can prevent development of this dreadful condition (15). The advent of active management of 3rd stage of labour (prophylactic uterotonics, early cord clamping and controlled cord traction to deliver the

placenta) decreases the incidence of PPH and reduce the need for maternal blood transfusion (16). The other management options of primary PPH are; Uterotonics with uterine compression, repair of perineal trauma, Evacuation of retained products of conceptions, uterine packing, uterine artery Ligation, obstetric hysterectomy and correction of coagulopathy (17).

A risk prediction model is a mathematical equation that employs risk factors/predictors to estimate the probability developing an event (18). They are multivariable processes which integrates several predictors used to predict individualized probability of development of outcome of interest (19). The use of risk prediction models in clinical reasoning and decision making in modern medicine are increasing through time for the diagnosis, prognosis, screening and management (19, 20).

Risk prediction models should be validated by either of internal validation methods which are split-sample, cross-validation, and bootstrapping methods to estimate the amount of overfitting or optimism(21, 22).

Prognosis in clinical practice is defined as a prediction of the course or outcome of a certain illness or condition, in a certain patient or individual. Clinically relevant prognoses are to be expressed as absolute risks, or absolute risk categories. Relative risks have no relevance to patients or physicians without reference to absolute probabilities (23).

Prognostic research is the use of an explicit risk score or prediction model or rule containing multiple prognostic determinants, representing the values of the predictors and their quantitative relationship to a certain prognostically relevant outcome. It is multivariable approach i,e uses a combination of factors to predict the probability of occurrence of outcome of interest in an individual client without reference to others (23). The goal of prognostic research is by nature prediction (description) of probability of health related outcome (usually dichotomous). The domain of a prognostic occurrence relation is individuals who are at risk of developing the outcome of interest (23).

1.2. Statement of the problem

The incidence of PPH has increased in both high and low income countries (24, 25). Worldwide, PPH affects about 5% of all deliveries and more than 50% of PPH associated deaths are preventable (1) . Obstetric hemorrhage is the world's leading cause of maternal mortality, responsible for an estimated 303,000 deaths annually (26). Reducing maternal mortality and morbidity from postpartum haemorrhage is a global challenge (27). Excessive bleeding after childbirth is a preventable but life threatening obstetric emergency requiring immediate response and a multidisciplinary approach (17).

Every single minute, a mother dies from complications of pregnancy and childbirth (5). Women with postpartum hemorrhage could die within 2 hours in the absence of timely and appropriate action. In the developed world, PPH is a largely preventable and manageable condition. According to reports of world health organization, in developing countries including Ethiopia, the possibility of maternal death caused by postpartum hemorrhage is 1 in 1000 deliveries. Furthermore, 60 to 99% of maternal mortality due to PPH occur in low- and middle-income countries (5, 28). Ethiopia is one of the ten countries with high maternal mortality rates which together account for 59% of all maternal deaths worldwide (29). Mothers are the center of her family's existence and maternal deaths as a result of PPH negatively affects both families and societies (30).

Ethiopia accepted and approved target 3 of the health related goals of sustainable development goals (SDGs) which aspires to reduce the maternal mortality ratio to less than 70 per 100,000 live births to be achieved by 2030 (31). Furthermore, Maternal, Newborn and Child Health were given great emphasis in the Ethiopian National Health Care Quality Strategy of 2016-2020 with a goal to reduce the maternal mortality ratio (MMR) from 412 to 199 per100,000 live births (32), but MMR was 401 per 100, 000 live births and unable to achieve the target (33). The overall maternal mortality ratio was 149 (95% CI: 136–162) in Ethiopian hospitals (34) and 412 per 100,000 livebirths according 2016 Ethiopian demographic and health survey (35). Hemorrhage is the leading cause of this direct maternal deaths (accounts for 29% of direct causes) in Ethiopia and it needs continued efforts to tackle the problem (36).

Ethiopia has developed policies and strategies that aid significant progress in maternal health care services which include; provision of misoprostol at community level, antenatal and

postnatal care, promotion of institutional births, training and availing of skilled birth attendants at all births, emergency and comprehensive obstetric care, practicing active management of the third stage of labor which reduces the incidence of PPH, and making all maternal services free of charge. (35). Despite this, the magnitude of primary postpartum hemorrhage in Ethiopia is still at its highest level and continues to remain the leading cause of maternal mortality in Ethiopia (2, 37) . This implies that Ethiopia needs much effort and evidence based decisions that guide clinical decision making regarding the causes of maternal mortality.

Majority of maternal deaths associated with PPH occur within the first 24 hrs. of birth and can be avoided through timely and appropriate management(38). Consequently, individualized risk prediction model for primary PPH could play additional role to achieve the SDG target of reducing the MMR by reducing obstetric hemorrhage related deaths in Ethiopia.

There are number of studies identifying individual risk factors for PPH but these don't reliably identify women at greatest risk by combining multiple risk factors (39-41). Additionally, literatures that tried to develop and validate individualized risk prediction model for PPH had conflicting results on the discriminatory power of the model (42-48). But, the ability to accurately predict the risk of PPH enable health professionals to take preventive and treatment measures that will decrease the frequency of PPH and the morbidity and mortality caused by it (44).

Almost all studies in Ethiopia investigate the magnitude and different factors associated with primary PPH and they are expressed interms of relative risks rather than absolute risks. Moreover, they only show the individual contribution of a factor and not the combined predictive accuracy of multiple determinants in predicting the future development of primary PPH (2, 37, 49, 50). But, it is clinically important to estimate the collective impact of different clinical and non-clinical factors together (prognostication), to support the identification of appropriate preventive and treatment measures timely (23). Nevertheless, there has been no prognostic study which integrates different factors into a risk prediction model/score to predict the probability of primary PPH in women within 24 hours of delivery up to my search. Therefore the this study is aimed at developing and internally validating a risk prediction model for primary PPH among mothers delivered at FHCSH.

1.3. Significance of the study

The results of this study will be used to predict the individualized risk of developing postpartum hemorrhage for mothers. It is also used to guide health professionals in the clinical decision making and for policy makers to design appropriate protocols for prevention, management of postpartum hemorrhage and maternal morbidity and mortality as a whole. Furthermore, it can serve as an input for researchers interested in the area.

2. LITERATURE REVIEW

2.1. Overview of Postpartum Hemorrhage

Postpartum haemorrhage (PPH) remains a primary cause of morbidity and mortality globally. In the United Kingdom, it was the second highest cause of direct maternal death in 2013–2015 (51). The incidence of PPH is higher in low and middle income countries but is also increasing in developed countries (52, 53). In a multicountry Survey on Maternal and Newborn Health the prevalence of PPH has been reported to be 1.2% and were estimated as significantly higher in the developing countries (40). In contrast, recent studies have shown an increase in the incidence of primary postpartum hemorrhage in the developed countries as well (54-56).

