Risk Factors for Secondary Postpartum Haemorrhage: A Retrospective Study

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ABSTRACT

Background: Secondary Postpartum Haemorrhage (SPPH) refers to any abnormal vaginal bleeding between 24 hours to 6 weeks postpartum. SPPH is a relatively unexplored issue and there is limited evidence, especially regarding risk factors. The aim of this study was to identify risk factors for SPPH.

Method: Patients readmitted with a diagnosis of SPPH between 2014 and 2018 at a tertiary hospital in Queensland, Australia were identified. These patients were compared with randomly selected controls that gave birth via vaginal delivery and caesarean section at the centre during the same time period. Logistic regression analyses were applied for categorical variables and T-test along for continuous variables.

Results: 110 cases of SPPH were identified and 225 patients that did not have SPPH were randomly allocated as controls. Incomplete placenta (p=0.005), Antepartum Haemorrhage (APH) (p=<0.001), antepartum (p=0.004) anticoagulation, along with previous obstetric complications (p=0.036) were found to be statistically significant risk factors for SPPH. Previous obstetric complications include conditions such as primary PPH, gestational diabetes and pre-eclampsia. Demographic factors of age and ethnicity did not express any predisposition to SPPH along with other factors such as BMI, parity and plurality. The average estimated blood loss within 24 hours of delivery in the SPPH case group was 350ml and control group was 300ml (p=0.038).

Conclusion: This study confirms that incomplete placenta, APH, antepartum anti-coagulation and previous obstetric complications are risk factors for secondary postpartum haemorrhage. Early identification of these risk factors could potentially prevent SPPH, allowing a safer postnatal journey for mothers.

Keywords:

Caesarean section, Maternal morbidity, Postpartum haemorrhage, Secondary Postpartum Haemorrhage (SPPH)

Introduction

An established definition of Secondary Post-Partum Haemorrhage (SPPH) or delayed haemorrhage is any abnormal uterine bleeding between 24 hours to 6 weeks postpartum [1]. Primary postpartum haemorrhage (PPH) has been extensively studied; however, in comparison there is limited literature on SPPH. Reported incidence rates of SPPH vary from 0.23% [2] to 1.4% of all deliveries [3].

A Cochrane review in 2002 did not identify any randomised controlled trials that sufficiently informed the management SPPH [4]. Since this review, there have been several studies outlining management options [5,6] however, in comparison limited studies have attempted to explore the risk factors, with only three key recent studies on this topic. Debost Legrand, et al. [2], identified Primary Postpartum Haemorrhage (PPH) and maternal age >35 years. Marchant et al. [7], included primary PPH, history of SPPH, prolonged or incomplete third stage, maternal smoking, incomplete third stage, third trimester hospital admission and vaginal bleeding prior to 24 weeks gestation as risk factors for the condition. Hoveyda and MacKenzie [8] showed primary PPH and manual removal of placenta to be associated with SPPH. Primary PPH appears to be the common risk factor between all the studies; however, other factors do not appear to be reproducible [2,7,8]. Thus, further research in this area is warranted. This study aims to identify risk factors for SPPH to inform clinical management and decrease maternal morbidity.

Materials and Methods

A nested case-control study design was used. The sampling frame comprised of patients listed in the obstetric and perinatal database who delivered at a tertiary level hospital in Queensland, Australia between June 2014 and December 2018. Cases were eligible for inclusion if they re-presented to the hospital with abnormal uterine bleeding between 24 hours and 6 weeks postpartum. Controls were randomly selected 2:1 without replacement from the sampling frame of eligible women who delivered at the centre.

Controls were women who had given birth at the same hospital during the time frame of June 2014 and December 2018 and were not known to represent with abnormal bleeding. The case and control groups excluded patients that delivered under 20 weeks gestation or delivered a fetus less than 400g. The definition of Antepartum Haemorrhage (APH) used to include patients with any bleeding from the genital tract after 20 weeks gestation. Data for cases and controls were extracted from patients' electronic medical records and by retrospective chart audit.

