Risk factors for postpartum hemorrhage among Saudi women

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ABSTRACT

الأهداف: تحديد المخاطر الصحية المؤدية لحدوث نزيف الخلاص (PPH) لدى النساء السعوديات وتقدير نسبة حدوث حالات النزيف الأولى منها PPH.

الطريقة: أجريت دراسة مقارنة خلال الفترة ما بين 1 يوليو2007 حتى 30 يونيو2008 في مدينة الملك عبد العزيز الطبية – الرياض – المملكة العربية السعودية. شملت هذه الدراسة 101 مريضة أصيبن ب PPH و 209 مريضة من مجموعة التحكم. درست العلاقة ما بين المتغيرات المؤدية لمختلف المخاطر المتعلقة بحدوث نزيف الخلاص PPHومن ثم التمييز إحصائيا لأهم هذه العوامل. تم إجراء تحليل الانحدار اللوجستي المتعدد لتحديد عوامل الخطر لحدوث مضاعفات الولادة.

النتائج: اقترن تعدد الولادات بزيادة حدوث نزيف الخلاص PPH بمقدار 17%. أدى تسمم الحمل لتضاعف حدوث هذا النزيف 6 مرات. كما يرفع تاريخ حدوث نزيف أثناء الحمل APH مخاطر PPH 8مرات. وهناك عوامل خطورة أخرى تم تمييزها مثل الحمل المتعدد، والولادة الطبيعية، وتطاول المرحلة الثالثة من المخاض، كذلك ووجود تغيرات غير طبيعية في تخطيط قلب الجنين (CTG).

خاتمة: إن عوامل الخطورة المؤدية لحدوث نزيف الخلاص PPH مابين النساء السعوديات كانت مشابهة لحد كبير لغيرها من الدراسات المنشورة عالميا مع ملاحظة أهمية كبرى لتعدد الولادات، ووجود نزيف أثناء الحمل APH، والحمل المتعدد، وحدوث تغيرات غير طبيعية في تخطيط قلب الجنين CTG إضافة إلى تطاول المرحلة الثانية من المخاض. إن هناك حاجة لتثقيف المريضات بما يخص أهمية تحديد النسل والمتابعة السريرية للحمل. وهناك حاجة لتثقيف الأطباء عن أهمية التدبير الفعال للمرحلة الثالثة من المخاض إضافة إلى التقييم الصحيح لفقدان الدم أثناء الولادة.

Objectives: To identify health-related risk factors for the development of post partum hemorrhage (PPH) in Saudi women and to estimate the incidence of primary PPH.

Methods: A case-control study was conducted between July 1, 2007 and June 30, 2008 at King Abdulaziz Medical City, Riyadh, Saudi Arabia. One hundred and one patients with PPH and 209 control patients were included. Bivariate associations between the different risk factors for the development of PPH were studied. Multivariate logistic regression analysis to identify significant risk factors for the occurrence of this obstetrics complication was carried out.

Results: High parity was associated with a 17% increased risk of PPH. Risk factors in preeclampsia was associated with >6-fold increase. History of antepartum hemorrhage (APH) increased the risk for PPH by >8-fold. Other factors were: multiple pregnancy, vaginal delivery, prolonged third stage of labor, and presence of cardiotocograph (CTG) abnormalities.

Conclusion: Risk factors for developing PPH among Saudi women are comparable to other reported studies with a greater influence of parity, presence of APH, multiple gestation, CTG abnormalities and prolonged third stage of labor. There is a need for patient education on family planning and antenatal care, physician education on active management of the third stage, and correct estimation of blood loss.

