Prevalence and Risk Factors of Severe Postpartum Hemorrhage: a Retrospective Cohort Study

Chenning Liu
Dongguan Maternal and Child Health Care Hospital
Fubing Yu
Dongguan Maternal and Child Health Care Hospital
Yunzhe Xu
Third Affiliated Hospital of Guangzhou Medical University
Jinsheng Li
Third Affiliated Hospital of Guangzhou Medical University
Zhihong Guan
Third Affiliated Hospital of Guangzhou Medical University
Manna Sun
Dongguan Maternal and Child Health Care Hospital
Chenan Liu
Shanxi Medical University
Fang He (hefangjnu@126.com)
Third Affiliated Hospital of Guangzhou Medical College https://orcid.org/0000-0003-3362-6002
Dunjin Chen
Third Affiliated Hospital of Guangzhou Medical University

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Prevalence and risk factors of severe postpartum hemorrhage: a retrospective cohort study

Chenning Liu[1,5], Fubing Yu[5], Yunzhe Xu[1], Jinsheng Li[1], Zhihong Guan[1], Manna Sun[1,5], Chenan Liu[6], Fang He[1,2,3*], Dunjin Chen[1,2,4*]

First authors: Chenning Liu and Fubing Yu contributed equally to this work.

Corresponding authors: Fang He and Dunjin Chen were co-corresponding authors of this work.

Correspondence: hefangjnu@126.com (F. He); chendunjin123@163.com (D. Chen).

[1]Department of Obstetrics, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou 510150, China

[2]Key Laboratory for Major Obstetric Diseases of Guangdong Province, Guangzhou 510150, China

Full list of author information is available at the end of the article.

Abstract

Background: Although maternal deaths are rare in developed regions, the morbidity associated with severe postpartum hemorrhage remains a major problem. To provide new insight into severe postpartum hemorrhage, we analyzed data of women giving birth in Guangzhou Medical Centre for Critical Pregnant Women, which received a large quantity of critically ill obstetric patients from other hospitals of Southern China.

Methods: In this study, we conducted a retrospective cohort by using the criteria of severe maternal morbidities, which was defined by estimation of blood loss volume and use of blood transfusion≥4 units, to determine the prevalence, risk factors and short-term complications of severe postpartum hemorrhage.

Results: Severe postpartum hemorrhage was observed in 532 mothers (1.56%) among the total population of 34 178 mothers. Placental related cause (55.83%) was the major identified cause of severe postpartum hemorrhage, while uterine atony without associated retention of placental tissues accounted for 38.91%. The risk factors for severe postpartum hemorrhage were maternal age<18 years, previous cesarean section, history of postpartum hemorrhage, conception through in vitro fertilization, pre-delivery anemia, stillbirth, prolonged labor, placenta previa, placental abruption, placenta accrete spectrum and macrosomia. The prevalence rates of admission to ICU, hysterectomy, acute renal failure and sepsis were significantly higher in women with severe postpartum hemorrhage.

Conclusion: The results of this study suggested that severe postpartum hemorrhage could be adopted as an indicator to assess the quality of obstetric care because of its severity and potential lethality. Extra vigilance during the antenatal and peripartum periods is needed to identify women

who have risk factors and enable early intervention to prevent severe postpartum hemorrhage. It's important to remember that we have to prepare for all mothers giving birth, as some get severe postpartum hemorrhage without any known risk factors.

Keywords: Postpartum hemorrhage, Causes, Risk factors, Short-term complications

Background

Severe postpartum hemorrhage (SPPH) is the leading cause of maternal deaths and severe maternal morbidities, which accounts for almost one fifth of maternal deaths worldwide, ranging from 8% in developed areas to 32% in Northern Africa [1]. The incidence of postpartum hemorrhage (PPH) ranges from 3% to 8% and continues to increase in recent years [2-4]. Severe complications such as hemorrhagic shock, acute respiratory distress syndrome, disseminated intravascular coagulation, acute renal failure, loss of fertility, pituitary necrosis (Sheehan syndrome), and even maternal death may be caused by delayed recognition or an improper clinical procedure.

