



Incidence, risk factors and outcome of Primary Postpartum Hemorrhage at Jigme Dorji Wangchuck National Referral Hospital: a retrospective case-control study

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ABSTRACT

Introduction: Primary postpartum hemorrhage is one of the leading causes of maternal death in Bhutan but data on the incidence and risk factors for primary postpartum hemorrhage are scarce. The purpose of this research is to look into the incidence, its associated risk factors and maternal outcome of primary postpartum hemorrhage among women who gave birth at the national referral hospital. **Methods:** The incidence of primary postpartum hemorrhage was estimated total number of primary postpartum hemorrhage cases of total deliveries during the study period. A case-control study was conducted to identify risk factors for primary postpartum hemorrhage. Cases of primary postpartum hemorrhage was defined by blood loss of ≥ 500 ml in vaginal delivery or ≥ 1000 ml for abdominal delivery within 24 hours of delivery. A multivariable logistic regression was used to identify associated risk factors of primary postpartum hemorrhage. **Results:** Among 9,221 deliveries, primary postpartum hemorrhage occurred in 180 cases (1.95%; 95% CI=1.68%-2.26%) during two year period. The significant risk factors for primary postpartum hemorrhage were, labor induction (adjusted OR=2.27; 95% CI= 1.11-31.47, $p=0.005$), current pregnancy complications (aOR=2.50; 95% CI: 1.32-4.74, $p=0.005$), and gestational age at term delivery (aOR=6.49; 95% CI:1.12-37.48, $p=0.037$). The significant causes of primary postpartum hemorrhage were uterine atony (aOR=72.57; 95% CI:5.95-885.76, $p=0.001$), retained placenta (aOR=18.08; 95% CI:2.66-122.81, $p=0.003$) and perineal and cervical tear (aOR=27.80; 95% CI: 15.13-51.07, $p<0.001$). **Conclusions:** The incidence of primary postpartum hemorrhage was 1.95% which is lower compared to other South East Asian countries. The causes and risk factors identified in this study may help predict primary postpartum hemorrhage and aid healthcare providers in better management of primary postpartum hemorrhage in all women giving birth.

Keywords: Case control; Incidence; Postpartum hemorrhage; Risk factor.

INTRODUCTION

Postpartum Hemorrhage (PPH) is a life-threatening event in a woman's life and it is the primary cause of maternal mortality in the majority of low-income countries, accounting for nearly a quarter of all maternal deaths in women and adolescent girls globally¹. In Bhutan the overall cumulative efforts of the Reproductive and Health program have gradually resulted in reduction of maternal mortality ratio (MMR) from 770 per 100,000 live births in 1984 to 89 per 100,000 live births in 2017. Similarly, maternal death due to PPH has declined from 45% in 2001 to 9% in 2012 according to MNDI reports 2001-12. However, more needs to be done to be able to achieve 2030 SDGs target of less than 70 per 100,000 live births. Primary PPH is one of the leading causes of maternal death in Bhutan². PPH is defined as the estimated blood loss of ≥ 500 ml after vaginal delivery and ≥ 1000 ml after cesarean

section. PPH within 24 hours of delivery is termed as early or primary postpartum hemorrhage; whereas hemorrhage 24 hours after delivery is called late or secondary postpartum hemorrhage. There are previous studies, attempting to identify predictors of PPH in different countries which includes history of previous PPH, multiple pregnancy, grand multiparity, pre-partum anemia, large baby, placenta previa, induction of labor, prolonged labor, preeclampsia, mothers age 35 or above years, multiparity, post term pregnancy and chorioamnionitis³. The most well-known post-delivery causes of PPH is uterine atony, but genital trauma (i.e. vaginal and cervical lacerations), uterine rupture, retained placental tissue and maternal coagulation disorders may also result in PPH.

Severe morbidities associated with PPH include anemia, disseminated intravascular coagulation, blood transfusion, hysterectomy and renal or liver failure⁴. The most heartbreaking outcome of PPH is maternal mortality, which affects every family member, especially the child who is left behind. It is encouraging that many literatures support the claim that PPH can be prevented and timely treatment of PPH can decrease the associated morbidity and mortality.

