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Meta-analysis of risk factors for maternal postpartum hemorrhage

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Abstract: *To systematically evaluate the risk factors of postpartum hemorrhage, the Chinese and English databases were searched by computer system, and the case-control studies on postpartum hemorrhage were found up to March 2022, Meta-analysis was performed with RevMan 5.4 after literature screening and quality evaluation. A total of 34 articles were included, and the statistically significant risk factors were cesarean delivery OR=6.08(3.67-10.08), anterior placenta OR=5.98(4.56-7.84), weak uterine contractions OR=5.41(4.37-6.70), placenta adhesion OR=3.75(2.89-4.86), hypertension during pregnancy OR=2.89(2.09-4.01), multifetal pregnancy OR=2.49(1.99-3.12), history of miscarriage OR=1.90(1.57-2.29) and giant baby OR=1.82(1.64-2.02). Cesarean delivery, anterior placenta, weak uterine contractions, placenta adhesion, hypertension during pregnancy, multifetal pregnancy, history of miscarriage and giant baby are the risk factors of postpartum hemorrhage.*

Keywords: *maternal; postpartum hemorrhage; risk factors; influencing factors; meta-analysis*

1. Introduction

Postpartum hemorrhage (PPH) refers to bleeding >1000 ml within 24 hours after delivery, regardless of vaginal or cesarean delivery [1]. Postpartum hemorrhage can lead to maternal coagulation disorders, shock, multi-organ failure, and even death, and is a common complication of pregnancy and a major cause of maternal death [2-3]. The incidence of postpartum hemorrhage in our country is about 6.4% [4]. In this study, the risk factors for postpartum hemorrhage were clarified through systematic evaluation to provide a basis for effective prevention of maternal postpartum hemorrhage.

2. Data and methods

2.1. Inclusion and exclusion criteria

Inclusion criteria: ① study subjects met the diagnostic criteria for PPH; ② study type was a case-control study; ③ Chinese literature or English literature. Exclusion criteria: ① original data were incomplete and OR values and 95% CIs could not be extracted; ② no statistical treatment of risk factors or improper application of statistical methods; ② duplicate publications; ③ literature with NOS scores below 7.

2.2. Search strategy

The PubMed, Web of Science, Cochrane Library, Embase, CBM, CNKI, Vipshop and Wanfang databases were searched using a computer system to retrieve case-control studies on risk factors for maternal postpartum hemorrhage published in China and abroad from the date of database construction to May 2023. Subject terms were searched in combination with free terms. Chinese search terms: maternal, postpartum hemorrhage, risk factor(s) or influencing factor(s) or etiology or related factor(s), etc.; English search terms: postpartum hemorrhage, case-control study, risk factor(s), etc.

2.3. Literature screening and quality evaluation

Two researchers independently screened the literature based on inclusion and exclusion criteria, and the results were finally proofread, with any disagreement decided by a third party. The NOS

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(Newcastle-Ottawa Scale) scale [5] was used to evaluate the quality of the literature with a score of 9 out of 10, which included: selection of study subjects (4 points), comparability of components (2 points), and outcome measures (3 points).

2.4. Statistical methods

Effect-value combining and heterogeneity tests were performed using RevMan 5.4. The combined ratio (OR) with 95% confidence interval (95% CI) was used to evaluate the association between each risk factor and postpartum hemorrhage, and the I^2 test was used to determine whether there was heterogeneity between studies: (i) if $I^2 \leq 50\%$, no heterogeneity between studies was considered, and the fixed-effect model was used. (ii) If $I^2 > 50\%$, a random-effects model was used. The validation of the bias test was performed with funnel plots, and sensitivity analysis was performed by comparing the ORs and 95% CIs of the random and fixed effects for each risk factor.

3. Results

3.1. Results of literature search

A total of 39 papers were included [6-39], and the search process is shown in Figure 1.

