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Original Research Article

Major postpartum hemorrhage after intra partum caesarean section: analysis of risk factors

Arfat Waheed^{1*}, Shakura Bhat², Andrea Perniola¹, Imran Khan³,
Rimple Tiwary⁴, Manish Kumar Tiwary¹

¹Department of Anesthesiology, Sheikh Khalifa Medical City Ajman, University Street, Ajman, United Arab Emirates

²Department of Obstetrics and Gynecology, Sheikh Khalifa Medical City Ajman, University Street, Ajman, United Arab Emirates

³Department of Biostatistics, Sher-e-Kashmir University of Agriculture Sciences and Technology, Srinagar, Jammu and Kashmir, India

⁴Department of Obstetrics and Gynecology, Sheikh Khalifa General Hospital, Umm Al Quwain, United Arab Emirates

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*Correspondence:

Dr. Arfat Waheed,

E-mail: arfatwaheed@gmail.com

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ABSTRACT

Background: Women who undergo intrapartum caesarean section (CS) are at increased risk of postpartum hemorrhage (PPH) compared to those undergoing elective caesarean. We aimed to find the risk factors for major post-partum hemorrhage in women undergoing intra-partum caesarean section.

Methods: A retrospective chart study was conducted to identify risk factors for severe PPH in intrapartum CS. Severe PPH was classified as an estimated blood loss (EBL) ≥ 1500 ml or receipt of a red blood cell (RBC) transfusion up to 48 hours after CS. Logistic regression was performed to identify the potential risk factors.

Results: 102 cases and 189 controls were studied. Average blood loss was 1530 ml in cases and 433 ml in controls. Among severe PPH cases, 46% of women had at least 1500 ml EBL, and 83% of women received RBC intraoperatively or within 48 hours post-CS. Most significant clinical factor for severe PPH during intrapartum CS was general anesthesia (OR 4.12; CI=3.05 to 8.17). Compared to parturients who underwent primary CS, those who had ≥ 3 CS had increased odds of severe PPH (OR 1.83; CI=2.11-4.08). Women aged ≥ 30 years had reduced odds of PPH compared to women aged less than 30 years (OR=0.52; 95% CI=0.32-0.86). Arab women had 2-fold increased odds of severe PPH as compared to non-Arab women in our study (OR 2.04; CI=1.25-3.31).

Conclusions: In patients undergoing intrapartum caesarean section, general anesthesia may be a risk factor for postpartum hemorrhage. The risk of severe postpartum hemorrhage may be increased in patients with, multiple previous caesareans (≥ 3) and multiple pregnancies. Arab ethnicity was also found to be a risk factor in this study but larger studies are needed to confirm our findings.

Keywords: Caesarean section, Intra partum, Post partum hemorrhage

INTRODUCTION

Postpartum hemorrhage (PPH) is reported as a complication of almost one-third of all cesarean deliveries depending on the population studied and the definition used.^{1,2} Even though the mortality rates are decreasing overall, the incidence of PPH is increasing even in high-

income countries. The United States reported a significant increase in the rate of atonic PPH among women undergoing CS after induction of labour, between 1994 and 2006.³ Increasing rates of CS and increased complications such as placenta previa, placental abruption, and need for emergency CS and general anesthesia (GA) may explain the increased incidence of PPH.^{4,5} Compared

to those parturients undergoing elective cesarean section, those who undergo intrapartum cesarean section or emergency cesarean section are at increased risk of postpartum hemorrhage.^{6,7}

High quality clinical studies are needed to understand relevant and potentially preventable risk factors associated with PPH as per The International PPH Collaborative group.⁴

It is well known that there is a high prevalence of obstetric risk factors like grand multiparity, multiple previous CS (>3), and gestational diabetes in Arab population.⁸⁻¹²

We tried to find a possible association between these risk factors and the incidence of severe PPH.

METHODS

After obtaining ethical committee approval from Sheikh Khalifa Medical City Ajman and the Ministry of Health, United Arab Emirates, the source population was defined as parturients delivering by intra-partum caesarean section (CS) at Women Hospital of SKMC Ajman which is a tertiary center based in the northern part of United Arab Emirates (UAE) from December 2015 to December 2020.