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Post partum hemorrhage (PPH) is the most common cause of maternal mortality and accounts for one-quarter of the maternal deaths worldwide.[1] All delivering women are potentially at risk for PPH. Apart from physiological and biological reasons, other issues related to the health care provided plays a major role in PPH occurrence. Sixty percent of all pregnancy-related maternal deaths occur during the postpartum period, 45% of them occur in the first 24-hours after delivery.[2] The optimal solution for the vast majority, if not all, is prevention throughout pregnancy. Identifying risk factors for PPH will help to assure that women are sufficiently healthy to withstand postpartum hemorrhage. The World Health Organization (WHO) conducted a review of the literature on PPH published between 1997 and 2002 to more precisely define PPH and its incidence.[3] Accurately defining PPH was difficult, and a wide variation in its incidence was observed, ranging from as low as 0.55% of deliveries in Qatar to as high as 17.5% in Honduras.[3] The risk of dying from PPH depends not only on the amount and rate of blood loss, but also on the health status of the woman.[4] Some of which are inevitable and unchangeable. Obstetric hemorrhage has been identified as a major factor contributing to maternal mortality in Saudi Arabia.[5] Saudi mothers pregnancies were occurring at the extremes of the reproductive age, associated with short birth intervals and short maternal stature. Furthermore, low educational status, poor utilization of antenatal services and a high rate of previous infant loss were of the characteristics features of Saudi women pregnancies.[6] These features may predispose Saudi women to PPH. The objective of this study was to identify health-related risk factors for the development of PPH in pregnant Saudi women as well as to estimate the incidence of primary PPH in Saudi Arabia.

Methods. We carried out a case-control study between July 1, 2007 and June 30, 2008 at the Department of Obstetrics and Gynecology, King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia. King Abdulaziz Medical City is a tertiary care referral center with more than 900 beds. Over 8500 patients were admitted and delivered yearly in our department, with a cesarean section (CS) rate of approximately 20%. The Research Committee and the Institutional Review Board of King Abdullah International Medical Research Center, Riyadh, Saudi Arabia approved the design to conduct the study.

Cases represented all Saudi patients who were admitted to our department for delivery during the study period and coded in the labor and delivery trigger book as having developed primary PPH. A diagnosis of PPH was given to patients with a visually estimated blood loss of ≥500 ml within the first 24 hours after vaginal delivery or loss of ≥1000 ml within the first 24 hours after CS delivery.[7] We excluded from our study non-Saudi patients, those who were <20 weeks gestational age, patients who developed PPH after 24 hours post-delivery, and patients referred to our institution post-delivery due to the development of PPH. Controls included in our study were Saudi patients who were admitted and delivered at/or after 20 weeks of gestation without the development of PPH. The controls were randomly selected from all patients who delivered vaginally or by CS without the development of primary PPH during the study period.

The criteria used to assess blood loss for both cases and controls who delivered vaginally was visual estimation of blood loss. This estimation was performed by the attending physician or midwife and documented on the delivery summary form. For those who delivered by CS, blood loss estimation was documented by the anesthetist based on the amount of blood collected in the suction bag and the number of surgical gauzes that were used to dry up the blood during surgery. There was no consent taken from the cases or the control as the research included only revision of their records without any intervention on human substance.

In order to assess risk factors for developing PPH, data collection included demographic data such as age, parity, body mass index (BMI), gestational age (GA), and booking status. The BMI was considered normal if within 18-24 kg/m^2, and obesity was diagnosed if BMI was >24 kg/m^2. We collected data on patient medical history, including diabetes, hypertension, anemia and idiopathic thrombocytopenia (ITP). Patients' obstetric history included history of CS, myomectomy, uterine rupture, PPH, antepartum hemorrhage (APH), and uterine fibroids. Information on current pregnancy characteristics included the presence of multiple pregnancy, large baby ≥4 kg, various degrees of placenta previa, abruptio placenta, and post-term delivery. Labor and delivery characteristics included whether labor was spontaneous or induced, CS delivery, instrumental delivery, and vaginal delivery. Length of various stages of labor, implementation of active management of third stage, CTG abnormalities and the occurrence of retained products of conception (RPOC) were also assessed. Finally, diagnosed causes of PPH as documented in medical records were identified these included uterine atony (vaginal, cervical, and uterine), tears, surgical bleeding, and retained placenta. During the study period, only 101 patients delivered and diagnosed with primary PPH that fulfilled our criteria for inclusion. We collected relevant data for 209 patients in the control arm. Continuous variables were categorized according to clinically relevant cut-off points.

