

Meta-analysis of the effect of duration of labour on postpartum haemorrhage

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ABSTRACT

Objectives: To evaluate the relationship between stages of labour and the risk of postpartum haemorrhage (PPH) and provide evidence for clinical application.

Material and methods: Manual searches were undertaken, and computer searches of PubMed, MEDLINE, Web of Science, CNKI, Wanfang and Wipu databases with a search window from database creation to April 2022 were conducted to procure relevant studies on the relationship between labour phase and PPH. The articles included in this study were evaluated for quality, and RevMan 5.3 software was used for meta-analysis.

Results: Meta-analysis showed that the incidence of PPH in women with weak uterine contractions was 27.5%, compared with 18.1% in women with normal contractions [relative risk (RR) = 1.60; 95% confidence interval (CI) 1.38, 1.85; $p < 0.01$]. There was a statistically significant difference in the incidence of PPH in pregnant women with a prolonged second stage of labour (≥ 2 h) (34.5%) compared with those whose second stage of labour was normal in duration (15.9%) (RR = 0.20; 95% CI 0.15, 0.25; $p < 0.01$). The incidence of PPH was 52.1% in pregnant women with a prolonged third stage of labour (≥ 15 min) compared with 20.9% in those whose third stage of labour was of normal duration (RR = 3.53; 95% CI 2.75, 4.52; $p < 0.01$). The difference in the incidence of a prolonged third stage of labour in pregnant women with weak contractions compared with those with normal contractions was statistically significant (72.3% vs 15.5%) (RR = 0.47; 95% CI 0.35, 0.60; $p < 0.01$).

Conclusions: Duration of labour is associated with the development of PPH, and the risk of PPH is increased in women with weak contractions or with a prolonged second or third stage of labour.

Keywords: postpartum haemorrhage; uterine atony; stage of labour

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INTRODUCTION

Mckinney et al. [1] reports that postpartum haemorrhage (PPH) is a serious complication of childbirth and is one leading causes of maternal death in developing nations. Souter et al. [2] contends that uterine inertia is the cause of 76.6% of PPH. Approximately 290,000 women worldwide died of PPH in 2010, according to data released by the World Health Organization in 2015 [3]. Studies have shown that PPH is a leading cause of maternal death, accounting for 27.1% of maternal mortality [2]. According to data from the 2018 National Maternal and infant Health Survey, death due to uterine inertia-related PPH has increased with different degrees [4].

Previous studies have suggested that the occurrence of uterine inertia is related to duration of labour and to a history of multiple pregnancies. It is well known that labour begins at the onset of regular contractions and continues until the complete delivery of the placenta and that its duration is primarily affected by characteristics of the birth canal, force of labour and mental factors [5]. Lei Yan et al. [6] assert that the labour process is divided into three stages: the first stage of labour refers to the onset of regular and gradually enhanced uterine contractions, which generally last for > 30 s (with a regularity of about 5–6 min) and are accompanied by progressive cervical canal disappearance and uterine mouth dilatation. Han Ningyu et al. [7, 8] claim that

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an increase in the duration of the second and third stages of labour is related to the development of PPH. Postpartum haemorrhage remains the leading cause of maternal death. Uterine inertia accounts for most cases of PPH and is related to duration of labour, a history of multiple pregnancies and other factors. Uterine inertia and duration of labour mutually affect each other. There is some research significance in the fact that no related meta-analysis exists to date on this topic, as it is relatively novel. This study evaluates the relationships between labour duration, uterine inertia and PPH through a systematic and comprehensive meta-analysis and aims to provide more effective guidance and serve as a reference for the clinical prevention of PPH.