Severe PPH was classified as an estimated blood loss ≥ 1500 ml or receipt of a red blood cell transfusion up to 48 hours post CS.^{2,6} RBC transfusion within 48 hours of CS was incorporated as a classifier for severe PPH to account for subjects in whom visually estimated blood loss (EBL) may have been underestimated. Women who had multiple deliveries in our hospital, the second and subsequent pregnancies were excluded to limit repeated correlated measurements. Controls were sampled from the same source population. Parturients with PPH were identified and were excluded. From the remaining list, two controls were randomly selected within the same year of delivery for each case. Each control had an EBL < 1500 ml and no transfusion. The medical records were reviewed for EBL and transfusion data to confirm the correct classification of each case and control. Women who had received a blood transfusion because of postpartum anemia, without any evidence of excessive hemorrhage were excluded.

Patient data was based on information from: 1) hospital medical records; 2) operation theatre records. Detailed information on studied risk factors was taken from the hospital electronic health records (Cerner Millennium) and supplemented with International Classification of Diseases, (ICD) codes. After obtaining and de-identifying the patient records, we assembled the clinical and transfusion data. Intrapartum CS inclusion criteria included parturients in labour as confirmed by painful contractions or induction of labor prior to CS. According to the literature review, we identified potential risk factors for PPH for consideration in our analyses. We looked for pre-pregnancy risk factors like age, ethnicity, previous CS, parity and current pregnancy conditions including gestational age, multiple pregnancy, body mass index

(BMI), hemoglobin (most approximate to delivery), presence of gestational diabetes (insulin-treated or diet regulated) and pregnancy-induced hypertension (PIH). Also, intrapartum factors included mode of delivery, time of delivery, induction of labor, dilatation of the cervix, labor augmentation with oxytocin, and type of anesthesia were studied. The final mode of anesthesia prior to surgical incision was designated as the mode of anesthesia in our analysis. Information for patients who required intraoperative conversion from neuraxial to general anesthesia was not included in our analyses. Women receiving anticoagulation preoperatively or patients with hematologic or coagulation disorders were excluded from the analysis. Analysis for variables like the history of previous PPH was not included as the data was missing for this information in a large proportion of cases. BMI was categorized using the World Health Organization (WHO)'s classification, with a BMI of 18.5-24.9 kg/m² as the reference.

Statistical analysis

Descriptive statistics provided the average blood loss and incidence of PPH. Quantitative data was analyzed using two-sample independent t-tests and one-way analysis of variance (ANOVA). Qualitative variables were assessed using Fisher's exact test and Pearson's Chi-Square test. Logistic regression was employed to examine the relationship between the binary dependent variable and the independent variables. A p value of <0.05 was considered statistically significant. The data analysis was performed using R software.

RESULTS

We identified 102 cases and 189 controls were studied. Controls were random patients selected from the same source population. Average blood loss was 1530 ml in cases and 433 ml in controls. Among severe PPH cases, 47 (46%) women had at least 1500 ml EBL, and 85 (83%) women received RBC transfusion intraoperatively or within 48 hours post-CS. Maternal, obstetric, intrapartum, and perioperative characteristics of women with and without severe PPH are presented in Table 1.

Logistic regression utilizing odds ratios for clinical factors is presented in Table 2.

In our study clinical factor with the highest odds for severe PPH was general anesthesia (OR 4.12; CI=3.05 to 8.17, reference group = spinal anesthesia). Compared to women who underwent primary CS, women who had ≥ 3 CS had increased odds of severe PPH (OR 1.83; CI 2.11-4.08) but women with one prior CS had reduced odds of severe PPH (OR=0.51; CI=0.17-1.36, reference = primary CS). Women aged ≥ 30 years had reduced odds of PPH compared to women aged less than 30 years (OR=0.52; 95% CI=0.32-0.86). Arab women had 2-fold increased odds of severe PPH compared to non-Arab women in our study (OR 2.04; CI=1.25-3.31).