The four major causes of PPH include; failure of the uterus to contract after delivery(tone), lacerations of the cervix, vagina and perineum (trauma), Retained products of conceptions (Tissue) and Coagulation abnormalities (Thrombin) (4, 7, 57)

In Ethiopia, the magnitude of PPH vary from 5.8 to 16.6% (2, 37, 50, 58, 59). Furthermore, according to two different studies which were done in Jima and Kersa revealed that postpartum hemorrhage was the first leading cause of maternal mortality which accounts for 54% and 46.5% maternal mortality respectively.(60, 61)

2.2. Predictors of Postpartum Hemorrhage

a. Socio-demographic Predictors

According to world health organization multi country survey on maternal and newborn health findings, mothers with advanced age were at increased risk of PPH (62). However, population based comparative cross-sectional study results in France and Canada indicated that, PPH risk was higher among young age group women (63). Likewise studies conducted on the association between advanced maternal age and risk of PPH in china (64) and United States of America (USA) (65) showed that the risk of PPH decreases gradually with the advancement of maternal age. Similarly, studies conducted Incidence and risk factors for postpartum hemorrhage in Uganda showed that women age of 35 or above years was a risk factor for PPH (24). However other studies indicated that risk of PPH increases at advanced maternal age (66-68). In contrast a meta-analysis study on the relation between maternal characteristics and PPH did not show a relationship between maternal age and risk of PPH (69). Primary postpartum hemorrhage may occur in women without risk factors (70, 71).

A number of studies in Ethiopia indicated that the risk of PPH increases with advanced maternal age (2, 37, 72).

b. Medical Factors

According to a retrospective cohort study among women on five indian hospitals, anemia was associated with increased risks of PPH (AOR) =9.45; 95% CI 2.62 to 34.05) **(73)**. Likewise, a retrospective report from Pakistan indicated that the risk of PPH was more common among anemic women. **(74)**. However, a retrospective cohort study conducted in Scottish population on maternal and neonatal outcomes of antenatal anemia showed that anemia was significantly associated with reduced risk of PPH **(75)**. Also, a case control study on the risk factors of PPH in noway (7) and Egypt (76) revealed that maternal anemia was a predictor of PPH**.** Moreover, a cross sectional study on the association between anemic women at labour and PPH and associated factors with PPH related maternal death in referral hospitals of Mali and Senegal indicated that anemia was positively associated with PPH (77).

In a study conducted in Uganda on the incidence and risk factors for PPH, HIV sero-positive women were more likely to develop PPH (78).

A study in Ethiopia showed that the risk of PPH increased with women who had *antepartum anemia* (37).

c. Past obstetric Predictors

In a A case-control study conducted in Thailand (79) and Norway (7) to examine the risk factors associated with PPH, women with past history of PPH were more likely to have increased risk of having PPH. Inaddition, a study on the prevalence and risk factors of PPH conducted in cammeron (80) and Egypt (76) showed that past history of PPH was a predictor of PPH. Another study indicated that presvious CS was a risk factor for primary PPH (81, 82).

A study in Ethiopia showed that the risk of PPH significantly associated with previous caesarian section (2), previous PPH (2, 37).

d. Current Obstetric predictors

Literatures indicated that increased number of pregnancy is a predictor of PPH (80, 83) while another study showed that prim gravida was positively associated with primary PPH (84).

A retrospective cohort study conducted in Israel on the risk factors for early PPH in the first vaginal delivery, and obstetrical outcomes in subsequent pregnancy, hypertensive disorders of pregnancy was found to be significant risk factor for primary PPH (85). Similarly, a prospective cohort study conducted in Japan on the incidence and risk factors for postpartum hemorrhage among transvaginal deliveries, HDP was a significant predictor of PPH (86). In a study conducted in Netherlands (46) and Norway (7)showed that preeclampsia is an independent prognostic factor for PPH.

Literatures in Norway (7, 87) and London (68) showed that the risk of PPH in multiple pregnancies were 2.11 and, 2.60 times the risk in singleton pregnancies respectively.

According to Systematic Review and Meta-Analysis study, the incidence of PPH is high in women with placenta Previa (88). Additionally, a retrospective Review study in Qatar revealed that placenta Previa and emergency CS were risk factors for massive PPH (89). According to a systematic review on the prevalence and risk factors of PPH in Africa multiparty was a significant risk factor for PPH (90).

According to a retrospective Cohort Study to predict PPH, cesarean delivery was a predictor of PPH (82). A case-control study conducted on risk factors of PPH in Norway in 2017 showed that both elective and in-labor cesarean delivery were predictors of primary PPH (7). Furthermore, a prospective cohort study in Uganda identified that delivery by CS, multiple pregnancies, and macrosomia were independent predictors of PPH (24). Moreover, labor induction (87, 91), prolonged labor (58, 80, 87, 91, 92), macrosomia (24, 76-78, 80, 93), operative vaginal delivery (55, 77), placenta Previa (76, 94), preeclampsia/eclampsia (39, 93, 95), retained placenta (76), multiple pregnancy (39, 78) were risk factors significantly associated with primary postpartum hemorrhage.

A study in Ethiopia showed that the risk of PPH associated with instrumental vaginal delivery was 5.3 times **(37)**. Similarly, prolonged labour (≥ 24 hours) **(58)**, delivery by CS **(58)**, instrumental delivery **(37)** multigravidity **(2)**, multiparty **(58)**, absence of ANC follow up **(58)** were significantly associated with postpartum hemorrhage. Likewise, a prospective cohort study in Northwest Ethiopia on the effects of gestational diabetes mellitus on risk of adverse maternal

outcomes in 2020 revealed that women with gestational diabetes mellitus had about 5 times increased risk of PPH **(96)**.

2.3. Predictive models of postpartum hemorrhage

Different models developed to predict PPH in different countries showed conflicting results on the discrimination power and calibration of models developed to predict it. A systematic review for predicting risk of postpartum haemorrhage revealed that some models can be used for clinical practice while others models would not be used due to risk of bias related with absence of internal validation, insufficient external validation, and absence of handling or reporting of missing data (41).

According to a single-center retrospective study to develop a risk model to predict severe postpartum hemorrhage in patients with placenta Previa in china in 2019 provided a high decision accuracy with sensitivity and specificity of 90% and 76.5% respectively and with excellent discrimination (area under the ROC curve = 0.84.2%) and total accuracy rate of 0.795 (43). Furthermore, antepartum and antepartum/ intrapartum prediction model of postpartum hemorrhage in women with gestational hypertension or mild preeclampsia at term in Netherlands yielded moderate discrimination and good to better calibration respectively (46). On the other hand, a study conducted to develop a risk score for predicting postpartum hemorrhage in association with cesarean delivery in Thailand, Bangkok indicated that a risk score created maternal clinical features could be a useful device for predicting PPH in cesarean delivery with AUC of 64.7%, and sensitivity, specificity, positive predictive value and negative predictive value of 60.2%, 18.1%, 7.7%, and 80.2% respectively (42).

However other predictive studies on PPH revealed that prediction models have low power or it is unable to predict PPH (45).