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Although, there is a wealth of literatures on this subject across the world. However, only limited studies have been conducted in Bhutan. The findings from this study therefore, would enable to estimate the burden of the primary PPH and its risk factors in relation to Bhutan. And also provide evidence for healthcare providers, reproductive health program at the ministry of health, and key stakeholders to develop appropriate policies and strategic interventions to improve the care of women during pregnancy, childbirth and after delivery to reduce the impact of primary PPH and its outcomes. The objective of this study was to determine the incidence, risk factors, and maternal outcomes of primary PPH at the Jigme Dorji Wangchuck National Referral Hospital (JDWNRH) in Bhutan.

METHODS

Ethical Consideration

The study was approved by Research Ethic Board of Bhutan vide letter no. REBH/Approval/2021/049 dated 21st June 2021.

Study design and population

This is a case-control study to determine the risk factors and outcomes of primary PPH cases. The source population was defined as all the women who delivered in JDWNRH between 1st January, 2018 and 31st December, 2019. From this source population, we identified all the cases of primary PPH from the birth register and case sheet/discharge summary sheet maintained with the record section and also from the electronic records of the patients. Primary PPH was defined as the cumulative blood loss of 500 ml or more following vaginal delivery or 1000ml or more following cesarean delivery. Any blood loss after delivery or cesarean section has to be recorded mandatorily in all the hospitals in Bhutan. Blood loss was estimated visually post-delivery by the attending physician or midwife and recorded in the case sheet and birth register either by nurse or doctors. All the cases of PPH among women aged 15-45 years with gestation age at delivery of 24 – 42 weeks during the study period was included in the study, comprising a total of 180 cases. An incidence of primary PPH was also estimated for the two-year period based on the historical data of delivery at the JDWNRH.

In order to remove the confounding effect of known confounder, a frequency matching was done in the selection of control by matching them to cases by gestation age (24-42 weeks), age at delivery (15-45 years) and time period (Jan 2018 to December 2019). We considered a minimum of case: control ratio of 1:2 to increase the power of the study, assuming a smaller number of cases even though all eligible cases were selected for this study. This study selected 180 case and 362 controls without PPH totaling to the sample size of 542 participants.

Variables consideration

In this study, presence or absence of primary PPH in cases and controls was the dependent variable while the demographic characteristics, presence or absence of the potential PPH risk

factors among PPH cases and controls were the independent variables. Based on published articles, a standard questionnaire was developed and modified into four parts to fulfill the study purpose. The first part consisted of socio-demographic characteristics such as age, level of education, occupation and average monthly income. The other information collected included obstetric history such as gravida (multi gravida indicates woman who had two or more pregnancies and grand multigravida is five or more pregnancies), BMI, previous history of abortion, history of previous cesarean section, multiple pregnancy (a pregnancy with more than one fetus), current pregnancy complication (e.g. Antepartum hemorrhage, Premature rupture of membrane, hypertensive disorders during the current pregnancy, gestational diabetes and polyhydramnios), whether spontaneous or induced labour, labor complications (e.g. prolong labor, malposition or obstructed labor], mode of delivery (spontaneous, instrumental or cesarean section), prepartum anemia, ruptured uterus, perineal tear, uterine atony and whether or not uterotonic was received. The part III of the questionnaire consisted of birth outcomes: gestational age and birth weight of babies at delivery. Lastly, part IV consisted of maternal outcomes: primary PPH, blood transfusion, laparotomy/hysterectomy, organ failure and whether the mother was alive or not. All the information was retrieved from the medical record section maintained at JDWNRH.

Statistical analysis

The incidence of primary PPH was estimated by dividing the total number of primary PPH by total number of deliveries for each year and two years combined. The only continuous variable age was categorized into a binary variable (<35 year and ≥35 years), and remaining descriptive statistic was generated for key variables for cases and controls. The significant differences in the proportion of each variable between cases and controls were compared using chi-squared test. An univariable logistic regression was used to estimate unadjusted odds ratios (OR) to identify significant individual risk factors and for the selection of the significant variable for multivariable model at liberal *p*-values of 0.20. A multivariable logistic regression model using a stepwise backward elimination procedure was performed to identify significant risk factors associated with primary PPH. A 5% significant level was used to retain the significant variable in the final multivariable model. The log likelihood ratio test was used to assess the significance of the variable in the final model where the reduced model (without a particular variable) is nested within a full model (with a particular variable), and overall Wald's test and Akaike information criterion (AIC) and the Bayesian information criterion (BIC) were used to determine the significance of a variable if the reduced model is not nested within a full model. The overall goodness of fit of the final model were assessed using Pearson's, deviance, and Hoshmer and Lemeshow goodness-of-fit test. The influential and outlying observations were evaluated using standardized Pearson's and deviance residuals and leverage values. The predictive performance of the final model was assessed using model sensitivity and specificity,

overall accuracy and model discrimination power by generating receiver operative curve (ROC). All statistical analyses were performed using STATA version 13.0 (Stata Corp, College Station, TX, USA).