The reported prevalence of SPPH varied, and was influenced by the definition, case ascertainment, clinical management and characteristics of the population. There are several definitions of PPH in use, and no single satisfactory definition exists. Commonly used definitions

of postpartum hemorrhage are based on estimations of blood loss within 24h of childbirth [5, 6]. The severity of PPH, however, depends not only on volume, but also on the rate of blood loss, physical conditions, physiological response to bleeding and medical conditions, making women more vulnerable to decompensation with bleeding around delivery [7, 8]. On the other hand, the inaccuracy estimation of blood loss suggests that PPH may not be fully diagnosed.

Although maternal deaths are rare in developed regions, the morbidity associated with SPPH remains a major problem. Therefore, SPPH is still an indicator to assess the quality of obstetric care in developed areas. Although severe obstetric hemorrhage may develop unexpectedly, many studies have attempted to alert doctors to severe obstetric hemorrhage by identifying specific high-risk factors for PPH. These factors include previous cesarean delivery, hypertensive disorders of pregnancy, fibroids, placenta previa, etc. [4, 9-11].

To provide new insight into SPPH, we analyzed a retrospective cohort of women giving birth in Guangzhou Medical Centre for Critical Pregnant Women, which received a large quantity of critically ill obstetric patients from other hospitals of Southern China. In this study, we used the criteria of severe maternal morbidities [12], which was defined by estimation of blood loss volume

and use of blood transfusion≥4 units, to determine the prevalence, risk factors and short-term complications of SPPH.

Methods

Study population

We used data on all women giving birth after 28 weeks of gestation in The Third Affiliated Hospital of Guangzhou Medical University (Guangzhou Medical Centre for Critical Pregnant Women) from January 2015 to August 2019 (34 178 mothers). From this population, we identified 532 cases of SPPH. SPPH was defined as a visually estimated blood loss exceeding 1000mL within 24h of childbirth, and women received either≥4 units of RBCs or a multicomponent blood transfusion. The deadline for eventual blood transfusion was the time of discharge. A multicomponent blood transfusion was defined as blood transfusion consisting of a combination of RBCs and fresh frozen plasma and/or platelet concentrates. Controls were a random sample from the same source of population and period, comprising a total of 33 646 mothers.

Based on a review of the relevant literature and clinical plausibility, we formulated a set of 27 candidate risk factors on maternal characteristics and comorbidities that potentially contributed to increased risk of SPPH. We restricted our analysis of potential risk factors that would likely be

identifiable during the antepartum period up to the time of admission for delivery and were not complications developed during the delivery admission. We defined the presence of each condition as having one or more corresponding codes during this period. In the study population of 34 178 mothers, there were 844 women excluded in the risk factor analysis because of an incomplete information (Figure 1). All diagnoses were identified by the presence of a diagnostic codes from the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM). Surgical procedures were identified using surgical codes.

The explanatory variables (explained in Appendix) included demographic, pre-gestational medical and obstetric-related factors. The demographic characteristics were as follows: age of delivery, history of cesarean delivery, parity, body mass index (BMI) before pregnancy and history of PPH. The pre-gestational medical variables were defined as medical diseases prior to pregnancy, and diseases including chronic hypertension, pre-gestational diabetes mellitus (PGDM) and cardiac diseases. The pregnancy-related variables were identified directly in ticked boxes, such as in vitro fertilization (IVF), regular or irregular prenatal examination, singleton or twins, hypertensive disorders of pregnancy, HELLP syndrome, gestational diabetes mellitus (GDM), fibroids, anemia, thrombocytopenia, blood coagulation disorder, stillbirth, placenta previa, placenta abruption,

placenta accrete spectrum (PAS) and macrosomia. The labor-related obstetric variables included induction of labor, prolonged labor, precipitate labor and mode of delivery.

Meanwhile, short-term postpartum complications, such as admission to ICU, hysterectomy, acute renal failure, sepsis and maternal death were analyzed between the SPPH group and controls.

Statistical analysis

Prevalence and causes of SPPH were expressed as number (n) and percentage (% or ‰). Cross-tabulations were used to show the proportions of demographic, medical and obstetric factors in women with SPPH and controls. Univariate logistic analysis was done to assess candidate variables as risk factors for SPPH, and the associations between potential risk factors and SPPH was quantified by the OR and 95% confidence interval (CI). All explanatory variables with a significance level of $P < 0.05$ in univariate analysis were included in multivariate logistic analysis using a fully stepwise selection algorithm. In consideration of previous reports and clinical plausibility, we especially included twins, thrombocytopenia, blood coagulation disorder, precipitate labor and macrosomia in multivariate analysis, despite $P \geq 0.05$ in univariate analysis. Finally, cross-tabulation and odds ratios were used to calculate differences in the frequency of severe

postpartum complications between mothers with SPPH and controls. The data were analyzed with SPSS version 24. Statistical significance was judged as $P<0.05$.