We carried out the descriptive analyses by calculating the number and percentage for the categorical variables, and mean ± SD for continuous variables. Bivariate analyses for the association between different factors and development of PPH were carried out, and p-values were calculated using the chi-square test or student's t-test, as appropriate. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for categorical variables, as well as for categorized continuous variables. Multivariate logistic regression analysis with stepwise selection of risk factors was carried out to identify significant risk factors for the development of PPH. For the risk factors, we calculated the adjusted OR and the 95% CI. A p-values of ≤0.05 were considered statistically significant. Data management and analyses were carried out using Statistical Analysis Software (SAS, Release 8, SAS Institute, Cary, NC, 1999).

Table 1 - Underlying reasons for postpartum hemorrhage (PPH) among Saudi women giving birth in a tertiary care facility in Riyadh, Saudi Arabia.

Causes of PPH	Controls n=209	Cases n=101
Vaginal tear	0	10 (9.9)
Cervical tear	0	5 (5.0)
Uterine rupture	0	1 (1.0)
Uterine atony	0	84 (83.2)
Chorioamnionitis	0	1 (1.0)
Coagulopathy	0	2 (2.0)
Retained products of conception	0	8 (7.9)
Broad ligament hematoma	0	1 (1.0)
Placental bed bleeding	0	3 (3.0)
Surgical bleeding	0	10 (9.9)
Retained placenta	0	7 (6.9)

Results. This study comprised 101 cases (patients diagnosed with PPH), and 209 controls (delivered without the development of PPH). During the one-year study period, 8350 deliveries took place at KAMC; hence, the primary PPH rate was 1.21 per 100 delivered women. The various reasons for the development of primary PPH are presented in **Table 1**; none of the controls developed any of these complications. Uterine atony emerged as the most important cause for the development of PPH among the cases (83.2%), followed by surgical bleeding and vaginal tears (9.9%). The mean blood loss among the PPH women was 1288.6 ± 979.5 ml as compared to a mean of 341.9 ± 192.6 ml blood loss in the control women. Demographic characteristics for PPH women and their controls as well as OR and 95% CI and p-values are presented in **Table 2**. There was a significant difference between the mean parity of the cases (3.5±2.6) as compared to the controls (2.8±2.4, p=0.04). Moreover, a parity of 3 or more was associated with an increased risk for the development of PPH). Finally, the mean GA for the cases was 37.7±4.0 as compared to 38.9±2.2 for the controls (p=0.0049). Pre-pregnancy and antenatal risk factors for the PPH cases and controls as well as OR, 95% CIs and p-values are presented in **Table 3**. None of the hypothesized medical risk factors were significantly related to the development of PPH. Conversely, several obstetric history-related risk factors (**Table 3**) were associated with the development of PPH. The development of PPH was significantly associated with previous history of PPH

Table 2 - Demographic characteristics of post-partum hemorrhage cases and controls.

Patient characteristic	Controls (n=209)	Cases (n=101)	OR (95% CI)	*P*-value
Age (years) (mean ± SD)	30.5 ± 6.4	31.0 ± 6.5	Not applicable	0.5
<30	102 (48.8)	40 (39.6)	Reference*	
30-39	88 (42.1)	51 (50.5)	1.48 (0.89-2.44)	0.3
≥40	19 (9.1)	10 (9.9)	1.34 (0.57-3.14)	
Parity (mean ± SD)	2.8 ± 2.4	3.5± 2.6	Not applicable	0.04
<3	116 (55.5)	42 (41.6)	Reference*	0.02
≥3	93 (44.5)	59 (58.4)	1.75 (1.08-2.83)	
Body mass index (kg/m²)	32.4± 5.3	33.6 ± 5.5	Not applicable	0.09
<24	15 (7.2)	5 (5.0)	Reference*	0.5
≥24	194 (92.8)	96 (95.1)	1.48 (0.52-4.21)	
Gestational age (weeks)	38.9 ± 2.2	37.7 ± 4.0	Not applicable	0.005
<38	38 (18.2)	25 (24.8)	Reference*	0.2
≥38	171 (81.8)	76 (75.3)	0.68 (0.38-1.20)	
Booking status	150 (71.8)	64 (64)	0.70 (0.42-1.16)	0.2

*Reference group for the calculation of the odds ratio (OR). CI - confidence interval

Table 3 - Pre-pregnancy and antenatal risk factors for post-partum hemorrhage (PPH) cases and controls.