Table 1: Clinical profile of women with severe PPH versus controls.

	Case (n=102)	Control (n=189)	P value
Gestational age(weeks)	35.88±3.86	37.64±2.61	≤0.0001*
Maternal age(years)	31.80±5.22	29.78±5.81	0.004*
BMI	32.06±5.78	31.97±5.70	0.898
Hb pre labour	10.72±1.50	11.39±1.36	≤0.0001*
	N (%)	N (%)	
Hypertensive (>130/89)	12 (11.8)	23 (12.2)	1.00
Gestational diabetes (fasting >5.6 mg/dl)	35 (34.3)	56 (29.6)	0.42
Pre-eclampsia (>140/90) with proteinuria	12 (11.8)	23 (12.2)	1.00
Cervical dilatation (9 cm)	85 (83.3)	173 (91.5)	0.051
Augmentation	17 (16.7)	20 (10.6)	0.125
BMI			
<30	36 (35.6)	65 (34.4)	0.70
30-40	53 (51.5)	105 (55.6)	
>40	13 (12.9)	19 (10.1)	
HB			
<8	2 (2.0)	2 (1.1)	0.005
8-11	55 (53.9)	66 (34.9)	
>11	45 (44.1)	121 (64.0)	

P value of less than 0.05 is significant.

Table 2: Odds ratio (OR) for variables associated with severe PPH during intrapartum CS.

Variables	Odds ratio (or)	P value
Maternal age		
<30 years	Reference	
>30 years	0.52 (0.32-0.86)	0.01
Gestational age		
>38 weeks	Reference	
<38 weeks	0.42 (0.24-0.73)	0.002
Race/ethnicity		
Non-Arabic	Reference	
Arabic	2.04 (1.25-3.31)	0.01
Number of previous CS		
0	Reference	
1	0.51 (0.17-1.36)	0.11
2	0.82 (0.49-1.70)	0.15
≥3	1.83 (2.11- 4.08)	0.002
Type of pregnancy		
Singleton	Reference	
Multiple	1.44 (2.27-5.15)	0.01
Parity		
0	Reference	
1	0.23 (0.74-1.11)	0.22
2	0.81 (0.83-1.22)	0.17
3	1.67 (2.02-4.57)	0.010
≥4	2.19 (3.41-5.33)	<0.0001
Mode of anesthesia		
Regional	Reference	
General	4.12 (3.05-8.17)	≤0.0001
Gdm	1.24 (0.74-2.07)	0.42
Pre-eclampsia	0.96 (0.45-2.02)	1.00
Oxytocin augmentation	1.8 (0.91-3.60)	0.10

P value of less than 0.05 is significant.

DISCUSSION

Reducing the prevalence of severe PPH continues to be a challenge. Post partum hemorrhage especially when severe is a common cause of maternal morbidity leading to complications like ARDS, shock, coagulopathy, renal failure, sometimes requiring hysterectomy. Exploring the risk factors for PPH is supposed to help us better understand the mechanisms operating that cause PPH and also to develop strategies to manage PPH. Clinical data obtained in our retrospective case control study was used to identify risk factors for severe PPH, some of them well studied and some will require further studies to clarify their role and importance in causing PPH. In this study it was found that, general anesthesia had higher odds of severe PPH compared with spinal anesthesia. Multiple studies have shown similar association with varying degrees of magnitude.^{7,13-15}