Results

SPPH was observed in 532 mothers (1.56%) among the total population of 34 178 mothers. The causes of SPPH are showed in Figure 2. Placental related cause (55.83%) was the primary identified cause of SPPH, while uterine atony without associated retention of placental tissues accounted for 38.91%. Trauma and coagulopathy could be identified for 2.82% and 1.13% of the SPPH cases, respectively.

Risk factors of SPPH

The study population comprised a total of 506 cases of SPPH and 32 828 controls without SPPH. The distribution of potential risk factors was presented in Table 1. In the univariate analysis, SPPH was more likely among mothers with the following characteristics: ≥35y, multipara, history of PPH, previous cesarean delivery, conception through IVF, irregular prenatal examination, GDM, anemia, stillbirth, prolonged labor, cesarean section, placental previa, placental abruption and PAS.

Table 1 Clinical profile of women with SPPH versus controls

	SPPH(n=506)	Controls (n=32 828)	OR	95%CI	*P*

Maternal age (y)					
<18	1·(0.20%)	20 (0.06%)	3.99	0.53-29.84	0.177
18-34.9	318 (62.85%)	25389 (77.34%)	Ref.		
35-39.9	149 (29.45%)	5883 (17.92%)	2.02	1.66-2.46	<0.001
≥40	38 (7.51%)	1536 (4.68%)	1.98	1.41-2.78	<0.001
Parity					
0	138 (27.27%)	17913 (54.57%)	Ref.		
1-2	355 (70.16%)	14698 (44.77%)	3.14	2.57-3.82	<0.001
≥3	13 (2.57%)	217 (0.66%)	7.78	4.34-13.95	<0.001
Previous cesarean delivery	302 (59.68%)	6323 (19.26%)	6.21	5.19-7.43	<0.001
BMI (kg/m^2)					
<18.5	41 (8.10%)	3239 (9.87%)	0.83	0.60-1.14	0.250
18.5-24.9	354 (69.96%)	23107 (70.39%)	Ref.		
25-29.9	91 (17.98%)	5531 (16.85%)	1.07	0.85-1.36	0.547
≥30	20 (3.95%)	951 (2.90%)	1.37	0.87-2.16	0.172
History of PPH	20 (3.95%)	161 (0.49%)	8.35	5.20-13.40	<0.001

Chronic hypertension	0 (0.00%)	79 (0.24%)	0.00	0.00	0.977
PGDM	0 (0.00%)	248 (0.76%)	0.00	0.00	0.995
Cardiac disease	8 (1.58%)	354 (1.08%)	1.47	0.73-2.99	0.282
IVF	84 (16.60%)	4283 (13.05%)	1.33	1.05-1.68	0.019
Irregular prenatal examination	282 (55.73%)	15524 (47.29%)	1.40	1.18-1.68	<0.001
Twins	34 (6.72%)	2186 (6.66%)	1.01	0.71-1.43	0.957
Hypertensive disorders of pregnancy					
Gestational hypertension	15 (2.96%)	706 (2.15%)	1.40	0.83-2.36	0.203
Preeclampsia	26 (5.14%)	1422 (4.33%)	1.21	0.81-1.80	0.356
Eclampsia	0 (0.00%)	18 (0.05%)	0.00	0.00	0.999
HELLP syndrome	2 (0.40%)	68 (0.21%)	1.91	0.47-7.82	0.367
GDM	105 (20.75%)	5369 (16.35%)	1.34	1.08-1.66	0.008
Fibroids	5 (0.99%)	172 (0.52%)	1.90	0.78-4.63	0.161
Anemia	158 (31.23%)	2954 (9.00%)	4.59	3.79-5.56	<0.001
Thrombocytopenia	6 (1.13%)	317 (0.97%)	1.23	0.55-2.77	0.617
Blood coagulation disorder	2 (0.40%)	43 (0.13%)	3.03	0.73-12.52	0.127