MATERIAL AND METHODS

Literature search

This meta-analysis follows Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The authors conducted a comprehensive search of the relevant literature on PubMed, MEDLINE, Scopus and Cochrane Library electronic databases from January 2000 to August 2022 using combinations of the following terms: 'labour duration management', 'vaginal delivery', 'second stage of labour', 'third stage of labour', 'postpartum haemorrhage', 'uterine atony', 'duration of labour', 'second duration of labour', 'third duration of labour' and 'immediate postpartum haemorrhage'. The reference lists of the selected articles and reviews were also included as additional studies, following the Population, Intervention, Comparison, Outcomes and Study principle.

Inclusion and exclusion criteria

The inclusion criteria for research articles were as follows: (1) randomised, controlled trials and clinical controlled trials; and (2) studies whose observation indicators included patients with a longer duration of labour (a second phase of labour ≥ 2 h and/or a third phase of labour ≥ 15 min) and postpartum bleeding (≥ 500 mL) and a control group with third phase of labour < 15 min and without bleeding or bleeding (< 500 mL).

The exclusion criteria were as follows: (1) articles that were not publicly published; (2) studies with no control group; (3) studies whose observation indicators were not classified, summarised and collected according to relevant international or national standards; and (4) Those published already literature data.

Data extraction of the included articles

Two literature evaluators conducted a literature search, data extraction and risk of bias evaluation of the collected articles based on the set inclusion and exclusion criteria and checked the consistency of the relevant documents.

In cases of disagreement, a third party made a final judgment. Extracted data included basic information and the research content of the selected articles, including number of study subjects and observation indicators.

Quality evaluation of the included articles

Two literature evaluation personnel evaluated the quality of the articles included in this study based on the Cochrane assessment tool for risk of bias. The tool evaluates each study item by item based on seven indicators, including the generation of random sequences and selective publication. An Ottawa scale was also constructed for quality assessment of the chosen articles (Tab. 1 [8–23]).

Statistical methods

RevMan 5.3 software was used to execute the meta-analysis following these steps:

1. A chi-squared (χ^2) test is performed to determine whether there is some heterogeneity among the results of the included articles. If some heterogeneity is present ($I^2 > 50\%$; $p < 0.1$), its potential sources are analysed tentatively.
2. If there is no clinical heterogeneity present, a random effect model is used for combined analysis.
3. If the heterogeneity among study results is very small ($I^2 \geq 50\%$) the combined effect size is calculated by a fixed effect model.
4. If a large clinical heterogeneity exists among study results, a simple elaboration analysis can be run. Count data are mainly described by the degree of relative risk (RR) and a confidence interval (CI) of 95%.

RESULTS

The included articles and screening process

A preliminary search turned out 60,818 documents. Of these, 62 documents were deemed relevant from a reading of their titles and abstracts. After irrelevant and duplicate articles were excluded, 26 documents remained. Following a reading of the full text of these documents, 17 articles were ultimately selected for this meta-analysis, including 2 in English and 15 in Chinese. The process described above is detailed in Figure 1.

Risk of bias assessment of the included studies

The quality of the included studies is illustrated in Figure 2.

Analysis of uterine inertia and PPH

Eight studies [8, 9, 13, 14, 20–23] were enlisted to compare the risk of PPH in pregnant women with uterine inertia to that in women with normal contractions. Meta-analysis showed a significant difference in the incidence of PPH between pregnant women with uterine inertia (27.5%) and those with normal contractions (18.1%) (RR = 1.60; 95%

Table 1. Characteristics of articles included in the review process [8–23]