Volatile anesthetics have relaxing effect on uterine smooth muscle, thereby increasing the possibility of uterine atony.^{16,17} Inhalational agents like halothane and sevoflurane and induction agents like propofol can also affect platelet function negatively.¹⁸ This may lead us to conclude that general anesthesia may be directly increasing chance of severe postpartum hemorrhage. However, still there is a possibility that patients with anticipated risk factors for PPH may be more likely to receive general anesthesia.^{19,20} A key limitation of our study like other observational studies is delineating any effect of anaesthesia mode on morbidity from various confounders, whether they are due to indication or severity. The current study found that Arab women had higher odds of severe PPH in comparison to non-Arab women. This association could be multifactorial, but the data identifying genetic and ethnic entities as potential independent risk factors for PPH is limited. There is recent interest in candidate genes and molecular mechanisms to understand how the uterus contracts in the 3rd stage of labor and to find possible targets to prevent PPH. A study by Bryant and colleagues found that Asians/Pacific Islanders were at higher risk of PPH as a cohort, but couldn't distinguish rates of PPH among the distinct ethnicities.²¹ The study suggested that differential expression of genes varying by race/ethnicity might contribute to the disparities found in the study. Being a retrospective study, the reason for this apparent association is unclear and needs further investigation. Another study by Al Zirqi and colleagues found the maternal age of ≥ 30 years, and south-east Asian ethnicity were significantly associated with an increased risk of PPH.¹¹ The study found risk is lower in women of Middle Eastern ethnicity, and significantly higher for multiple pregnancies, von Willebrand's disease and anemia (hemoglobin < 9 gm/dl) during pregnancy

In a case-control study from northern Thailand, Burmese nationality was found to be a risk factor for severe PPH but not for non-severe PPH. The study indicated that Burmese women were less likely to have PPH as compared to Thai

women, but whenever they do, the hemorrhage is severe.²² In a German study, Asian women had a higher risk of bleeding compared to German women, who in turn had higher chances of bleeding as compared to women from Middle Eastern region. Study tried to link inadequate prenatal care to hysterectomy in Asian, African, Latin American, and other women, but not in Middle Eastern women.²³

In our study women with more than 3 previous cesareans had higher odds of having severe PPH, but women with a history of one prior CS had lower adjusted odds of severe PPH compared to women with no prior CS. Few studies have discussed this, a meta-analysis by Keag showed increased rates of abruptio placenta and ante partum bleeding but not PPH in patients with previous cesarean section.²⁴ A study by Butwick and others showed that patients with less than 2 cesareans had actually lesser rates of PPH.⁶ For women undergoing trial of labor after prior CS, obstetricians are less likely to consider augmentation of labor or longer trials fearing uterine rupture. This can be a possible explanation for why these women were at lower risk of severe PPH compared to those without a history of prior CS.

This study showed that in women with high parity and multiple pregnancies, there are higher odds of major PPH. Grand multiparity (GMP) is defined as a parity of five or more as per recent literature.^{25,26} Previous studies have shown an association between high parity and PPH.^{27,28} However some previous studies showed that grand multiparity was not associated with PPH.^{10,29} Further research is needed to determine if the differences found were caused by provider cognitive bias, socioeconomic factors, language barriers, and/or other factors.

Previous studies have suggested that gestational hypertension, gestational diabetes and maternal BMI are closely related to postpartum hemorrhage, but our study could not find gestational hypertension, gestational diabetes, and maternal BMI as risk factors for severe PPH.^{30,31}

Previous studies showed IVF as a risk factor for severe early PPH.^{32,33} Few studies showed association between severe PPH and assisted reproductive technology (ART) due to alteration in gene expression in the human placenta. This can lead to early placental separation and uterine atony causing severe PPH. Anticoagulants are common medications used for patients with pregnancy after ART compared to spontaneous pregnancies, which also contribute to increased risk of PPH. The limitation of this study is a retrospective observational design. Only data that were easily queried through electronic medical records were collected. This original study was not designed to investigate racial and ethnic disparities or potential reasons for the differences that were found. Other limitations are single-centre study, biases of retrospective studies: selection, recall, incomplete data, confounding, etc. As with any impact study that compares historical

controls, differing clinical practices and patient populations may impact study results.

CONCLUSION

In patients undergoing intrapartum caesarean section, general anesthesia may be a risk factor for postpartum hemorrhage. The risk of severe postpartum hemorrhage may be increased in patients with, multiple previous caesareans (≥ 3) and multiple pregnancies. Arab ethnicity was also found to be a risk factor in this study but larger studies are needed to confirm our findings.

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