Risk factor	Controls n=209		Cases n=101		OR	(95% CI)	*P*-value
Medical history							
Diabetes	6	(2.9)	4	(4.0)	1.40	(0.38 - 5.06)	0.73
GDM	25	(12)	6	(5.9)	0.46	(0.18 - 1.17)	0.10
PET	3	(1.4)	4	(4%)	2.83	(0.62 - 12.90)	0.22
Essential hypertension	7	(3.4)	5	(5.0)	1.50	(0.47 - 4.86)	0.54
HELLP syndrome	1	(0.5)	0	(0.0)	NA	NA	1.00
ITP	1	(0.5)	1	(1.0)	2.08	(0.13 - 33.60)	0.55
IDA	14	(6.7)	7	(6.9)	1.04	(0.41 - 2.66)	0.94
Obstetric history							
Previous CS	49	(23.4)	25	(24.8)	1.07	(0.62 - 1.87)	0.80
Number of CS, mean (SD)	0.4	(0.8)	0.3	(0.8)	NA	NA	0.71
Previous myomectomy	1	(0.5)	1	(1.0)	2.08	(0.13 - 33.60)	0.55
Previous PPH	3	(1.4)	6	(5.9)	4.34	(1.06 - 17.71)	0.06
Previous APH	2	(1.0)	5	(5.0)	5.39	(1.03 - 28.28)	0.04
Uterine fibroid	3	(1.4)	1	(1.0)	0.69	(0.07 - 6.68)	1.00
Pregnancy characteristics							
Multiple pregnancy	3	(1.4)	8	(7.9)	5.91	(1.53 - 22.77)	0.01
Large baby	5	(2.4)	3	(3.0)	1.25	(0.29 - 5.33)	0.72
Placenta previa	3	(1.4)	5	(5.0)	3.58	(0.84 - 15.27)	0.12
Abruptio placenta	1	(0.5)	5	(5.0)	10.8	(1.25 - 93.99)	0.02
Post date	64	(30.6)	23	(22.8)	0.67	(0.39 - 1.16)	0.15

GDM - gestational diabetes mellitus, PET - pre-eclampsia, ITP - idiopathic thrombocytopenia, CS - cesarian section, HELLP - hemolysis, elevated liver enzymes, low platelets, NA - not applicable, IDA - iron deficiency anemia, APH - ante partum hemorrhage

Table 4 - Intra-partum and post-partum risk factors for post-partum hemorrhage (PPH) cases and controls.

Intra- and post- partum risk factors for PPH	Controls n=209		Cases n=101		OR (95% CI)	*P*-value
Spontaneous labor	119	(56.9)	68	(67.3)	1.56 (0.95-2.56)	0.08
Induction by PGE2	29	(13.9)	8	(7.9)	0.53 (0.23-1.21)	0.1
Induction by Syntocinon	11	(5.3)	5	(5.0)	0.94 (0.32-2.77)	0.9
Induction by both	5	(2.4)	3	(3.0)	1.26 (0.30-5.39)	0.7
Elective CS	31	(14.8)	4	(4.0)	0.24 (0.08-0.69)	0.005
Emergency CS	43	(20.6)	17	(16.8)	0.78 (0.42-1.45)	0.4
Ventouse delivery	6	(2.9)	3	(3.0)	1.04 (0.25-4.23)	1.0
Forceps delivery	2	(1.0)	0	(0)	NA	1.0
SVD	114	(54.6)	74	(73.3)	2.28 (1.36-3.83)	0.002
Length of labor						
Length of first stage (minute)	210.7	(199.6)	287.2	(353.1)	NA	0.04
<180	99	(47.4)	43	(42.6)	Reference*	0.4
≥180	110	(52.6)	58	(57.4)	1.21 (0.75-1.96)	
Length of second stage (minute)	18.6	(26.7)	23.8	(36.1)	NA	0.2
<60	193	(92.3)	91	(90.1)	Reference*	0.5
≥60	16	(7.7)	10	(9.9)	1.33 (0.58-3.04)	
Length of third stage (minute)	4.3	(3.9)	13	(33.7)	NA	0.01
<30 or <5	208	(99.5)	93	(92.1)	Reference*	0.0001
≥30 or ≥5	1	(0.5)	8	(7.9)	17.9 (2.2-145.1)	
Active management, third stage	131	(62.7)	76	(75.3)	1.8 (1.1-3.1)	0.03
CTG abnormalities	54	(25.8)	41	(40.6)	2.0 (1.2-3.3)	0.01
Retained placenta	1	(0.5)	7	(6.9)	15.5 (1.9-127.7)	0.002
RPOC	0	(0)	5	(5.0)	NA	0.004