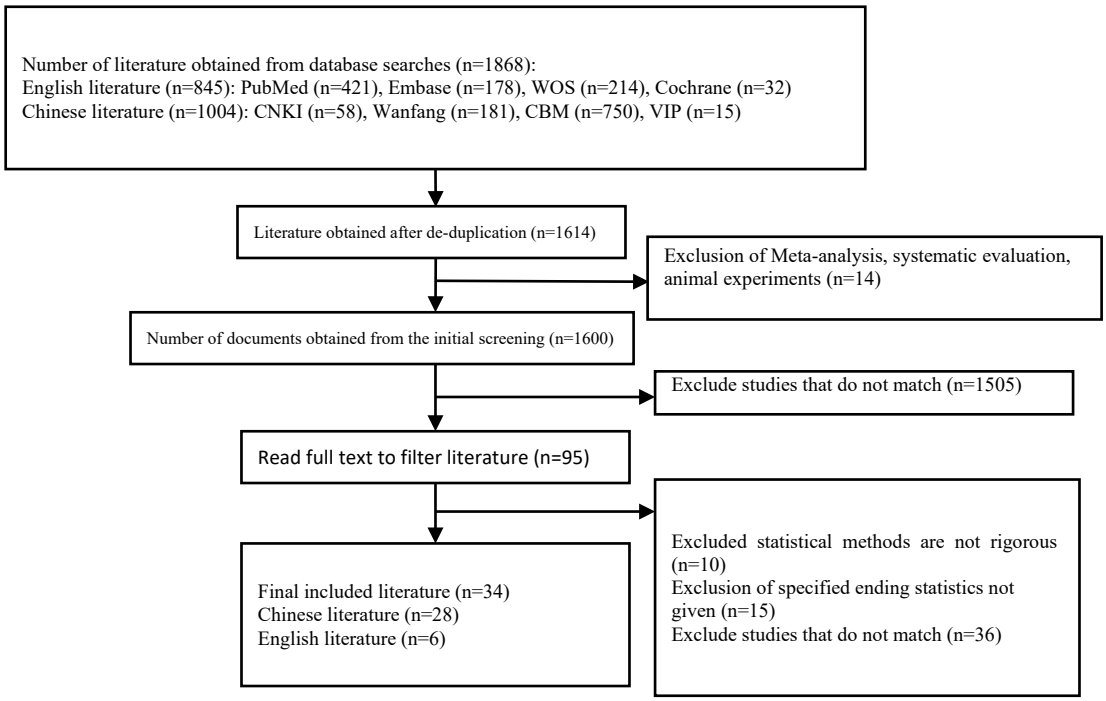

Figure 1: Literature search process for postpartum hemorrhage.

3.2. Basic characteristics and quality of included studies

Thirty-four papers were included, 27 in Chinese and 7 in English, with 7,111 cases in the case group and 12,570 in the control group, involving 8 risk factors. The NOS scores of the included literature were 7 to 9. Among them, 23 articles scored 8 and 11 articles scored 7. As shown in Table 1.

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Table 1: Basic characteristics and quality of the included literature.