Stillbirth	7 (1.38%)	132 (0.40%)	3.48	1.62-7.47	0.001
Induction of labor	22 (4.35%)	3045 (9.28%)	0.45	0.29-0.68	<0.001
Prolonged labor	18 (3.56%)	583 (1.78%)	2.04	1.27-3.29	0.003
Precipitate labor	1 (0.20%)	219 (0.67%)	0.30	0.04-2.11	0.223
Mode of delivery					
Vaginal delivery	370 (73.12%)	27780 (84.62%)	Ref.		
Cesarean section	136 (26.88%)	5408 (16.47%)	2.02	1.66-2.47	<0.001
Placenta previa	311 (61.46%)	1392 (4.24%)	36.02	29.88-43.42	<0.001
Placental abruption	11 (2.17%)	337 (1.03%)	2.14	1.17-3.93	0.014
PAS	283 (55.93%)	1076 (3.28%)	37.45	31.10-45.09	<0.001
Macrosomia	41 (8.10%)	2553 (7.78%)	1.05	0.76-1.44	0.79

Risk factors independently associated with SPPH were showed in Table 2. The risk of SPPH increased significantly as age<18y (adjusted ratio (aOR)=11.52). The risk of mothers who had history of PPH and previous cesarean section elevated, and the aOR was 4.94 and 2.57, respectively. Placental factors were associated with SPPH significantly; placental previa had the highest adjusted odds ratio of SPPH (9.75), followed by PAS (8.00) and placental abruption (3.85). Other obstetric

risk factors were prolonged labor (aOR=5.24), stillbirth (aOR=2.61), anemia (aOR=2.37), macrosomia (aOR=2.30), and IVF (aOR=1.78). Besides, cesarean section was a protective factor in this study, which had an aOR of 0.58.

Table 2 Multivariable logistic model for SPPH

Independent risk factors	Adjusted OR	95% CI	*P*
Maternal age<18y	11.52	1.51-87.62	0.018
Previous cesarean section	2.57	1.90-3.47	<0.001
History of PPH	4.94	2.63-9.29	<0.001
IVF	1.78	1.31-2.43	<0.001
Anemia	2.37	1.88-3.00	<0.001
Stillbirth	2.61	1.02-6.69	0.045
Prolonged labor	5.24	3.10-8.86	<0.001
Cesarean section	0.58	0.46-0.74	<0.001
Placenta previa	9.75	7.45-12.75	<0.001
Placental abruption	3.85	1.91-7.76	<0.001
PAS	8.00	6.20-10.33	<0.001

Macrosomia	2.30	1.38-3.83	0.001

Maternal morbidity of SPPH

The prevalence rates of admission to ICU, hysterectomy, acute renal failure and sepsis were significantly higher in women with SPPH (Table 3). SPPH increased the prevalence of admission to ICU and hysterectomy by 8.97 and 180.37 times, respectively. Meanwhile, the risk of acute renal failure and sepsis elevated by 31.74 and 6.53 times in SPPH group. During the period of the present study, only one woman with SPPH developed to death (1.9‰), and eight women in controls (0.2‰). Severe postpartum hemorrhage accounted for 11.11% of maternal deaths, and there were no statistically significant differences between the two groups in maternal mortality.

Table 3 Association between SPPH and severe postpartum complications

postpartum complication	SPPH(n=532)		Controls (n=33 646)		OR	95%CI	*P*
	No.	Percentage (‰)	No.	Percentage (‰)			
ICU admission	39	73.3	294	8.7	8.97	6.35-12.68	<0.01
Hysterectomy	109	204.9	48	1.4	180.37	126.75-256.67	<0.01
Acute renal failure	2	3.8	4	0.1	31.74	5.80-173.65	<0.01
Sepsis	4	7.5	39	1.2	6.53	2.33-18.33	<0.01

Discussion

Prevalence of SPPH

In our study, the prevalence of SPPH was 1.56%, which was following a known prevalence of 0.3-5.1% [4, 10, 11, 13]. The incidence of SPPH varied among reports, which might be partly due to different definitions, discrepancies of areas and recording practices. The most commonly accepted definition of PPH is based on the amount of blood loss after birth. The WHO recommends visual estimation of blood loss as the standard for blood loss measurement; yet, visual estimate underestimates blood loss volume by 33-50% when compared with spectrophotometry [14, 15]. We used a cutoff for SPPH of blood loss volume≥1000mL and blood transfusions≥4 units to make our results more reliable. Most of the previous studies included pregnancies from 24 weeks, while our study consisted of mothers from 28 weeks. Such factors might explain the different prevalence in our population.