*Reference group for the calculation of the odds ratio (OR). CI - confidence interval, PGE2 - prostaglandin E2, SVD - spontaneous vaginal delivery, RPOC - retained products of conception, CS - cesarean delivery, CTG - cardiotocograph, NA - not applicable

Table 5 - Multiple logistic regression results for the risk factors of the development of post partum hemorrhage (PPH), with odds ratio and 95% confidence intervals (CI) and p-values.

Variable	aOR	95% CI	P-value
Parity	1.17	1.05 - 1.30	0.006
GDM	0.40	0.13 - 1.21	0.1
PET	6.11	1.14 - 32.71	0.03
Previous APH	8.15	1.43 - 46.46	0.02
Multiple pregnancy	11.01	2.45 - 49.42	0.002
SVD	1.93	1.04 - 3.57	0.04
Length of third stage	1.08	1.02 - 1.13	0.006
CTG abnormality	2.41	1.34 - 4.31	0.003

aOR - adjusted odds ratio, GDM - gestational diabetes mellitus, PET - pre-eclampsia, SVD - spontaneous vaginal delivery, APH - ante partum hemorrhage, CTG - cardiotocograph

and history of APH. The development of PPH was significantly associated with the following pregnancy related factors: multiple gestation and abruptio placenta. Intra-partum and post-partum risk factors for cases and controls as well as OR, 95% CIs, and p-values are presented in **Table 4**. Elective CS delivery was a significant protective factor against the development of PPH as compared to emergency CS (OR=0.24, 95% CI=0.08-0.69). A similar significant protective benefit was associated with spontaneous vaginal delivery compared to cesarean delivery. A prolonged third stage of more than 30 minutes was associated with an 18-fold increased risk for the development of PPH, while lack of active management of the third stage of labor was associated with almost double the risk of PPH. Finally, retained placenta and retained RPOC were associated with significant increases in the risk of the development of PPH (p=0.002 and p=0.003). The results of the stepwise multivariate logistic regression analysis are presented in **Table 5**. It was found that high parity (≥3) was associated with a 17% increased risk for the development of PPH. The development of preeclampsia was found to be associated with a more than 6-fold increase in the risk of development of PPH. Previous history of APH was found to increase the risk for PPH by more than an 8-fold. Other factors associated with the risk of developing PPH were multiple pregnancy, vaginal delivery, prolonged third stage, and presence of CTG abnormalities.