The overall goodness-of-fit tests showed not significant model specification error (*p*-values for Pearson’s chi-square test, deviance chi-square test and Hosmer and Lemeshow goodness-of-fit test were 0.110, 0.087 and 0.374, respectively. Residual diagnostic showed only one covariate pattern with standardized Pearson’s residual of ≥ 3 , suggesting no outlying observations, except for one covariate pattern containing 11 cases and one control observations. Excluding these observations had significant impact on model coefficients pregnancy complication (52%), labor onset (25%), late term gestural age (-612%). However, there is no reason to exclude them as their values of risk factors were of expected range.

At the cut-off value of 0.5 predicted probabilities, the model sensitivity was 68.2%, specificity was 91.22 and overall correctly classified was 84.4% showing the model has reasonable predictability power. The value of area under ROC was 0.91 demonstrating the discrimination power of the model was very high.

RESULTS

From the source population of 9,221 deliveries occurred during the two-year period between January 2018 and December 2019, we identified 180 women (1.95%, 95% CI 1.68-2.26%) with primary PPH of ≥ 500 cc or ≥ 1000 cc for vaginal and cesarean delivery respectively. Of the total 180 identified PPH cases, there was 84 PPH cases in 2018 of which 2 were following cesarean delivery and in 2019 there were 96 PPH cases of which 4 were related to cesarean delivery. Table 1 presents demographic characteristics of women in cases and controls by age, education level, occupation and income, which are similar in nature. Most of the cases (95.6%) and controls (93.4%) were below 35 years. Similarly, majority of the women in cases and controls did not undergo previous cesarean section or had history of abortion and nearly everyone delivered singleton babies. Table 2 shows distribution of clinical characteristics of study participants by cases and control and results of their unconditional association with primary PPH (unadjusted ORs). The unconditional association showed that the primary PPH was significantly associated with current pregnancy complication, labor onset (spontaneous or induced), complication in labor, delivery mode, uterine atony, retained placenta (ROP), perineal or cervical tear during delivery, and gestational age.

The results of the multivariable logistic regression showed the significant risk factors for primary PPH were current pregnancy complications, labor induction, ROP, perineal or cervical tear, and gestational age (aORs and *p* value are presented in (Table 3). Although, mode of delivery and labor complication were significant at unadjusted analysis, were not associated with primary PPH after controlling for other factors.

Table 1. Socio-demographic characteristics of women experiencing Postpartum Hemorrhage (cases vs control) in the National Referral Hospital, Bhutan, 2018-2019 (n=542)

Characteristics	PPH cases n=180	Controls n=362	<i>p</i> -value
Total			
Age			0.309
<35 years	172 (95.6%)	338 (93.4%)	
35 years and above	8 (4.4%)	24 (6.6%)	
Education Level			<0.001
None	31 (17.2%)	71 (19.6%)	
Primary or secondary level	110 (61.1%)	159 (43.9%)	
Higher secondary or above	39 (21.7%)	132 (36.5%)	
Occupation			0.478
Civil servant	31 (17.2%)	70 (19.3%)	
Home maker	119 (66.1%)	222 (61.3%)	
Business	16 (8.9%)	46 (12.7%)	
Others	14 (7.8%)	24 (6.6%)	
Average Monthly Income			0.207
<6000	22 (12.2%)	63(17.4%)	
6000-8000	5 (2.8%)	11 (3%)	
8001-10,000	75 (41.7%)	117 (32.3%)	
>10,000	78 (43.3%)	171 (47.2%)	
Referred in from district hospitals			0.104
Yes	16 (8.9%)	19 (5.2%)	
No	164 (91.1%)	343 (94.8%)	

The odds of developing primary PPH was as high as seventy-two times in childbearing women who experience uterine atony compared with those without uterine atony (aOR 72.57, 95% CI 5.95-885.76). However, the sample size was small. The risk of primary PPH was eighteen times higher among women with retained placenta than in those without it (aOR 18.08, 95% CI 2.66-122.81). The risk is twenty-seven times more with genital organ laceration (aOR 27.80, 95% CI 15.13-51.07). We did not look at the problem of coagulopathy due to lack of data.