Continuous variables were summarised using the mean (SD) if approximately normally distributed and tested between cases and controls using Student's t-test, or summarised using the median (IQR) and tested using Wilcoxon's rank-sum test otherwise. Categorical variables were summarised using frequencies (%) and tested between groups using Pearson's chi-square test or Fisher's exact test. Logistic regression analysis was used to quantify the effects of variables associated with SPPH. Analyses were performed using the Stata statistical software package (version 15).

The study was granted exemption from full ethics review by the Human Research Ethics Committee on 22nd september 2020.

Results

Of the 17,581 deliveries at the centre between June, 2014 and December, 2018, 110 cases of SSPH were identified and 225 controls were included in the analyses. Of the 110 cases, 80 (73%) had vaginal deliveries and 30 (27%) underwent caesarean sections. 10 of these caesareans were conducted as an emergency and 10 as elective caesareans. Of the 225 controls, 133 (59%) had vaginal deliveries and 92 (41%) underwent caesarean sections. 57 of the caesareans in the control group were conducted as an emergency and 35 as electives.

Demographic features were similar between the two groups (Table 1). Mean age of the case group was 31 years and 30 years for the control. The mean Body Mass Index (BMI) was 23kg/m2 for both groups. Previous obstetric complications varied significantly between case and controls with 24 patients (22%) in the case group and 28 patients (12%) in the control group OR: 2.0 (95% CI 1.1-3.6, p-value 0.04). The case group included 57 (52%) multiparous women and 53 (48%) primiparous, and the control group had 113 (50.2%) multiparous women and 112 (49.8%) primiparous. Of the 110 cases, 5 (5%) were multiple pregnancies with 2 triplets and 3 twins, whereas the control group had 3 (1%) twin pregnancies (p-value 0.07).

Table 1: Maternal demographics and medical conditions of the SPPH case group and control group.

Variable	Category	Control	Case	p-value
		(N=225)	(N=110)	
Age[a]		30 (6)	31 (5)	0.21
Ethnicity[b]	Caucasian	159 (71%)	75 (68%)	0.43
	Australian	7 (3%)	4 (4%)	
	aboriginal			
	Pacific Islander	5 (2%)	5 (5%)	
	Asian	18 (8%)	5 (5%)	
	South east Asian	11 (5%)	10 (9%)	
	Other	25 (11%)	11 (10%)	
Marital status[b]	Divorced	2 (1%)	4 (4%)	0.12
	Married/ de facto	172 (76%)	88 (80%)	
	Never married	49 (22%)	16 (15%)	
	Separated	2 (1%)	2 (2%)	
Body Mass Index (BMI)[c]		23 (21-27)	23 (20-27)	0.45
Smoking[b]		28 (12%)	13 (12%)	0.94
Drugs[b]		5 (2%)	5 (5%)	0.24
Plurality[b]		3 (1%)	5 (5%)	0.07
Gestation at delivery[c]		39 (38-40)	39 (37-40)	0.32
Gravida[c]		2 (1-3)	2 (1-3)	0.39
Parity[c]		1 (0-1)	1 (0-1)	0.8
Antenatal anti-coagulation[b]		4 (2%)	9 (8%)	0.004
Previous mode of delivery[b]	Caesarean section	34 (15%)	12 (11%)	0.027
	Forceps	5 (2%)	3 (3%)	
	Spontaneous vaginal delivery	66 (29%)	34 (31%)	
	Vacuum extraction	2 (1%)	8 (7%)	

Previous obstetric complications[b]		28 (12%)	24 (22%)	0.036
Previous miscarriage[b]		70 (31%)	43 (39%)	0.18
Medical condition: Haematology[b]		9 (4%)	6 (5%)	0.58
Medical conditions: Autoimmune[b]		20 (9%)	10 (9%)	1
Medical conditions: Mental Health[b]		41 (18%)	26 (24%)	0.25
Medical conditions: Cardio-respiratory[b]		34 (15%)	17 (16%)	1
Medical conditions: Gynaecological[b]		22 (10%)	34 (31%)	1
[a]Mean (SD), p-value from Student's t-test; N(%), [b]p-value from Pearson's chi-square test; [c]median (IQR), p-value from Wilcoxon's rank-sum test				

Analysis of the haematological medical conditions found that the SPPH case group included 3 patients with thrombocytopenia, 1 patient with a hyper-coagulopathic disorder and 2 with other haematological conditions. The control group included 3 patients with thrombocytopenia, 3 with hyper-coagulopathic disorders and 3 other haematological conditions. Haematological conditions in pregnancy were also assessed and the case group was found to have 9 patients (8%) with anaemia and 1 patient (0.9%) with a deep venous thrombus diagnosed in pregnancy, whereas the control group had 17 (7.5%) patients with anaemia and no reported cases of venous thromboembolism.