3. Conceptual framework

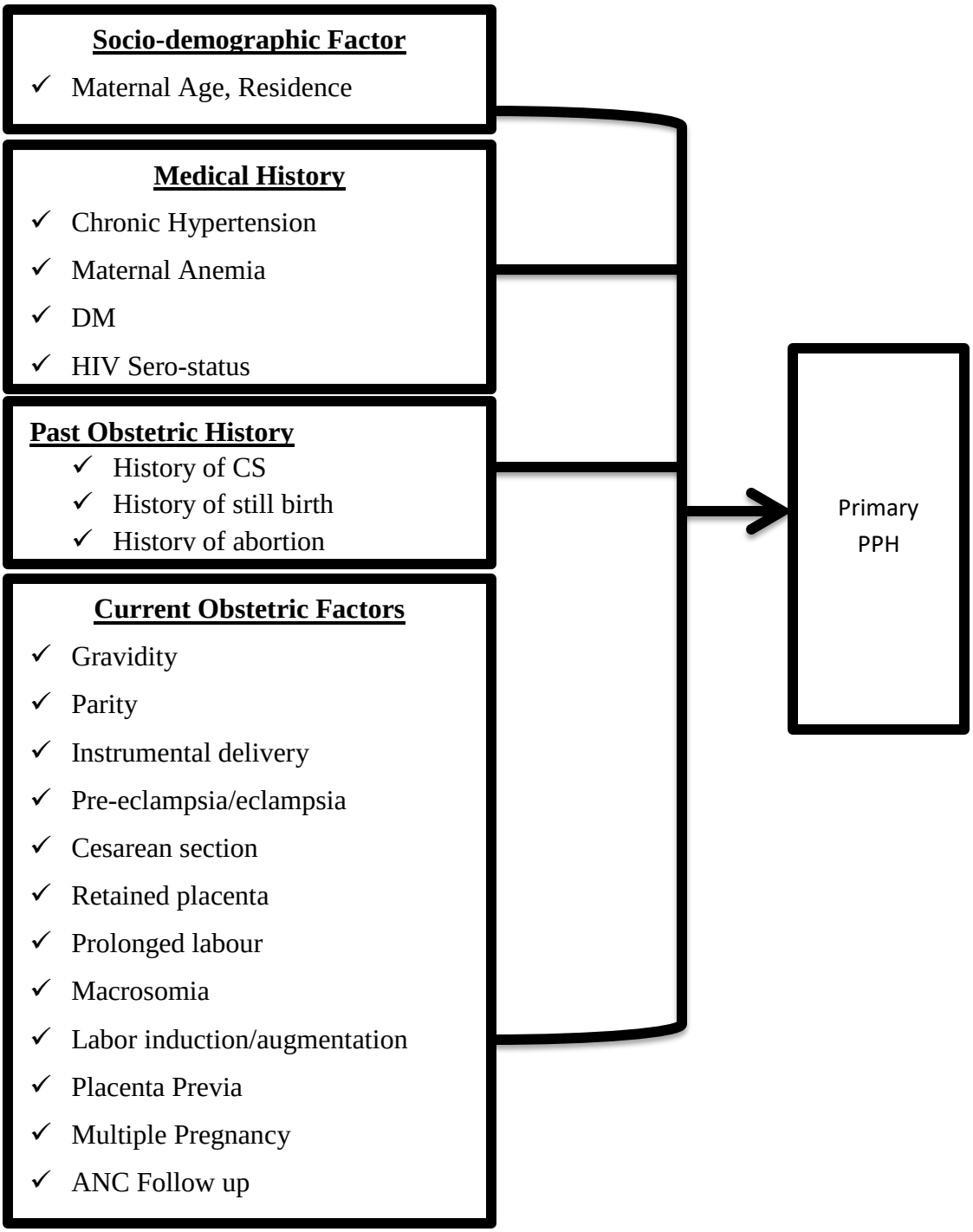

Figure 1. Conceptual framework for development and validation of a risk prediction model for primary PPH among mothers delivered at FHCSH, NW Ethiopia, 2021 adapted from literatures(7, 37, 42, 82, 88, 97).

4. OBJECTIVES OF THE STUDY

4.1. General objective

To develop a risk prediction model for primary postpartum hemorrhage among mothers delivered at FHCSH, Bahir Dar city, Northwest Ethiopia, 2021.

4.2. Specific Objectives

- ✓ To develop risk prediction model for primary postpartum hemorrhage using maternal characterstics.
- ✓ To quantify risk score for primary postpartum hemorrhage

5. Methods and Materials

5.1. Study design

An institution based unmatched case-control study will be conducted.

5.2. Study setting and period

The study will be conducted from April to March 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. FHCSH 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 northern end of the city near Lake Tana and aspires to see a healthy, productive and prosperous society and become a centre of medical service Excellency by 2029. During its establishment, it was planned to serve for 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 man power (5 obstetrician and gynecologist and 63 midwives among others) in different disciplines. It has a total 500 formal beds, 11 wards (emergency ward and Inpatient wards such as Gynecological &Obstetric, Surgical, orthopedics, Medical, Pediatric, L&D, Eye unit, NICU, psychiatrics, 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 (98).

5.3. Population of the Study

5.3.1. Source population

All mothers who give birth at FHCSH will be the source population.

5.3.2. Study population

All mothers who give birth at FCSH between April 20/2019 and April 20/2021 will be the study population.

5.3.3. Study Unit

Cases: The study unit will be selected mothers with primary postpartum hemorrhage who

delivered FHCSH in the last two years.

Controls: The study units will be selected mothers without primary postpartum hemorrhage who delivered FHCSH in the last two years.

5.4. Eligibility criteria (inclusion, exclusion)

5.4.1. Inclusion Criteria

All mothers delivered at FHCSH will be included in the study.

5.4.2. Exclusion Criteria

Mothers who delivered but have had their ANC in other health institutions, and mothers with incomplete data records will be excluded from the study.

5.5. Variables of the Study

5.5.1. Dependent variable

- ✓ Primary postpartum hemorrhage

5.5.2. Independent Variables

Socio-demographic variables

- ✓ Maternal age, residence

Medical History Factors

- ✓ Chronic Hypertension, , Maternal Anemia, DM, HIV Sero-status

Past Obstetric History

- ✓ Previous history of CS, history of still birth, history of abortion

Current Obstetric Factors

- ✓ Gravidity, parity, multiple pregnancy, pre-eclampsia/eclampsia, Macrosomia, GDM, episiotomy, mode of delivery, Labor augmentation/induction, prolonged labor, abnormal placentation, Retained placenta

5.6. Operational definition

PPH: An abnormal bleeding after vaginal delivery of ≥ 500ml or ≥ 1000ml after cesarean delivery OR bleeding that causes maternal hemodynamic instability (38).

Primary PPH: Bleeding that occurs within 24 hours of delivery

Late PPH: Abnormal bleeding from the vaginal tract that occurs from 24 hours to 6 weeks of postpartum period (38).

Sever PPH: Severe PPH was defined as blood loss ≥100 ml after vaginal delivery or ≥1500 mL after CS delivery OR bleeding necessitating need for blood transfusion for excessive bleeding at the time of delivery

Macrosomia: A baby who weighs more than 8 pounds, 13 ounces (4,000 grams) at birth, regardless of his or her gestational age (99)

Gestational Diabetes Mellitus: glucose intolerance (fasting plasma glucose 5.1 mmol/l (92 mg/dl) or 2-h plasma glucose 8.5 mmol/l (153 mg/dl) following a 75 g oral glucose load) first detected during pregnancy (100).

Pre-eclampsia: HTN and proteinuria (≥2 on dipstick) and/or end-organ damage which occurs after 20 completed weeks of gestation and resolves 6 weeks postpartum (101).

Eclampsia: grand mal seizure or comma that occurs during pregnancy, labor or within 7 days of postpartum unrelated to other cerebral conditions (101).

Ascertainment of cases: For this study the occurrence of primary PPH will be ascertained based on the information charted. If PPH is reported on the chart, it will be included in list of cases.

5.7. Sample size and sampling methods

5.7.1. Sample size Determination

The sample size will be determined by using double population proportion formula using open Epi software with the assumption of 95% confidence interval, 80% power, and 5% margin of error, with 1:2 ratio of cases to controls. Variables that were associated with PPH in different literatures will be used to calculate the sample size and the variables' proportions/odds ratios which give highest sample size will be used as the final sample size for the study.

$$n1 = \frac{[Za/2\sqrt{(1 + 1/r)\, pq} + Z\beta\sqrt{\mathrm{p1q1} + p2q2/r}]2}{(p1 - p2)2}$$

Where; $n_2 = n_1 r$ and $p = (p_1 + rp_2)/(1+r)$

Table 1. Sample size determination for the development and validation of risk prediction model for primary PPH among mothers delivered at FHCSH, Northwest Ethiopia, 2021.