Common causes of PPH are uterine atony, placental cause, trauma and failure of the blood coagulation system. In our study, uterine atony without other associated causes was identified in only 38.91% of mothers, which was much lower than the reported prevalence of 70-80% [4, 16, 17]. Meanwhile, abnormal placentation was responsible for the majority (55.83%) of SPPH, which was

much higher than the previously reported prevalence of 10% [4, 17]. This might be explained by our rules of classification and the special population in our hospital. In our study, women who had atony due to retained placental tissues were categorized in the group of placental related cause. For another reason, our hospital was Guangzhou Medical Centre for Critical Pregnant Women, which received a large quantity of critically ill obstetric patients transferred from other hospitals of Southern China, including a high proportion of PAS and dangerous placenta previa. As previous studies reported, the prevalence of PAS and placenta previa were 0.1-11 per 1000 deliveries and 5.5 per 1000 deliveries, respectively [18]. In our study, there were 306 mothers (57.52%) with PAS and 332 cases (62.41%) with placenta previa in SPPH group, which were much higher than other hospitals. Our findings suggested that placental related cause might be a more prominent cause of SPPH than previous reports. Trauma accounted for only 2.82%, which was less than the figure reported of 20% [11]. This could be partly due to proper obstetric care though labor and vaginal delivery procedures. Coagulopathy prevalence was relatively in accordance with a known prevalence of 1% [11].

Risk factors for SPPH

The risk factors for SPPH were maternal age<18y, previous cesarean section, history of PPH, conception through IVF, pre-delivery anemia, stillbirth, prolonged labor, placenta previa, placental abruption, PAS and macrosomia. Previous cesarean section, pre-delivery anemia, stillbirth, prolong labor and macrosomia were associated with SPPH, which were compatible with previous reports [4, 9-11, 19-21]. With antenatal anemia affecting up to 25% pregnant women, initiatives may be necessary to promote anemia correction [22]. Severe societies, including The Royal College of Obstetricians and Gynecologists (UK) and the French College of Gynecologists and Obstetricians, have published PPH guidelines recommending that a hemoglobin level above 8g/dL is a therapeutic goal [23]. Macrosomia is known to over-distend the uterus which is associated with uterine atony. Macrosomia is an increasingly common lifestyle problem needing public health intervention, and is associated with high BMI, elderly pregnant women and diabetes mellitus [24, 25].

Numerous studies have reported that elderly maternal age (≥35y or ≥40y) was a risk factor of PPH, while few studies suggested that young age might be a risk factor as well [26]. In our study, the results showed that elderly maternal age (≥35y) increased the incidence of SPPH in univariate analysis. Nevertheless, maternal age<18y was actually associated with increased SPPH. Women with a history of PPH had 4.94-fold increased odds of SPPH. Likewise, a study from Australia

reported a recurrence rate of 28% from medical audits [27]. A study from Sweden reported that the recurrence of PPH might be explained by environmental and genetic factors [28]. The risk of SPPH elevated in women who conceived through IVF, which was in accordance with previous studies. Zhu et al. reported that placental adherence occurred more frequently in a group after using assisted reproductive technology [29].

Our study showed that cesarean section was associated with SPPH, together with an increased incidence of SPPH in the univariate analysis. However, the risk of SPPH decreased by 43% in women with cesarean delivery in the multivariate model. The protective effect of cesarean section was contrary to the results in most previous studies. However, a few studies reported the protective effect of cesarean section against PPH when compared with vaginal births [30]. Our study showed that the risk of SPPH elevated significantly for women with placenta previa, placental abruption and PAS, which was consistent with previous studies [4, 9-11, 19-21]. Placenta related factors contributed significantly to severe forms of PPH, such as PPH with blood transfusion and PPH with hysterectomy.