Serial number	Inclusion of studies and years	Study site	Case group	Control group	Risk factors	NOS
1	Guihua Zeng[6]2013	Qinghai	76	88	①	8
2	Suqing Hao[7]2013	Hainan	159	318	③⑤	7
3	Xuefang Huang[8]2014	Guangdong	50	50	①	8
4	Yuefang Huang[9]2010	Sichuan	122	144	①⑥	7
5	Hui Jin[10]1995	Shaanxi	162	162	⑤	7
6	Lei Jin[11]2013	Suzhou	100	200	⑤⑥	8
7	Wu Li[12]2010	Guangdong	36	36	⑧	8
8	Yanping Li[13]2018	Shaanxi	300	600	②③⑦	8
9	Gaixin Liu[14]2009	Guangdong	94	94	④	7
10	Honglei Liu[15]2010	Shenzhen	46	57	⑧	8
11	Jingxia Liu[16]2016	Neimenggu	125	125	①③	8
12	Yanping Liu[17]2016	Heilongjiang	118	118	①	8
13	Chunyi Ma[18]2015	Shenzhen	89	89	③⑤⑥	8
14	Huan Ren[19]2013	Hubei	124	124	①⑧	8
15	Sujuan Shen[20]2014	Henan	170	340	⑦	8
16	Xueqin Tian[21]2019	Ningxia	240	240	④	8
17	Hongju Wan[22]2014	Henan	120	240	②⑥	8
18	Qiaoying Wang[23]2016	Sichuan	50	50	⑦	8
19	Yonghua Wang[24]2020	Henan	37	91	②⑦	8
20	Jiuling Wu[25]2009	Henan	92	92	⑧	8
21	Yuying Xia[26]2003	Guangdong	1976	3952	①④⑧	7
22	Zhongping Xu[27]2018	Zhejiang	96	200	①③④	8
23	JianyingYa[28]2012	Fujian	212	424	③④⑤	8
24	Qunfang Ying[29]2014	Zhejiang	220	220	②	8
25	Qingxiang Zhao[30]2015	Chongqing	50	100	①⑤	8
26	Xiangjuan Zha[31]2012	Haerbin	67	139	①③	8
27	Zhengwen Zhu[32]2012	Guizhou	122	244	②⑥	8
28	Bazirete, O.[33]2022	Africa	108	322	①	7
29	Helman, S.[34]2015	Israel	122	488	⑥⑦	7
30	Henry, A.[35]2005	Australia	125	125	④⑥	7
31	Nyflot, L. T.[36]2017	Norway	1064	2059	⑥	7
32	Selo-Ojeme, D. O.[37]1997	United States	107	107	⑥	8
33	Wandabwa, J.[38]2008	Africa	106	500	④	7
34	Wang, X.[39]2014	Hunan	132	132	③	7
Note:①weak uterine contractions; ② giant babies; ③placenta praevia; ④hypertension in pregnancy;⑤ placental adhesions; ⑥multiple pregnancies;⑦history of miscarriage; ⑧cesarean delivery						

3.3. Meta-analysis results

A total of 8 risk factors were involved in 34 studies, and Meta-analysis showed that all 8 factors were risk factors for postpartum hemorrhage. As shown in Table 2.

Table 2: Meta-analysis results of a case-control study of risk factors for postpartum hemorrhage.

Risk factors	*Number of Literature*	*Heterogeneity test*		*Models*	*Merger effect value*	
		I^2(%)	*P*		*OR(95%CI)*	*P*
Weak uterine contractions	10	2.0	P<0.01	Fixed	5.41(4.37-6.70)	P<0.01
Giant baby	5	0.0	P<0.01	Fixed	1.82(1.64-2.02)	P<0.01
Anterior placenta	8	0.0	P<0.01	Fixed	5.98(4.56-7.84)	P<0.01
Hypertension during pregnancy	7	0.0	P<0.01	Fixed	2.89(2.09-4.01)	P<0.01
Multifetal pregnancy	8	0.0	P<0.01	Fixed	2.49(1.99-3.12)	P<0.01
Placental adhesions	6	0.0	P<0.01	Fixed	3.75(2.89-4.86)	P<0.01
Cesarean delivery	5	21.0	P<0.01	Fixed	6.08(3.67-10.08)	P<0.01
History of miscarriage	5	0.0	P<0.01	Fixed	1.90(1.57-2.29)	P<0.01

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3.4. Sensitivity analysis

The funnel plots for placental factors, macrosomia, multiple pregnancy, uterine systole, placenta praevia, gestational hypertension, placental adhesions, cesarean section, and history of miscarriage were largely symmetrical. Stable results for each risk factor were found by sensitivity analysis, as shown in Table 3.

Table 3: Sensitivity analysis of risk factors for postpartum hemorrhage.