Induction of labour rates were 52% in the case group and 45% in the control group (Table 2). Antepartum haemorrhage was observed in only one control patient (0.4%) compared to 12 (11%) of cases (p<0.01). Primary PPH was observed in 21% of cases and 16% of controls OR1.4 (95%CI: 0.8-2.4, p-value 0.22). Incomplete placenta was only reported in vaginal births and with significantly higher occurrence in cases (9% vs 2%; OR: 4.4; 95% CI: 1.4-13; p-value <0.01). Two patients in the SPPH case group required Manual Removal of Placenta (MROP) whereas one patient in control group underwent an MROP. The estimated median blood loss within 24 hours was 300mls in the control group and 350mls in the SPPH case group (p-value 0.038).

Table 2: Pregnancy complications, intrapartum and postpartum factors of the SPPH case group and control group.

Variable	Category	Control	Case	Total	p-value
		(N=225)	(N=110)	(N=335)	
Hypertensives disorders of pregnancy[a]	Gestational hypertension	6 (3%)	6 (6%)	12 (4%)	0.11
	Pre-eclampsia	13 (6%)	6 (6%)	19 (6%)	
Endocrine and gastrointestinal disorders[a]	Hyperemesis	14 (4%)	7 (6%)	21 (4%)	0.15
	Gestational hypertension	31 (8%)	14 (13%)	45 (9%)	
	Cholestasis of pregnancy	2 (1%)	0 (0%)	2 (0%)	
Early rupture of membranes[a]		37 (16%)	18 (17%)	55 (17%)	1
Antepartum haemorrhage[a]		1 (0%)	12 (11%)	13 (4%)	0.001
Fetal abnormalities[a]		51 (23%)	30 (27%)	81 (24%)	0.42
Group B Streptococcus[a]		8 (4%)	7 (6%)	15 (4%)	0.27
Decreased fetal movements[a]		58 (26%)	30 (27%)	88 (26%)	0.79
Uteroplacental complications[a]		11 (5%)	11 (10%)	22 (7%)	0.098
Induction of labour[a]		101 (45%)	57 (52%)	158 (47%)	0.23
Induction of labour with syntocinon[a]		68 (30%)	34 (31%)	102 (30%)	0.9
Mode of birth[a]	Emergency caesarean	57 (25%)	10 (9%)	67 (20%)	0.005
	Elective caesarean	35 (16%)	20 (18%)	55 (16%)	
	Forceps	4 (2%)	6 (5%)	10 (3%)	
	Spontaneous vaginal delivery	112 (50%)	65 (59%)	177 (53%)	
	Vacuum extraction	17 (8%)	9 (8%)	26 (8%)	
First stage of labour duration (mins)[b] (n=207)		270 (165-455)	240 (145-390)	270 (158-420)	0.44
Second stage of labour duration (mins) [b](n=133)		23 (11-79)	37 (14-83)	30 (11-79))	0.42

Third stage of labour duration (mins)[b](n=131)		10 (7-15)	12 (7-22)	10 (7-18)	0.053
Total labour duration[b]		140 (0-368)	212 (0-420)	169 (0-390)	0.2
Active third stage[a]		208 (93%)	107 (97%)	315 (94%)	0.1
Perineal laceration[a]	Nil tear	130 (58%)	50 (45%)	180 (54%)	
	First degree	21 (9%)	12 (11%)	33 (10%)	
	Second degree	40 (18%)	31 (28%)	71 (21%)	
	Episiotomy	30 (13%)	15 (14%)	45 (13%)	
	Third degree	4 (2%)	2 (2%)	6 (2%)	
Antibiotics in labour[a]	101 (45%)	40 (37%)	141 (42%)	101 (45%)	0.16
Infective complications in labour[a]		12 (5%)	4 (4%)	16 (5%)	0.52
Incomplete placenta[a]		5 (2%)	10 (9%)	15 (5%)	0.005
Primary postpartum haemorrhage[a]		35 (16%)	23 (21%)	58 (17%)	0.22
Estimated blood loss within 24 hours (mlns) [b]		300 (200-450)	350 (250-500)	300 (200-500)	0.038
Postpartum anticoagulation[a]		95 (42%)	30 (27%)	125 (37%)	0.008
[a]N(%),p-value from Pearson's chi-square test; [b]median (IQR), p-value from Wilcoxon's rank-sum test					