Short-term postpartum morbidities associated with SPPH

Among women with SPPH, the higher frequencies of admission to ICU, peripartum hysterectomy, acute renal failure and sepsis reflected the severity and potential lethality of this complication. Mothers with SPPH had 6.53 times the risk of sepsis compared with controls. The association between SPPH and sepsis is partly explained by underlying factors or procedures such as prolonged labor, manual removal of placenta, injuries and surgical interventions to stop bleeding [31]. In addition, the consequent anemia increases the risk of postpartum infections and consequently sepsis. The risk of acute renal was 31.74 times higher in mothers with SPPH, implying the severe hypoperfusion of organs. In our study, the rate of maternal death increased in SPPH group (1.9‰) compared with controls (0.2‰), but there was no statistical difference between the two groups. Only one mother developed to death because of SPPH, which might get benefit from the early-warning system and rapid response team we established. The high rates of emergency peripartum hysterectomy and admission to ICU in SPPH were evidence that mothers were associated with severe morbidity. It is clear that SPPH affects the mothers, their newborns, families and the finances of the healthcare system.

Strengths and limitations

Our study has two strengths, as well as some limitations. First, a large cohort of women in Guangzhou Medical Centre for Critical Pregnant Women ensured an obstetric critical representative sample of Southern China. Second, we diagnosed SPPH by combining blood loss volume with blood transfusion to minimize selection bias, thus analyzed the causes, risk factors and complications of SPPH comprehensively and objectively.

The limitation of our study was the absence of data on instrumental/spontaneous vaginal delivery and emergency/elective cesarean section. Although surgery codes existed for forceps, vacuum, assisted breech and emergency or elective cesarean section, the operations sometimes were coded by other broader surgery codes and thus failed to identify the substantial proportion of different modes of delivery, which prevented us from studying the contribution of delivery mode to the occurrence of SPPH. For another, we did not analyze the impact of smoking or drinking to SPPH, since it was rarely among our population. Absolutely, assessing risk factors in retrospect was also a limitation in our study.

Conclusions

The results of this study suggested that SPPH could be adopted as an indicator to assess the quality of obstetric care because of its severity and potential lethality. Maternal age<18y, previous

cesarean section, history of PPH, conception through IVF, pre-delivery anemia, stillbirth, prolonged labor, placenta previa, placental abruption, PAS and macrosomia were risk factors of SPPH. Extra vigilance during the antenatal and peripartum periods is needed to identify women who have risk factors and enable early intervention to prevent SPPH. It's important to remember that we have to prepare for all mothers giving birth, as some get SPPH without any known risk factors.

Figure1 Profile of the study population

Figure 2 Causes of severe postpartum hemorrhage

Abbreviations

PPH: Postpartum hemorrhage; SPPH: Severe postpartum hemorrhage; PAS: placenta accrete spectrum; GDM: gestational diabetes mellitus; PGDM: pre-gestational diabetes mellitus; BMI: Body mass index; HELLP: Hemolysis elevated liver enzymes, low platelet count; IVF: In vitro fertilization; OR: Odds ratio; aOR: adjusted odds ratio; CI: Confidence interval

Ethics approval and consent to participate

The study was approved by the medical research ethics committee of the third affiliated hospital of Guangzhou Medical University. The approval reference number is 2020107. All information obtained from the patients' medical records was anonymized and de-identified prior to analysis.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding authors on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

Fang He and Dunjin Chen were responsible for conception, study design and approved the final version. Chenning Liu and Fubing Yu monitored data collection, analyzed the data, drafted and revised the paper. Yunzhe Chen, Jinsheng Li and Zhihong Guan collected data. Mana Sun and Chenan Liu analyzed the data.

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Author details

[1]Department of Obstetrics, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China. [2]Key Laboratory for Major Obstetric Diseases of Guangdong Province, Guangzhou, China. [3]Guangzhou Medical Centre for Critical Pregnant Women, Guangzhou, China. [4]Quality Control Center of Obstetrics of Guangdong Province, Guangzhou, China. [5]Dongguan Maternal and Child Health Care Hospital, Dongguan, China. [6]Shanxi Medical University, Taiyuan, China.

Appendix. Part of variables investigated in analysis

Variable	Explanation
Maternal age (y)	age of delivery; categorized into four groups: <18, 18-34.9, 35-39.9 and≥40 years.
Parity	grouped into no previous deliveries (0), 1-2 previous deliveries, and ≥3 previous deliveries.
BMI (kg/m^2)	low weight<18.5; normal: 18.5-24.9; overweight: 25-29.9; obesity≥30.