Risk factors	*Random effects model*	*Fixed effects model*
Cesarean delivery	6.26(3.53-11.13)	6.08(3.67-10.08)
Weak uterine contractions	5.39(4.32-6.71)	5.41(4.37-6.70)
Placenta praevia	5.98(4.56-7.84)	5.98(4.56-7.84)
Placental adhesions	3.75(2.89-4.86)	3.75(2.89-4.86)
Hypertension during pregnancy	2.89(2.09-4.01)	2.89(2.09-4.01)
Multiple pregnancy	2.49(1.99-3.12)	2.49(1.99-3.12)
history of miscarriage	1.90(1.57-2.29)	1.90(1.57-2.29)
Giant baby	1.82(1.64-2.02)	1.82(1.64-2.02)

4. Discussion

4.1. Cesarean delivery, weak uterine contractions

This study shows that cesarean delivery and weak uterine contractions are risk factors for postpartum hemorrhage. Cesarean section causes different degrees of maternal endometrial damage, which not only makes the uterus contraction weak but also causes placental adhesions and incisional injuries. Weak contractions can result in the inability of the uterine muscle fibers in different directions to effectively contract the blood vessels between the muscle bundles, which in turn can cause bleeding.

4.2. Hypertension during pregnancy, giant babies, multiple pregnancies

Gestational hypertension, macrosomia and multiple pregnancies were risk factors for maternal postpartum hemorrhage in this study. Gestational hypertension causes vasospasm of small arteries and increased vascular pressure, which also leads to uterine dysplasia, which in turn causes postpartum hemorrhage. A giant baby is a fetus weighing ≥4 kg at birth, and when a mother delivers a giant baby, she is prone to soft birth canal injury, weak contractions and placental adhesions. This in turn causes bleeding. Multiple pregnancy refers to two or more fetuses in the uterine cavity, which causes overexpansion of the uterus, increased pressure in the uterine cavity, overextension of the uterine muscle fibers, and difficulty in effective contraction of the uterus, causing postpartum hemorrhage.

4.3. Placental factors, history of miscarriage

This study suggests that placental factors and a history of miscarriage are risk factors for maternal postpartum hemorrhage. Placental factors include placenta praevia, placental adhesions, retained placenta, and placental implantation, all of which are abnormal manifestations of endometrial damage, all of which inhibit contractions and affect the closure of the blood sinuses in the uterine wall, causing bleeding. Anterior placenta, due to the special position of the placenta, makes it difficult for the uterus to contract after abruption and the blood sinuses cannot close properly, causing bleeding. After placental adhesions maternal chorionic tissue penetrates deep into the myometrium, it affects the contraction of the myometrium and causes bleeding after placental abruption. Wang Jun showed that the incidence of postpartum hemorrhage from placental adhesions was positively correlated with the number of miscarriages. Zheng Han demonstrated that miscarried women are prone to damage the endometrium and have an increased risk of placenta praevia and placental adhesions, which in turn lead to postpartum hemorrhage. However, one study showed that a history of miscarriage was not significantly associated with maternal postpartum hemorrhage. This risk factor is controversial and may be related to individual maternal fitness and psychological quality, which needs to be further demonstrated.

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5. Conclusions

Prevention of postpartum hemorrhage is important. We should do a good job of prenatal education on pregnancy health care, plan births and avoid multiple abortions; strictly grasp the indications for cesarean delivery and reduce unnecessary cesarean deliveries. For women with hypertension during pregnancy, multiple births and huge babies, they should actively control their weight and develop a reasonable diet and exercise plan. During labor, observe the progress of labor closely to prevent prolonged labor from causing weak contractions; avoid pulling the umbilical cord and pressing the fundus too early after the second stage of labor to avoid placenta retention and adhesions. After delivery of the placenta, make sure the placenta and fetal membranes are intact. Closely observe the uterine contractions and vaginal bleeding after delivery; urge the mother to empty the bladder in time to avoid postpartum bleeding due to contractions.

Acknowledgements

Limitations of this study:①Only Chinese literature and English literature were included. ②The type of study was a case-control study, and there may be language bias and implementation bias. ③ There may be geographical differences between studies, differences in hospital rank, or other confounding factors.

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