Anticoagulant use in the antenatal period was more frequent in the SPPH case group (8% vs 2% p-value=0.004). One patient in the case group was on therapeutic anticoagulation in the antenatal period with Enoxaparin due to a deep venous thromboembolism. Postpartum anticoagulation use was significantly reduced in the SPPH case group (27% vs 42%; p <0.01) (Table 2).

Discussion

Debost-Legrand, et al. [2], Marchant, et al. [7] and Hoveyda, et al. [8], are key studies that have previously examined risk factors for SPPH. All three studies confirm that primary PPH is a risk factor for SPPH. However, we did not find a significant statistical association between primary PPH and SPPH (p-value=0.22). However, the SPPH case group median estimated blood loss in the first 24 hours was 50mls more than the control group. Primary PPH not indicating a statistically significant association with SPPH in this study could be attributed to the routine use of active third stage management at the centre. Active third stage includes administration of an uterotonic and assisting delivery of the placenta, and has been shown to decrease the risk of primary PPH [9]. 94% of patients in the study had active third stage as part of their care (Table 2). This could potentially have an effect on decreasing the primary PPH rates in the cohort.

Previous obstetric complications were found to be a statistically significant risk factor in developing secondary postpartum haemorrhage. Previous obstetric complications primarily included previous primary PPH along with gestational diabetes and pre-eclampsia. As previous studies have shown that primary PPH increases risk of a repeat primary PPH in the next pregnancy, it may also be risk for SPPH [1].

Demographic features were not found to have an increased association with SPPH. Marchant et al. [7], observed a correlation with increased BMI; however, this study and Debost-Legrand, et al [2], did not find any association with BMI.

This study found the use of antenatal anticoagulation a risk factor for SPPH. Anticoagulation use during the antenatal period included aspirin, enoxaparin or combined aspirin and enoxaparin. Of the patients on anticoagulation, most patients were commenced on a prophylactic dose of enoxaparin to prevent a Venous Thromboembolism (VTE) as per the local guidelines [10]. However, one patient in the SPPH case group was on therapeutic doses due to a deep venous thromboembolism diagnosed in pregnancy. A study by Wang et al. [11], supports the finding of increased haemorrhagic risk with antenatal use of therapeutic and prophylactic anticoagulation.

Incomplete placenta had an increased association with SPPH in this study. This is similar to Debost-Legrand et al's findings and is further supported by King et al's [12] finding of retained placenta being more likely in patients with secondary haemorrhage. Marchant et al. [7], also found an incomplete third stage being associated with SPPH.

Antepartum haemorrhage was found to have an increased occurrence in the SPPH case group [13]. Previous studies have not investigated the relationship between APH and SPPH. Marchant et al. [7], found an increased risk of SPPH in patients that had vaginal bleeding prior to 24 weeks; however, did not investigate after 24 weeks.

Conclusion

This study is consistent with the current literature that identified factors such as incomplete placenta and antenatal anti-coagulation as increasing the risk of SPPH. It also identifies antepartum haemorrhage and previous obstetric complications as possible risk factors that have not been previously investigated. Identification of these risk factors could lead to a change in clinical practise. SPPH could potentially be prevented by modification of procedures found to increased risk. Additionally, it could also assist in identifying women at increased risk of SPPH early in their antenatal period and targeting education along with shorter term follow-up postpartum. Thus, further investigation is warranted to identify if antepartum haemorrhage and

previous obstetric complications such primary PPH have an association with SPPH. Limitations of this study are the small sample size and single centre data. Further investigation with a larger sample size, multicentre incorporation and perspective data could further improve on the current data.

Conflict of Interest

The authors declare no competing financial interest.

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