Predictor variable	**Percent of exposure among control**	**Percent of exposure among cases**	**OR**	**Case to control ratio**	**Sample size**
Mode of delivery (instrumental vaginal) (7)	12.2%	20.0%	2.26	1:2	404
Severe pre-eclampsia or HELLP syndrome (7)	2.6%	8..72%	3.58	1:2	534
Mode of delivery(In-labor cesarean) (7)	11.9%	59.9%	2.71	1:2	266
Anemia (Hgb ≤ 9.0 g/dL) (7)	1.9%	7.0%	4.11	1:2	555
Labor augmentation (7)	38.7%	55.2%	1.95	1:2	348
Oxytocin during labour (102)	49%	68.8%	2.3	1:2	239
Parity (0) (7)	48.9	59.57	1.54	1:2	810

Consequently, the sample size calculated using parity 0 (7) as a risk factor for postpartum hemorrhage yielded the largest sample size which was 810. Therefore, it will be the final sample size for this study.

5.7.2. Sampling methods and procedure

Systematic random sampling method will be employed to select cases and controls using registration number of delivered mothers. First all mothers delivered at FHCSH from April 30/2016 to 30/2021 will be identified from the delivery registration book. Then cases (women who develop primary PPH) and controls (women who didn't develop primary PPH) will be identified. After that mothers who meet the exclusion criteria will be excluded from the study. Thereafter, a separate sampling frame will be prepared for cases and controls who meet the eligibility criteria. Finally cases will be selected by a sampling interval k= 3 (811/270 ≈ 3) and controls will be selected by a sampling interval k= 14 (7980/540 =14).

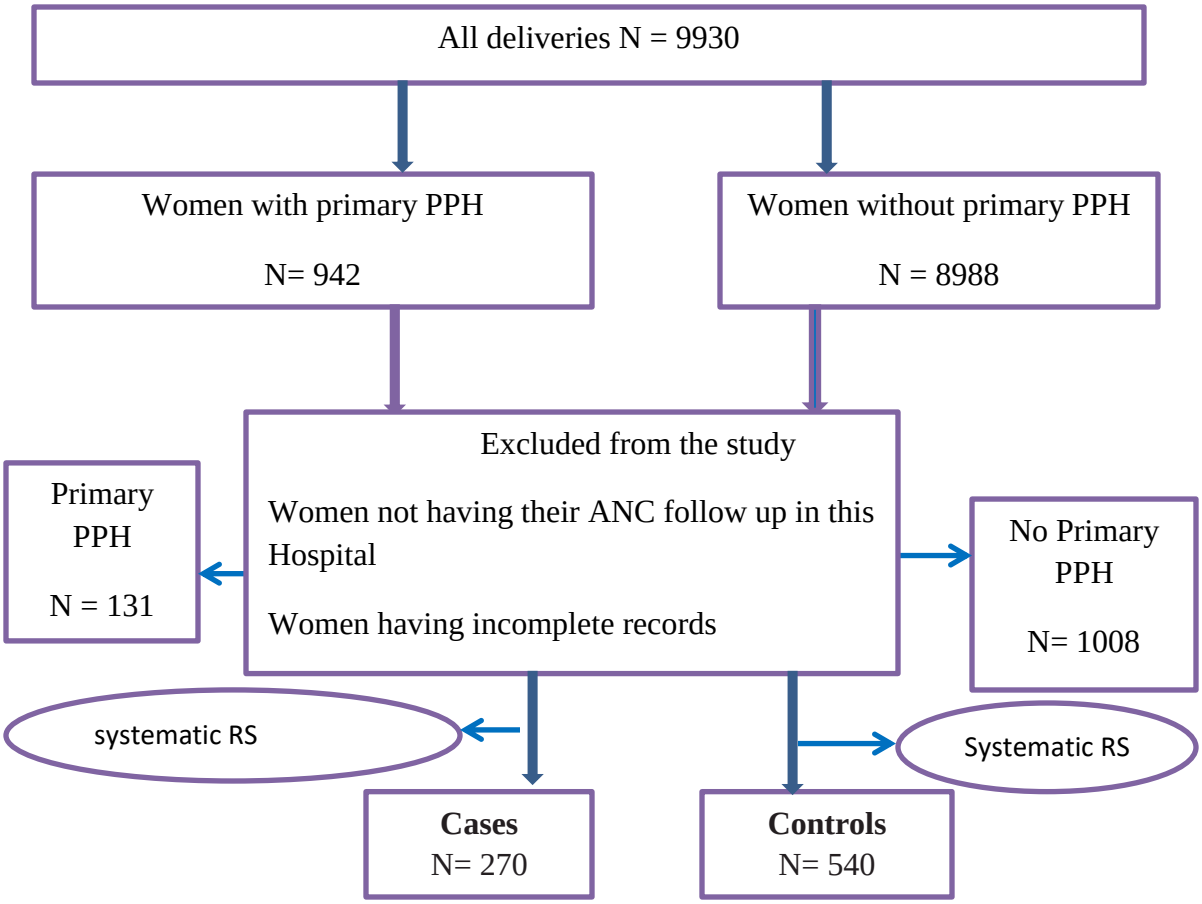

Figure 2: Schematic presentation of sampling procedure among women delivered at FHCSH, Bahir Dar city, North West Ethiopia, 2021.

5.8. Survey instruments and procedures

Data will be collected using structured checklist through chart review. The checklist will be developed after reviewing of various relevant literatures. It consists of socio-demographic (Maternal age, Educational status, Residence, marital status) medical history such as; HTN, DM, anemia (hgb/hematocrit measurements in red blood cells), ANC utilization, past obstetric history (history of still birth and abortion, previous history CS, history of PPH) and current obstetric factors such as; gravidity, parity, multiple pregnancy, pre-eclampsia/eclampsia, placenta previa, GDM, mode of delivery. The dependent variable will be ascertained with a diagnosis PPH by a physician, midwife or other health professionals and recorded on womens' medical charts.

5.9. Data management and analysis

Data will be entered into EPI DATA version 3.2 Software and then exported to STATA version 14 software for analyzsis. Missing data will be assumed as missing at random and will be managed by multiple imputations. Sensitivity analysis will be done to check whether the assumption of missing at random (MAR) is valid or not. Descriptive statistics will be presented by using frequencies, proportions, graph and tables. Bivariable analysis will be conducted to screen the possible determinants of primary PPH and variables with p-values of ≤ 0.2 and important variables for the objective of the study based on literature review will be entered to the multivariable model. Binary logistic regression model will be used to identify associated factors and backward stepwise variable selection method will be employed. In multi-variable binary logistic regression analysis, factors associated with primary PPH will be identified and retained using their Adjusted Odds Ratio (AOR) with the corresponding 95% CI. Predictors that will have association with the dependent variable will be reported using their coefficients, odds ratios, risk scores and 95% CIs. The model accuracy will be assessed by computing discrimination (area under the receiver operating characteristic curve (ROC AUC)), calibration (by calibration plot). An AUC value of greater than 0.5 will be considered a measure of the good performance of the model. The regression coefficients, ORs with its 95% confidence levels, and the AUC will be adjusted for over fitting or over-optimism using bootstrapping technique. Model goodness of fit test (calibration) will be assessed by Hosmer- Lemeshow test. The model will be assumed to be well fitted when Hosmer-Lemeshow goodness of fit test p-value is greater than 0.05. Internal validation for the model will be performed by bootstrapping method which can be calculated by bootstrapping 2000 samples with replacement. Primary PPH score will be developed by dividing each variables'AORs by the smallest significant odds ratio and rounding to the nearest integers. Finally, the total score for each woman will be calculated by assigning the points for each variable present and summing them up. Multicollinearity will be checked by variance inflation factor (VIF) and assumed to be problematic when the VIF exceeds 10.