Discussion. The major cause of primary PPH in our sample was uterine atony 84 (83.2%). This is in agreement with other studies where uterine atony was found to be the major cause of PPH.[8,9] The second identified cause in our study was vaginal tears and episiotomy, the literature shows that episiotomy can bleed heavily. [4,10] Observational studies suggest that the relative risk of postpartum hemorrhage is increased by 4-5 times if an episiotomy was performed.[4,10] Therefore, a recommendation to avoid elective episiotomy should be established. Increased parity of ≥3 was associated with 17% increased risk for the development of primary PPH in our patients, which is consistent with other studies.[4] In a study on parity-related sociodemographic factors and contraceptive use in Saudi Arabia, Sibai et al[11] found a significant relationship between high parity and low educational attainment of the observed couples. Grand-multiparity has already been identified as a risk factor for the development of PPH in the Saudi population.[12] Such a finding, highlights the importance of patient education on family planning. The labor and delivery protocol at KAMC indicates that the length of the third stage should not exceed 30 minutes. Therefore, the effect of third stage prolongation was not prominent in this study (8% increased risk of PPH). A randomized trial comparing 20 versus 30 minutes length of the third stage was stopped after an interim analysis because only 8 of 1607 patients' placentas had not delivered by 20 minutes and a third stage of labor that exceeded 10 minutes was observed to be significantly correlated with an increased risk of post-partum hemorrhage.[13] Furthermore, meta-analytical reviews of randomized controlled trials of the role of active management of third stage in the prevention of PPH[14] revealed a trend towards a decreased need for therapeutic oxytocin (RR=0.50, 95% CI=0.39-0.64) in those who received prophylactic oxytocin.[15] Preeclampsia increased the risk of PPH by 6 times in our cases as compared to the controls. Witlin et al[16] found that the incidence of postpartum hemorrhage was approximately 4-fold greater in the magnesium sulfate group for patients with preeclampsia (RR=4.1, 95% CI=0.5-35.4); this was not statistically significant. The development of preeclampsia was a prominent and statistically significant risk factor for PPH among the women in our study. Further work investigating this risk on a larger sample of preeclamptic patients is needed. The presence of APH increased our patients' risk of developing 8-fold PPH. Several important studies showed that presence of APH increased the chance of PPH by 3-13 folds.[10,17,18] Therefore, our studied APH patients were at a comparable risk for the development of PPH as seen in other populations. Multiple pregnancies were associated with an 11-fold increase in the risk for the development of PPH. Epidemiological studies suggest that twins and higher-order pregnancies are at increased risk for PPH. In a large retrospective cohort study in Canada, multiple pregnancies were associated with almost double the risk for PPH.[19] Our twin gestation women carried a 5-times greater risk of developing PPH as compared to similar Western women; therefore extra

care should be taken during antenatal and intrapartum when preparing multiple gestation patients for delivery. In our data, CTG abnormalities were associated with a 2.5-fold increased risk of developing PPH. This could be explained by the increased risk of emergency CS delivery and instrumental vaginal delivery. Magann et al[17] found that PPH occurrence is higher in emergency CS deliveries while operative vaginal delivery is associated with a 66% increase in PPH occurrence.[4] Therefore, extra care should be taken for PPH prevention when a decision for emergency delivery is made. The reported rate of primary PPH in our study, 1.21 per 100 delivered women, is among the lowest. While this rate may be valid, it could also reflect lack of documentation, being in a tertiary care center with strict roles for active management of labor, or it may be a result of underestimation of blood loss using a visual method. Direct measurements of blood loss gives rise to primary postpartum hemorrhage rates of between 22% and 29%, as compared to rates of 5-8% with visual estimation.[20] This reflects an urgent need to implement a protocol that correctly estimate blood loss, as failing to do so may contribute negatively to patients' mortality and morbidity.

Two primary limitations of this study are the low number of women who developed PPH, and that the patient base was from one tertiary care center, a population whose risks for developing PPH may not be equivalent to those among all Saudi women. On the other hand, such work can be considered as a baseline study that can serve as a comparison for further studies incorporating a nationally representative sample.

In conclusion, risk factors for the development of PPH among Saudi pregnant women vary but are comparable to women of other nationalities, with a greater focus on parity, presence of APH, multiple gestation, CTG abnormalities and prolonged third stage of more than 30 minutes. There is a great need for patient education on the role of family planning and antenatal care in predicting and reducing the risk of PPH. Furthermore, physician education on active management of the third stage, appropriate preparation of patients for safe labor and delivery, and correct estimation of blood loss may contribute positively to the reduction of maternal morbidity and mortality resulting from PPH.

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