Hypertensive disorders of pregnancy	categorized into gestational hypertension, preeclampsia and eclampsia; gestational hypertension was defined as only if she did not have codes for pre-existing hypertension or preeclampsia or eclampsia.
Anemia	hemoglobin<9g/dL before delivery.
Thrombocytopenia	platelet count<$100*10^9$/L.
Prolonged labor	prolonged first stage of labor was determined as deviation of cervical dilatation from the normal rate of 1 cm/hour in the active phase or slow progress of the descent of the presenting part through birth canal; prolonged second stage of labor was>1hour from complete cervical dilation to delivery if multiparous and>2hours between complete cervical dilation and delivery if nulliparous.
Precipitate labor	3 hours or less from the onset of regular contractions to birth.
Macrosomia	substituted by a birthweight of ≥4kg.

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Figures

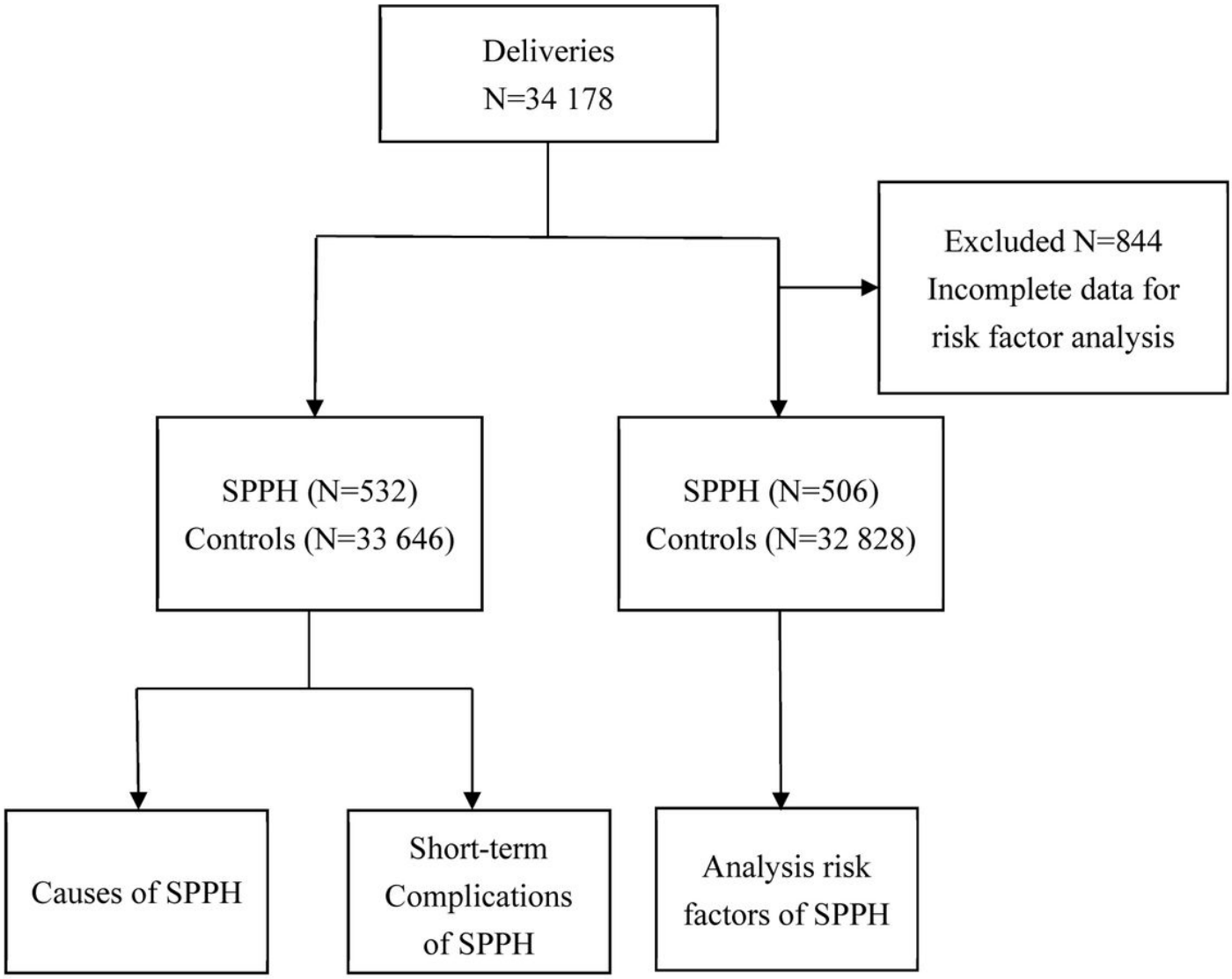

Figure 1

Profile of the study population

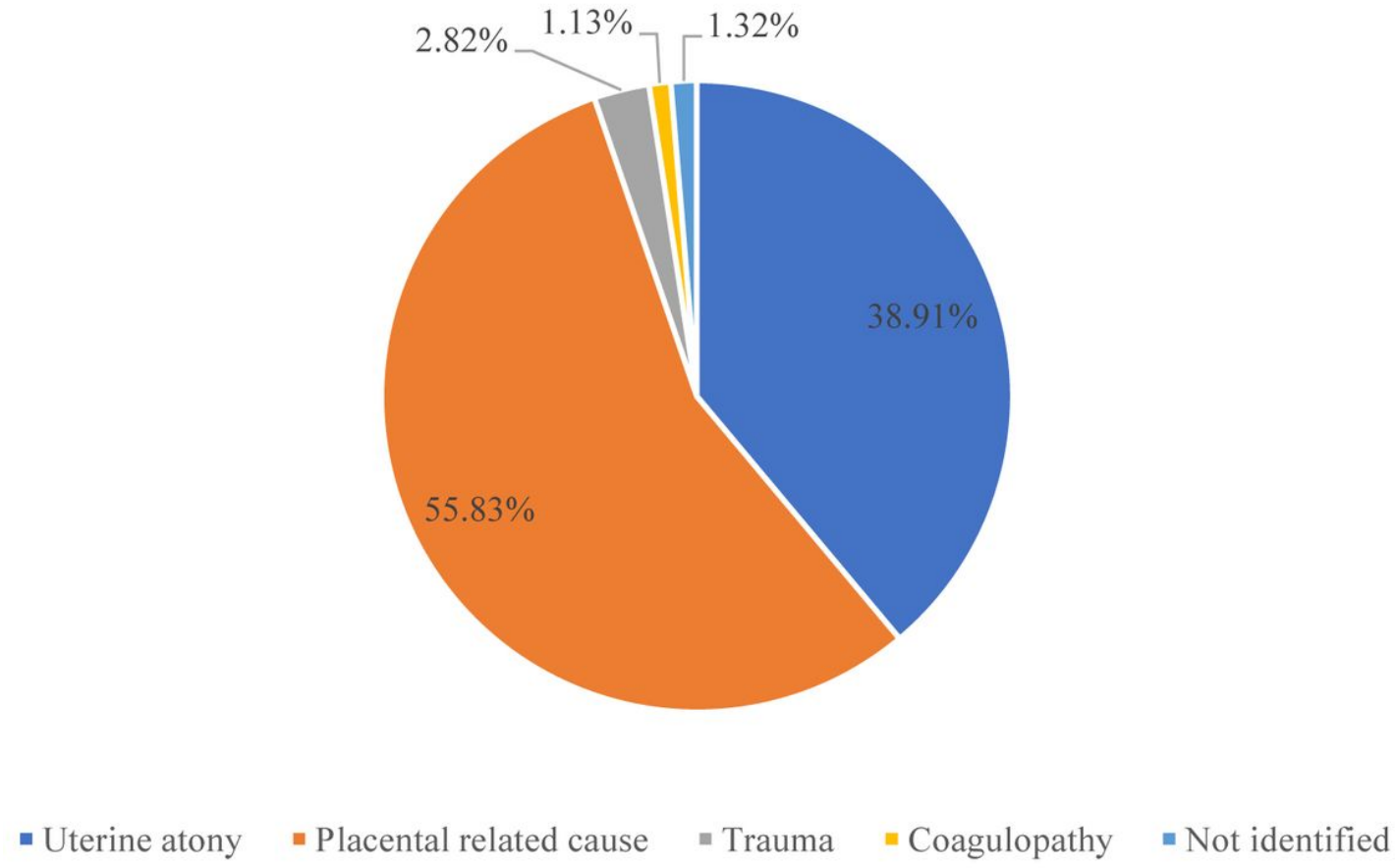

Figure 2

Causes of severe postpartum hemorrhage