5.10. Data quality assurance

Data quality assurance measures will be undertaken before, during and after data collection. Before data collection, a structured, pretested data extraction checklist will be prepared by the principal investigator. The pretest will be conducted at 28 (9 cases and 19 controls) mothers deliverd at Tibebe Gion specialized teaching hospital (TGSTH). Furthermore, data collectors

(six Bsc. midwives) will be recruited and given 2 days training on the objectives of the study, overall data collection procedures and contents of the checklist by the principal investigator and one personnel, who own Bachelor of Science (BSc) Degree in Midwifery, will supervise the data collection.

During the data collection process, data will be checked daily by the supervisors for completeness, eligibility, and appropriateness. Any inconsistent or missing data will be detected and the questionnaire/checklist will be returned to the data collectors for checks and corrections. The principal investigator will select 3% of the checklists completed and crosschecked it with the maternal records to check whether the information was collected accurately.

5.11. Ethical considerations

Before the start of the study, the proposal will be approved by and ethical clearance letter obtained from Ethical Review Board (IRB) of Bahir Dar University. Written collaboration and consent letter will be obtained from Felege Hiwot Comprehenssive Specialized Hospital. The data extraction checklist did not include personal identifiers in order to protect confidentiality of patients.

6. WORK PLAN AND BUDGET BREAKDOWN

6.1. Work plan

Table 2. Timeline for the study of development and validation of risk prediction model for primary postpartum hemorrhage among mothers delivered at FHCSH, Northwest Ethiopia, 2021.

No	Tasks to be performed	Responsible person(S)	Months of the work plan							
			Nov.	Dec	Jan.	Feb.	Mar.	Apr.	May	Jun.
1	Title selection	Investigator								
2	Title defense and submission	Investigator								
3	Proposal development	Investigator								
4	1st draft proposal submission	Investigator								
5	Advisor send back commented document	Advisors								
6	Second draft proposal submission	Investigator								
7	Advisor send back commented document	Advisors								
8	Final proposal submission	Investigator								
9	Proposal defense	Investigator								
10	Submitting final proposal to the dep.	Investigator								
11	Obtain Ethical clearance	IRB of BDU								
12	Reviewing data collection tools	Investigator								

13	**Duplication of questionnaire & Pretest**	**Investigator**								
14	**Data collection**	**Data collector**								
15	**Data entry & analysis**	**Investigator**								
16	**1st & 2nd draft thesis submission**	**Investigator**								
17	**Advisors send back commented document**	**Advisors**								
18	**Submitting final thesis to Dep.**	**Investigator**								
19	**Mock defense**	**Investigator**								
20	**Final thesis defense**	**Investigator**								

6.2. Budget breakdown

Table 1: budget breakdown for development an d validation of risk prediction model for PPH, FHCSH, Northwest Ethiopia, 2021

Budget Category	**Personnel/item**	**Multiplying factor**	**Unit Cost in birr**	**Total Cost (Birr)**
1. Training				
Trainer	1 persons	1 day	150	150
Data collector & supervisor	7 persons	1day	100	700
Refreshment(tea break and launch)			1000	1000
Subtotal				**1,850**
2. Personnel				
Pretest	1person	41 questioner	15br/questioner	615
Data collector	6 persons	810 questioner	25br/questioner	16,200
Supervisor	1 persons	810 questioner	15br/questioner	12,150
Subtotal				**28,965**
3. **Transportation *Subtotal***				**300**
4. Communication				**800**
5. Supplies				
Pen	Each	12	10	120
Pencil	Each	12	3	36
Sanitizer	Bottle	23	30	690
Face mask	Each	23	10	230
Duplicate questionnaire	Page	3240	1	3,240
Subtotal				**4,316**
Total	**36,231**			
10% contingency	**3,623**			
Grand total	**39,854 ETB**			

7. REFERENCES

1. Organization WH. WHO recommendations for the prevention and treatment of postpartum haemorrhage: World Health Organization; 2012.
2. Habitamu D, Goshu YA, Zeleke LB. The magnitude and associated factors of postpartum hemorrhage among mothers who delivered at Debre Tabor general hospital 2018. BMC Research Notes. 2019;12(1):618.
3. Oyelese Y, Ananth CV. Postpartum hemorrhage: epidemiology, risk factors, and causes. Clinical obstetrics and gynecology. 2010;53(1):147-56.
4. Evensen A, Anderson JM, Fontaine P. Postpartum hemorrhage: prevention and treatment. American family physician. 2017;95(7):442-9.
5. Organization WH. Reducing the global burden: postpartum haemorrhage. Making Pregnancy Safer. 2007;4:1-8.
6. https://ashpublications.org/hematology/article/2020/1/542/474319/Prevention-and-treatment-of-postpartum-hemorrhage
7. Nyfløt LT, Sandven I, Stray-Pedersen B, Pettersen S, Al-Zirqi I, Rosenberg M, et al. Risk factors for severe postpartum hemorrhage: a case-control study. BMC pregnancy and childbirth. 2017;17(1):17.
8. Ford J, Roberts C, Simpson J, Vaughan J, Cameron C. Increased postpartum hemorrhage rates in Australia. International Journal of Gynecology & Obstetrics. 2007;98(3):237-43.
9. Fyfe EM, Thompson JM, Anderson NH, Groom KM, McCowan LM. Maternal obesity and postpartum haemorrhage after vaginal and caesarean delivery among nulliparous women at term: a retrospective cohort study. BMC pregnancy and childbirth. 2012;12(1):112.
10. Blomberg M. Maternal obesity and risk of postpartum hemorrhage. Obstetrics & Gynecology. 2011;118(3):561-8.
11. Ahmadzia HK, Phillips JM, Katler QS, James AH. Tranexamic acid for prevention and treatment of postpartum hemorrhage: An update on management and clinical outcomes. Obstetrical & gynecological survey. 2018;73(10):587-94.
12. Ford JB, Patterson JA, Seeho SK, Roberts CL. Trends and outcomes of postpartum haemorrhage, 2003-2011. BMC pregnancy and childbirth. 2015;15(1):334.

13. Dunning T, Harris J, Sandall J. Women and their birth partners' experiences following a primary postpartum haemorrhage: a qualitative study. BMC pregnancy and childbirth. 2016;16(1):80.
14. Milman N. Postpartum anemia I: definition, prevalence, causes, and consequences. Annals of hematology. 2011;90(11):1247-53.
15. https://medcraveonline.com/OGIJ/postpartum-hemorrhage-a-major-killer-of-woman-review-of-current-scenario.html
16. Begley CM, Gyte GM, Devane D, McGuire W, Weeks A, Biesty LM. Active versus expectant management for women in the third stage of labour. Cochrane database of systematic reviews. 2019(2).
17. Sultana R, Manzoor S, Humayun S. Primary postpartum hemorrhage: risk factors, causes and maternal outcome. Journal of the Society of Obstetrics and Gynaecologists of Pakistan. 2020;10(1):40-6.
18. Grant SW, Collins GS, Nashef SAM. Statistical Primer: developing and validating a risk prediction model†. European Journal of Cardio-Thoracic Surgery. 2018;54(2):203-8.
19. Collins GS, Mallett S, Omar O, Yu L-M. Developing risk prediction models for type 2 diabetes: a systematic review of methodology and reporting. BMC medicine. 2011;9(1):103.
20. Moons KG, Kengne AP, Woodward M, Royston P, Vergouwe Y, Altman DG, et al. Risk prediction models: I. Development, internal validation, and assessing the incremental value of a new (bio) marker. Heart. 2012;98(9):683-90.
21. Steyerberg EW, Harrell Jr FE, Borsboom GJ, Eijkemans M, Vergouwe Y, Habbema JDF. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. Journal of clinical epidemiology. 2001;54(8):774-81.
22. Wolbers M, Koller MT, Witteman JC, Steyerberg EW. Prognostic models with competing risks: methods and application to coronary risk prediction. Epidemiology. 2009:555-61.
23. Grobbee DE, Hoes AW. Clinical epidemiology: principles, methods, and applications for clinical research: Jones & Bartlett Publishers; 2014.
24. Ononge S, Mirembe F, Wandabwa J, Campbell OM. Incidence and risk factors for postpartum hemorrhage in Uganda. Reprod Health. 2016;13:38.