Everyone in the study received uterotonic which includes the administration of an oxytocic drug soon after the baby is born and before the placenta is expelled. It is part of active management of the third stage of labor in all deliveries. In our study, among women who experienced PPH, 29% had received blood transfusion, 4% had to remove placenta manually and the PPH had adverse outcome such as laparotomy/hysterectomy in 3% (Figure 1). All the cases of primary PPH survived the condition.

Table 2. Univariate analysis: Clinical profile of women associated with postpartum hemorrhage (case vs controls) in the National Referral Hospital, Bhutan, 2018-2019 (n=542)

Variable	PPH cases (n=180)	Controls (n=362)	OR	95% CI	p-value
Age					
<35 years	172 (95.6%)	338 (93.4%)	Ref	-	-
35 years and above	8 (4.4%)	24 (6.6%)	0.65	0.29, 1.49	0.298
Gravida					
Primi gravida	79 (43.9%)	180 (49.7%)	Ref	-	0.4380*
Multi gravida	100 (55.6%)	180 (49.7%)	1.27	0.88, 1.81	0.200
Grand multigravida	1 (0.6%)	2 (0.6%)	1.14	0.10,12.75	0.916
BMI					
18.5 - 24.9 (normal wt.)	94 (52.2%)	203 (56.1%)	Ref	-	0.8240*
<18.5 (underweight)	8 (4.4%)	18 (5%)	0.96	0.40, 2.29	0.926
25 - 29.9 (overweight)	41 (22.8%)	102 (28.2%)	0.87	0.56, 1.34	0.526
≥30 (obese)	11 (6.1%)	32 (8.8%)	0.74	0.36, 1.54	0.422
History of abortion					
No	166 (92.2%)	343 (94.7%)	Ref	-	-
Yes	14 (7.8%)	19 (5.3%)	1.52	0.74, 3.11	0.255
History of previous C/S					
No	178 (98.9%)	357 (98.6%)	Ref	-	-
Yes	2 (1.1%)	5 (1.4%)	0.80	0.15, 4.17	0.791
Multiple pregnancy					
No	180 (100%)	359 (99.2%)	Ref	-	-
Yes	0	3 (0.8%)	1	-	-
Current pregnancy complication					
No	75 (41.7%)	102 (28.2%)	Ref	-	-
Yes	105 (58.3%)	260 (71.8%)	1.82	1.25, 2.65	0.002
Labor onset					
Spontaneous	130 (72.2%)	308 (85.1%)	Ref	-	-
Induced	49 (27.2%)	52 (14.4%)	2.23	1.44, 3.47	<0.001
Labor complications					
No	156 (86.7%)	335 (92.5%)	Ref	-	-
Yes	24 (13.3%)	27 (7.5%)	1.91	1.07, 3.41	0.031
Delivery mode					
Spontaneous Vg. delivery	155 (86.1%)	310 (85.9%)	Ref	-	0.0005*
Cesarean delivery	6 (3.3%)	36 (9.9%)	0.33	0.14, 0.81	0.015
Instrumental delivery	19 (10.6%)	15 (4.2%)	2.53	1.25, 5.12	0.010
Uterine atony					
No	140 (77.8%)	361 (99.7%)	Ref	-	-
Yes	15 (8.3%)	1 (0.3%)	38.68	5.06, 295.56	<0.001

Cont.....