25. Esteves-Pereira AP, Deneux-Tharaux C, Nakamura-Pereira M, Saucedo M, Bouvier-Colle M-H, Leal MdC. Caesarean delivery and postpartum maternal mortality: a population-based case control study in Brazil. PloS one. 2016;11(4):e0153396.
26. Bongaarts J. WHO, UNICEF, UNFPA, World Bank Group, and United Nations Population Division Trends in Maternal Mortality: 1990 to 2015 Geneva: World Health Organization, 2015. Population and Development Review. 2016;42(4):726-.
27. Finlayson K, Downe S, Vogel JP, Oladapo OT. What matters to women and healthcare providers in relation to interventions for the prevention of postpartum haemorrhage: a qualitative systematic review. PloS one. 2019;14(5):e0215919.
28. Organization WH. Priority diseases and reasons for inclusion. Postpartum haemorrhage. 2018.
29. Organization WH. Trends in maternal mortality: 1990-2015: estimates from WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division: World Health Organization; 2015.
30. B-Lynch C, Keith L, Lalonde A, Karoshi M. A Textbook of Postpartum Hemorrhage: A Comprehensive Guide to Evaluation. Management and Surgical Intervention. 2006.
31. DU CR. Sustainable development goals. 2016.
32. ETHIOPIAN NATIONAL HEALTH CARE QUALITY STRATEGY I 2016-2020: Transforming the Quality of Health Care in Ethiopia. 2016.
33. WHO U. UNFPA, World Bank Group, and the United Nations Population Division. Trends in Maternal Mortality: 2000 to 2017. Geneva. World Health Organization. 2019.
34. Geleto A, Chojenta C, Taddele T, Loxton D. Association between maternal mortality and caesarean section in Ethiopia: a national cross-sectional study. BMC Pregnancy and Childbirth. 2020;20(1):1-11.
35. Csa I. Central statistical agency (CSA)[Ethiopia] and ICF. Ethiopia demographic and health survey, Addis Ababa, Ethiopia and Calverton, Maryland, USA. 2016.
36. Mekonnen W, Gebremariam A. Causes of maternal death in Ethiopia between 1990 and 2016: systematic review with meta-analysis. Ethiopian Journal of Health Development. 2018;32(4).

37. Kebede BA, Abdo RA, Anshebo AA, Gebremariam BM. Prevalence and predictors of primary postpartum hemorrhage: An implication for designing effective intervention at selected hospitals, Southern Ethiopia. PloS one. 2019;14(10):e0224579.
38. Organization WH. WHO recommendations for the prevention and treatment of postpartum haemorrhage: Evidence base. WHO Guidelines Approved by the Guidelines Review Committee Geneva, Switzerland: WHO Library. 2012;48.
39. Nyfløt LT, Sandven I, Stray-Pedersen B, Pettersen S, Al-Zirqi I, Rosenberg M, et al. Risk factors for severe postpartum hemorrhage: a case-control study. BMC Pregnancy Childbirth. 2017;17(1):17.
40. Sheldon W, Blum J, Vogel J, Souza J, Gülmezoglu A, Winikoff B, et al. Postpartum haemorrhage management, risks, and maternal outcomes: findings from the World Health Organization Multicountry Survey on Maternal and Newborn Health. BJOG: An International Journal of Obstetrics & Gynaecology. 2014;121:5-13.
41. Neary C, Naheed S, McLernon DJ, Black M. Predicting risk of postpartum haemorrhage: a systematic review. BJOG : an international journal of obstetrics and gynaecology. 2021;128(1):46-53.
42. Suta J, Phaloprakarn C. A risk score for predicting postpartum hemorrhage in association with cesarean delivery. Thai Journal of Obstetrics and Gynaecology. 2015:3-11.
43. Chen C, Liu X, Chen D, Huang S, Yan X, Liu H, et al. A risk model to predict severe postpartum hemorrhage in patients with placenta previa: a single-center retrospective study. Annals of Palliative Medicine. 2019;8(5):611-21.
44. Dunkerton SE, Jeve YB, Walkinshaw N, Breslin E, Singhal T. Predicting postpartum hemorrhage (PPH) during cesarean delivery using the Leicester PPH Predict tool: a retrospective cohort study. American journal of perinatology. 2018;35(2):163-9.
45. Prata N, Hamza S, Bell S, Karasek D, Vahidnia F, Holston M. Inability to predict postpartum hemorrhage: insights from Egyptian intervention data. BMC pregnancy and childbirth. 2011;11(1):97.
46. Koopmans CM, Van der Tuuk K, Groen H, Doornbos JP, De Graaf IM, Van Der Salm PC, et al. Prediction of postpartum hemorrhage in women with gestational hypertension or mild preeclampsia at term. Acta obstetricia et gynecologica Scandinavica. 2014;93(4):399-407.

47. Goad L, Fabbri SE, Rockhill K, Heyborne K. Developing and Validating a Prediction Model for Postpartum Hemorrhage at a Single Safety-net Tertiary Care Center [11M]. Obstetrics & Gynecology. 2020;135:137S.
48. Neary C, Naheed S, McLernon DJ, Black M. Predicting risk of postpartum haemorrhage: a systematic review. BJOG: An International Journal of Obstetrics & Gynaecology. 2020;128(1):46-53.
49. Bekele G, Terefe G, Sinaga M, Belina S. Utilization of non-pneumatic anti-shock garment and associated factors for postpartum hemorrhage management among health care professionals' in public hospitals of Jimma zone, south-West Ethiopia, 2019. Reproductive Health. 2020;17(1):1-10.
50. Gudeta T, Kebede D, Nigeria G, Dow M, Hassen S. Magnitude of post-partum hemorrhage among women who received postpartum care at Bedele hospital south west, Ethiopia, 2018. J Preg Child Health. 2018;5(396):2.
51. Knight M, Kenyon S, Brocklehurst P, Neilson J, Shakespeare J, Kurinczuk J. Saving lives, improving mothers' care: lessons learned to inform future maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2009-2012. 2017.
52. Maswime S, Buchmann E. Causes and avoidable factors in maternal death due to cesarean-related hemorrhage in South Africa. International Journal of Gynecology & Obstetrics. 2016;134(3):320-3.
53. van Stralen G, von Schmidt auf Altenstadt JF, Bloemenkamp KW, van Roosmalen J, Hukkelhoven CW. Increasing incidence of postpartum hemorrhage: the Dutch piece of the puzzle. Acta obstetricia et gynecologica Scandinavica. 2016;95(10):1104-10.
54. Lutomski J, Byrne B, Devane D, Greene R. Increasing trends in atonic postpartum haemorrhage in Ireland: an 11-year population-based cohort study. BJOG: An International Journal of Obstetrics & Gynaecology. 2012;119(3):306-14.
55. Nakagawa K, Yamada T, Cho K, Akaishi R, Kohgo Y, Hanatani K. Independent risk factors for postpartum haemorrhage. Critical Care Obstetrics and Gynecology. 2016;2(2):10.
56. Goueslard K, Revert M, Iacobelli S, Cotenet J, Roussot A, Combier E. Incidence and Risk Factors of Severe Post-Partum Haemorrhage: A Nationwide Population-Based Study from a Hospital Database. Quality in Primary Care. 2017;25(2):55-62.

57. National Partnership for Maternal Safety Consensus Bundle on Obstetric Hemorrhage. Journal of midwifery & women's health. 2015;60(6):789.
58. Temesgen M. Magnitude of Postpartum Hemorrhage among Women Delivered at Dessie Referral Hospital, South Woll, Amhara Region, Ethiopia. J Women's Health Care. 2017;6(391):2167-0420.1000391.
59. Tiruneh B, McLelland G, Plummer V. Incidence and Mortality Associated with Primary Postpartum Haemorrhage Following In-Hospital Births in Northwest Ethiopia. Available at SSRN 3566174. 2020.
60. Legesse T, Abdulahi M, Dirar A. Trends and causes of maternal mortality in Jimma University specialized hospital, Southwest Ethiopia: a matched case–control study. International journal of women's health. 2017;9:307.
61. Tesfaye G, Loxton D, Chojenta C, Assefa N, Smith R. Magnitude, trends and causes of maternal mortality among reproductive aged women in Kersa health and demographic surveillance system, eastern Ethiopia. BMC women's health. 2018;18(1):198.
62. Sheldon WR, Blum J, Vogel JP, Souza JP, Gülmezoglu AM, Winikoff B. Postpartum haemorrhage management, risks, and maternal outcomes: findings from the World Health Organization Multicountry Survey on Maternal and Newborn Health. BJOG : an international journal of obstetrics and gynaecology. 2014;121 Suppl 1:5-13.
63. Bonnet MP, Basso O, Bouvier-Colle MH, Dupont C, Rudigoz RC, Fuhrer R, et al. Postpartum haemorrhage in Canada and France: a population-based comparison. PLoS One. 2013;8(6):e66882.
64. Lao TT, Sahota DS, Cheng YK, Law LW, Leung TY. Advanced maternal age and postpartum hemorrhage - risk factor or red herring? The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2014;27(3):243-6.
65. Cavazos-Rehg PA, Krauss MJ, Spitznagel EL, Bommarito K, Madden T, Olsen MA, et al. Maternal age and risk of labor and delivery complications. Matern Child Health J. 2015;19(6):1202-11.
66. Arya S, Mulla ZD, Plavsic SK. Outcomes of women delivering at very advanced maternal age. Journal of Women's Health. 2018;27(11):1378-84.

67. Radoń-Pokracka M, Adrianowicz B, Płonka M, Danił P, Nowak M, Huras H. Evaluation of Pregnancy Outcomes at Advanced Maternal Age. Open Access Macedonian Journal of Medical Sciences. 2019;7(12):1951.
68. Briley A, Seed PT, Tydeman G, Ballard H, Waterstone M, Sandall J, et al. Reporting errors, incidence and risk factors for postpartum haemorrhage and progression to severe PPH: a prospective observational study. BJOG : an international journal of obstetrics and gynaecology. 2014;121(7):876-88.
69. Durmaz A, Komurcu N. Relationship between maternal characteristics and postpartum hemorrhage: a meta-analysis study. LWW; 2018.
70. Bateman BT, Berman MF, Riley LE, Leffert LR. The epidemiology of postpartum hemorrhage in a large, nationwide sample of deliveries. Anesthesia and analgesia. 2010;110(5):1368-73.
71. James AH, McLintock C, Lockhart E. Postpartum hemorrhage: when uterotonics and sutures fail. American journal of hematology. 2012;87 Suppl 1:S16-22.
72. Asefa U, Ayele WM. Adverse Obstetrical and Perinatal Outcomes Among Advanced Age Pregnant Mothers in Northeast Ethiopia: A Comparative Cross-Sectional Study. International Journal of Women's Health. 2020;12:1161.
73. Nair M, Choudhury MK, Choudhury SS, Kakoty SD, Sarma UC, Webster P, et al. Association between maternal anaemia and pregnancy outcomes: a cohort study in Assam, India. BMJ Global Health. 2016;1(1).
74. Mahmood T, Rehman AU, Tserenpil G, Siddiqui F, Ahmed M, Siraj F, et al. The association between Iron-deficiency Anemia and adverse pregnancy outcomes: a retrospective report from Pakistan. Cureus. 2019;11(10).
75. Rukuni R, Bhattacharya S, Murphy MF, Roberts D, Stanworth SJ, Knight M. Maternal and neonatal outcomes of antenatal anemia in a Scottish population: a retrospective cohort study. Acta obstetricia et gynecologica Scandinavica. 2016;95(5):555-64.
76. El Badawy A, Waly E, Zaitoun N, Abo-Elwan Y. Assessment of Risk Factors for Primary Postpartum Hemorrhage at Zagazig University Hospitals. Zagazig University Medical Journal. 2017;23(2):1-9.

77. Tort J, Rozenberg P, Traoré M, Fournier P, Dumont A. Factors associated with postpartum hemorrhage maternal death in referral hospitals in Senegal and Mali: a cross-sectional epidemiological survey. BMC pregnancy and childbirth. 2015;15(1):235.
78. Ononge S, Mirembe F, Wandabwa J, Campbell OM. Incidence and risk factors for postpartum hemorrhage in Uganda. Reproductive health. 2016;13(1):1-7.
79. Prapawichar P, Ratinthorn A, Utriyaprasit K, Viwatwongkasem C. Maternal and health service predictors of postpartum hemorrhage across 14 district, general and regional hospitals in Thailand. BMC Pregnancy and Childbirth. 2020;20(1):172.
80. Halle-Ekane G, Emade F, Bechem N, Palle J, Fongaing D, Essome H, et al. Prevalence and risk factors of primary postpartum hemorrhage after vaginal deliveries in the Bonassama District Hospital, Cameroon. International Journal of Tropical Disease & Health. 2016;13(2):1-12.
81. Ekin A, Gezer C, Solmaz U, Taner CE, Dogan A, Ozeren M. Predictors of severity in primary postpartum hemorrhage. Arch Gynecol Obstet. 2015;292(6):1247-54.
82. Dunkerton SE, Jeve YB, Walkinshaw N, Breslin E, Singhal T. Predicting Postpartum Hemorrhage (PPH) during Cesarean Delivery Using the Leicester PPH Predict Tool: A Retrospective Cohort Study. Am J Perinatol. 2018;35(2):163-9.
83. Shan D, Qiu P-Y, Wu Y-X, Chen Q, Li A-L, Ramadoss S, et al. Pregnancy outcomes in women of advanced maternal age: a retrospective cohort study from China. Scientific reports. 2018;8(1):1-9.
84. Mousa HA, Blum J, Abou El Senoun G, Shakur H, Alfirevic Z. Treatment for primary postpartum haemorrhage. The Cochrane database of systematic reviews. 2014;2014(2):Cd003249.
85. Buzaglo N, Harlev A, Sergienko R, Sheiner E. Risk factors for early postpartum hemorrhage (PPH) in the first vaginal delivery, and obstetrical outcomes in subsequent pregnancy. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2015;28(8):932-7.
86. Fukami T, Koga H, Goto M, Ando M, Matsuoka S, Tohyama A, et al. Incidence and risk factors for postpartum hemorrhage among transvaginal deliveries at a tertiary perinatal medical facility in Japan. PLoS One. 2019;14(1):e0208873.