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Variable	PPH cases (n=180)	Controls (n=362)	OR	95% CI	p-value
Retained placenta					
No	146 (81.1%)	360 (99.5%)	Ref	-	-
Yes	13 (7.2%)	2 (0.5%)	16.03	3.57, 71.91	<0.001
Perineal/cervical tear					
No	54 (30%)	329 (90.9%)	Ref	-	-
Yes	102 (56.7%)	33 (9.1%)	18.83	11.57, 30.64	<0.001
Gestational Age					
Preterm	9 (5%)	17 (4.7%)	Ref	-	0.0000*
Term	147 (81.7%)	156 (43.1%)	1.78	0.77, 4.12	0.178
Late-term	22 (12.2%)	189 (52.2%)	0.22	0.09, 0.55	<0.001
Uterotonic received					
No	0	0			
Yes	163 (90.6%)	362 (100%)	1	-	
Birth weight					
Normal birth wt.	156 (86.7%)	325 (89.8%)	Ref	-	0.430*
Low birth wt.	10 (5.5%)	19 (5.3%)	1.10	0.50, 2.41	0.819
High birth wt.	14 (7.8%)	18 (4.9%)	1.62	0.79, 3.34	0.191

*Overall P values of the categorical variable. Totals do not always add to 542 due to missing data.

Table 3. Multivariate Analysis: Factors associated with primary PPH among women delivered at the National Referral Hospital, Bhutan, 2018-2019 (n=540)

Variable	Coefficient (95% CI)	Adjusted OR (95% CI)	p-value
Current pregnancy complication	0.92 (0.28-1.56)	2.50 (1.32-4.74)	0.005
Labor induction	0.822 (0.10-1.54)	2.27 (1.11-4.67)	0.025
Uterine atony	4.29 (1.78- 6.79)	72.57 (5.95-885.76)	0.001
Retained placenta	2.89 (0.98-4.81)	18.08 (2.66-122.81)	0.003
Perineal/cervical tear	3.32 (2.72-3.93)	27.80 (15.13-51.07)	<0.001
Gestational Age			
Preterm	-	Reference	<0.001*
Term	1.87 (0.12-3.62)	6.49 (1.12-37.48)	0.037
Late-term	-0.33 (-2.07-1.42)	0.72 (0.12-4.12)	0.711
Intercept	-3.78 (-5.59- - 1.96)	0.02 (0.00-0.14)	

* Over all P value of the categorical variables with more than two values

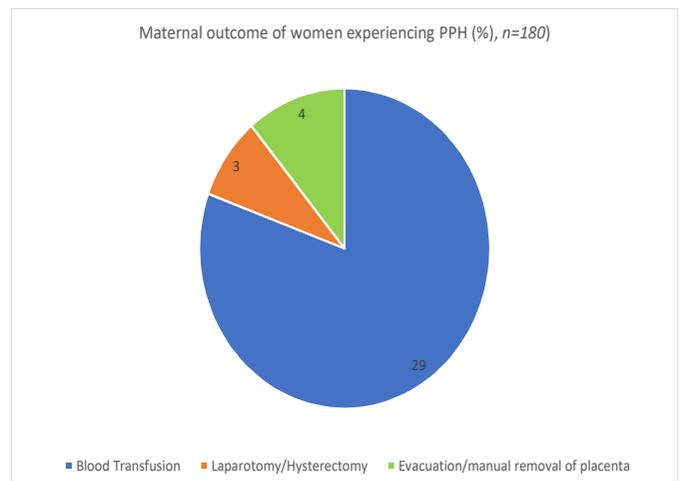


Figure 1. Maternal outcome of primary PPH among women delivered at Jigme Dorji Wangchuck National Referral Hospital, Bhutan, 2018-2019 (n=180).

Total do not add to 100% as remaining 64% of the PPH cases were managed through routine active management of third stage labor

DISCUSSION

This study presents one of the relatively large-scale case-control study that identified the risk factors of the primary PPH among Bhutanese women who delivered at Jigme Dorji Wangchuck National Referral Hospital (JDWNRH) during the two-year period, along with the incidence of primary PPH. The incidence

of primary PPH was 1.95% which is lower compared with that of other Southeast Asian countries at 4.88%⁵. Globally the incidence of PPH is 6 % by Carroli et al and 10.8% as reported by Calvert et al^{6,7}. The variation in the finding might be due to the difference in study design, cultural difference and accessibility to maternal health care services⁵. In our setting, the low incidence of primary PPH could be explained in part by the method of estimating blood loss by the nurse or doctor post-delivery. The visual estimation of blood loss may underestimate true blood loss sometimes by 30-50%⁸. The use of calibrated drape in assessment of postpartum bleeding reports the apparent high rate of PPH.

In our study labor induction, current pregnancy complication and gestational age at term pregnancy were the three factors that significantly increased the risk of primary PPH. This finding calls for more vigilance among healthcare providers, attending labor and births to identify women at risk and plan for early interventions to prevent the primary PPH.