87. Hiersch L, Bergel-Bson R, Asher D, Aviram A, Gabby-Benziv R, Yogev Y, et al. Risk factors for post-partum hemorrhage following vacuum assisted vaginal delivery. Archives of Gynecology and Obstetrics. 2017;295(1):75-80.
88. Fan D, Xia Q, Liu L, Wu S, Tian G, Wang W, et al. The Incidence of Postpartum Hemorrhage in Pregnant Women with Placenta Previa: A Systematic Review and Meta-Analysis. PLoS One. 2017;12(1):e0170194.
89. Amu O, Saleh H, Al Ibrahim A. "Incidence and Determinants of Massive Post Partum Haemorrhage: A Two Year Retrospective Review from a Multiethnic Population". EC Gynaecology 8.4 (2019): 205-214. 2019.
90. Bestman PL, Pan X, Luo J. The Prevalence and Risk Factors of Post-Partum Haemorrhage in Africa: A systematic review. 2019.
91. Traoré Y, Téguété I, Bocoum A, Traoré M, Dao S, Bomini MK, et al. Management and Prognosis of Early Postpartum Hemorrhage in African Low Setting Health. Open Journal of Obstetrics and Gynecology. 2018;8(1):1-9.
92. Ngwenya S. Postpartum hemorrhage: incidence, risk factors, and outcomes in a low-resource setting. Int J Womens Health. 2016;8:647-50.
93. Fukami T, Koga H, Goto M, Ando M, Matsuoka S, Tohyama A, et al. Incidence and risk factors for postpartum hemorrhage among transvaginal deliveries at a tertiary perinatal medical facility in Japan. PloS one. 2019;14(1):e0208873.
94. Huang Y, Bao Y, Qu X, Yuan L, Ying H. Factors associated with different levels of postpartum hemorrhage in patients experiencing blood transfusion during cesarean section. Int J Clin Exp Med. 2016;9(8):16675-81.
95. Ngwenya S. Postpartum hemorrhage: incidence, risk factors, and outcomes in a low-resource setting. International journal of women's health. 2016;8:647.
96. Muche AA, Olayemi OO, Gete YK. Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia. BMC pregnancy and childbirth. 2020;20(1):73.
97. Lao TT, Sahota DS, Cheng YK, Law LW, Leung TY. Advanced maternal age and postpartum hemorrhage–risk factor or red herring? The Journal of Maternal-Fetal & Neonatal Medicine. 2014;27(3):243-6.
98. Felege Hiwot Comprehensive Specialized Hospital 2012 EFY Annual Report. 2012 E.C.

99. Ye J, Torloni MR, Ota E, Jayaratne K, Pileggi-Castro C, Ortiz-Panozo E, et al. Searching for the definition of macrosomia through an outcome-based approach in low-and middle-income countries: a secondary analysis of the WHO Global Survey in Africa, Asia and Latin America. BMC pregnancy and childbirth. 2015;15(1):1-10.
100. Organization WH. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. World Health Organization, 2013.
101. Obstetricians ACo, Gynecologists. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. Obstetrics and gynecology. 2013;122(5):1122-31.
102. Belghiti J, Kayem G, Dupont C, Rudigoz R-C, Bouvier-Colle M-H, Deneux-Tharaux C. Oxytocin during labour and risk of severe postpartum haemorrhage: a population-based, cohort-nested case–control study. BMJ open. 2011;1(2).

ANNEXES

Annex 1: Information Sheet

Title of the Research Project: Development of a risk prediction model for primary postpartum hemorrhage among mothers delivered at FHCSH, Bahir Dar city, Northwest Ethiopia, 2021.

Name of Investigator: Anteneh Kassa (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: To develop a risk prediction model for primary postpartum hemorrhage among mothers delivered at FHCSH, Bahir Dar city, Northwest Ethiopia, 2021.

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

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from the medical chart, it will 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 will be 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 for those who survived and other starting hemodialysis., the research work will have a paramount direct benefit for health care planners and managers.

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

Person to contact: This research project will be 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.

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

Cell phone: +251- 9 18314019, E-mail: weproud16@gmail.com

Yihun Mulugeta (Associate professor of epidemiology and global health), Bahir Dar University, College of Health Science and Medicine, School of Public Health, Department of Biostatistics and Epidemiology, main advisor; Email Adress: yihun.mulugeta@yahoo.com

Abebaw Gedef (Assisstant professor of Biostatistics), Bahir Dar University, College of Health Science and Medicine, School of Public Health, Department of Biostatistics and Epidemiology, co-advisor; Email Adress: abebaw2516@gmail.com

Annex 2: Data extraction Checklist

Part I: Sociodemographic characterstics

Code	Questions	Possible Answers	Skip
101	Age	_____ years	
102	Address	_____	
103	Marital status	1. Married 2. Single 3. Divorced 4. Widowed 5. Others	
104	Educational status	1. Can't read and write 2. Primary education 3. Secondary education 4. College and above	
105	Occupation	1. House wife 2. government employee 3. Self employed 4. merchant 5. others (specify)	

PART II: Medical Factors

Code	Possible Answers	
201	HIV Sero-status	1. Positive 2. Negative
202	Maternal Anemia	1. Yes 2. No
203	DM	1. Yes 2. No
204	HTN	1. Yes 2. No

Part III. Obstetric History

Code	Questions	Possible Answers	Skip
301	History of still birth	1. Yes 2. No	
302	History of abortion	1. Yes 2. No	If 2, skip to Q206
303	If yes, how many times?	_____	
304	History of previous C/S	1. Yes 2. No	
305	If yes to Q206, how many times	_____	
306	History of previous postpartum Hemorrhage	1. Yes 2. No	

Part IV. Current Obstetric Factors

Code	Questions	Possible Answers	Skip
401	Gravidity/ Parity	_____/_____	
402	Gestational age (weeks)	1. _____wks. 2. Unknown	
403	Abruption placenta	1. Yes 2. No	
404	Placenta Previa	1. Yes 2. No	
405	Ante partum hemorrhage	1. Yes 2. No	
406	Multiple pregnancy	1. Yes 2. No	
407	Pregnancy induced hypertension(pre-eclampsia, eclampsia …)	1. Yes 2. No	
	Gestational DM	1. Yes 2. No	

408	Onset of Labour	1. Spontaneous 2. Induced	If 1, skip to Q403
409	If spontaneous, is labor augmented	1.Yes 2. No	
410	Obstructed labor	1. Yes 2. No	
411	Prolonged labor	1. Yes 2. No	
412	Mode of delivery	1. Spontaneous vaginal 2. Instrumental vaginal 3. C/S	
414	Retained Placenta	1. Yes 2. No	
415	Episiotomy	1. Yes 2. No	If no, skip to Q410
416	If yes, is there episiotomy extension	1. Yes 2. No	
417	Genital tract trauma other than episiotomy	1. Vaginal wall laceration 2. Perineal tear 3. cervical tear 4. absent	
418	Retained products of conception	1. Yes 2. Yes	
419	Uterine atony	1. Yes 2. No	
420	Coagulopathy	1. Yes 2. No	