We found that induction of labor was independently associated with two times higher risk of primary PPH compared to women who delivered spontaneously. Our finding agrees with several studies that determined PPH risk factors and found a significant association between labor induction and hemorrhage^{9,10}. Induction of labor is a common obstetric procedure which is medically indicated in woman to prevent the risks associated with the prolongation of pregnancy and SOP in JDWNRH has list of indications. Studies have hypothetically explained that the drugs used to induce labor might have a direct effect on the uterine muscle and by causing supra physiological contractions, act as a fatigue factor on the myometrium muscle and thus lead to postpartum atony and PPH¹¹.

Epidemiologic data on the potential association between gestation age and postpartum hemorrhage is conflicting. Some studies suggested that post term pregnancies are at risk for atonic hemorrhage due to reduced contractility in myometrium¹². At the same time other data suggested that due to impaired placentation, postpartum hemorrhage risk may be higher in women who deliver preterm¹³. In our study the odds of developing primary PPH was more than six times in term delivery compared to preterm deliveries. Our finding indicates that gestation age at delivery influences the maternal risk of PPH.

Risk factor for PPH are dependent on etiology of hemorrhage. In our study the current pregnancy complication included antepartum hemorrhage, pre-rupture of membrane, hypertensive disorders in pregnancy, gestational diabetes and polyhydramnios, some of which are risk factor for uterine atony¹⁴. We found that the risk of developing primary PPH is more than two times in women with current pregnancy complication compared to women without any complication.

The risk is twenty-seven times more with genital organ laceration. Perineal (including the vaginal tear and episiotomy) or cervical tear is one of the most common cause of the PPH in our study. This finding is consistent with the previous findings which showed that episiotomy and suture were also the risk factors

among many others reported to be associated with postpartum hemorrhage. Damage to the vagina, cervix, uterus or perineum causes bleeding. Using instruments like forceps or vacuum extraction during delivery can increase the risk of uterine trauma. Sometimes, a hematoma (collection of blood) can form in a concealed area and cause bleeding hours or days after delivery¹⁰.

The risk of developing primary PPH is as high as seventy-two times in childbearing women experiencing uterine atony than in birth not complicated by uterine atony. Uterine atony is the primary direct cause of maternal morbidity globally. The active management of the third stage of labour with uterotonics reduces the risk of postpartum hemorrhage. Oxytocin and ergometrine are drugs widely used for the purpose. In our hospital, the third stage of labour is managed with oxytocin as the main uterotonic agent. The risk of primary PPH was eighteen times higher among women with retained placenta than in those without. Evidence suggests that retained placenta accounts for nearly 20% of severe cases of PPH¹⁵. Similar to studies conducted in Cameroon, Zimbabwe, Cote D'Ivoire and Ethiopia.

Primary PPH has resulted in 4% of the mothers undergoing manual removal of placenta, 3% had to undergo laparotomy or hysterectomy, 29% of the diagnosed cases received blood transfusion, and none had died because of the PPH.

Limitations of the study

The retrospective nature of data collection, particularly routine visual estimation of blood loss by care providers, may have resulted in some cases of PPH being misclassified, ignored, or underreported, as there are no standard methods for quantifying the amount of bleeding. The study might not be a representative for the entire Bhutanese population since only the women delivered at JDWNRH were included in the study, and needs to be extrapolated cautiously. Populations living in other districts which are remote and less affluent may influence the quality and level of antenatal care, nutrition and other factors driving these risk factor.

CONCLUSIONS

The overall incidence of PPH was 1.95%. Labor induction, pregnancy complication and gestation age at term delivery were prevalent risk factors in primary PPH. The common causes of PPH were perineal/cervical tear, uterine atony and retained placenta. Visual estimation of blood loss more often underestimates the blood loss and therefore, increasing the accuracy of blood loss through standard measurement is crucial step in early detection of PPH and treatment. A feasibility study for accurate measurement of blood loss by use of calibrated pouch or other standard measurement is recommended. Concerted efforts are required from policy makers, health managers and service providers, to improve quality of proactive prevention of PPH through early identification of women at risk of primary PPH.

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AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

PW: Concept, design, data collection and analysis, manuscript writing

JC: Design, data analysis, manuscript writing

SW: Design, data collection and analysis, manuscript writing

Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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None