No	Author	Type of study	Samples	Results
1	Shao JP et al. /2014/	Four-group, double-blind, randomized controlled trial	525 pregnant women referring to Hospital of Sichuan	Long labor time frames and postpartum hemorrhage postpartum hemorrhage ($p < 0.001$)
2	Bai S et al. /2010/	Two-group, double-blind, randomized controlled trial	67 pregnant women referring to Hospital of Nanjing first	Long time of three postpartum hemorrhage stage ($p > 0.001$)
3	Wei L et al. /2017/	Four-group, double-blind, randomized controlled trial	345 pregnant women referring to Hospital of Zhejiang second	A prolonged second stage of labor (≥ 2 h) ($p < 0.001$)
4	Han NY et al. /2020/	Two-group, double-blind, randomized controlled trial	754 pregnant women referring to Hospital of Nanchang concerning	A prolonged three stage of labor ($p < 0.05$)
5	Lin Q et al. /2019/	Three-group, double-blind, randomized controlled trial	567 pregnant women referring to Hospital of Sichuan	A prolonged second stage of labor (≥ 24 h) ($p < 0.05$)
6	Zhu CT et al. /2012/	Two-group, double-blind, randomized controlled trial	853 pregnant women referring to Hospital of Zhengzhou first	Long time of three postpartum hemorrhage stage ($p > 0.05$)
7	Ma WF et al. /2019/	Two-group, double-blind, randomized controlled trial	532 pregnant women referring to Hospital of Wuhan university first	Long labor time frames ($p < 0.001$)
8	Zhang JH et al. /2017/	Two-group, double-blind, randomized controlled trial	432 pregnant women referring to Hospital of Xiang Tan	Long time of second postpartum hemorrhage stage (≥ 2 h) ($p < 0.01$)
9	Zhu TY et al. /2021/	Two-group, double-blind, randomized controlled trial	435 pregnant women referring to Hospital of Beijing university first	Long time of three postpartum hemorrhage stage (≥ 15 min) ($p > 0.05$)
10	Zhao RF et al. /2015/	Two-group, double-blind, randomized controlled trial	632 pregnant women referring to Hospital of Beijing university second	Long time of three postpartum hemorrhage stage (≥ 24 h) ($p < 0.05$)
11	Frolova AI et al. /2016/	Four-group, double-blind, randomized controlled trial	234 pregnant women referring to Hospital of Sichuan	Long time of second postpartum hemorrhage stage (≥ 2 h) ($p < 0.05$)
12	Magann EF et al. /2008/	Two-group, double-blind, randomized controlled trial	425 pregnant women referring to Hospital of Sichuan	Long time of three postpartum hemorrhage stage (≥ 24 h) ($p < 0.05$)
13	Zhou P et al. /2013/	Four-group, double-blind, randomized controlled trial	253 pregnant women referring to Hospital of Chong Qin Second	Long time of three postpartum hemorrhage stage ($p < 0.01$)
14	Qiu BQ et al. /2013/	Two-group, double-blind, randomized controlled trial	423 pregnant women referring to Hospital of Sichuan	Long time of second postpartum hemorrhage stage (≥ 2 h) ($p < 0.05$)
15	Li HM et al. /2019/	Two-group, double-blind, randomized controlled trial	586 pregnant women referring to Hospital of Sichuan	Long time of three postpartum hemorrhage stage (≥ 24 h) ($p < 0.01$)
16	Ban YZ et al. /2019/	Two-group, double-blind, randomized controlled trial	386 pregnant women referring to Hospital of Sichuan	Long time of three postpartum hemorrhage stage (≥ 24 h) ($p < 0.001$)

CI 1.38, 1.85; $p < 0.01$). The heterogeneity test result was $I^2 = 0\%$; $p = 0.44$ (Fig. 3).

Analysis of duration of labour and PPH risk

Five studies [11, 12, 15, 17, 24] were enlisted to compare the risk of PPH in pregnant women with a second stage of labour of extended duration (≥ 2 h) to that in women with a second labour stage of normal duration. Meta-analysis revealed the difference in the incidence of PPH between these two groups to be 34.5% and 15.9%, respectively, and the results were statistically significant ($RR = 0.20$; 95% CI 0.15, 0.25; $p < 0.01$). The heterogeneity test result was $I^2 = 14\%$, $p = 0.32$ (Fig. 4).

Seven studies [18–20, 22, 23, 25] were enlisted to determine the risk of PPH in pregnant women with a prolonged third stage of labour (≥ 15 min) compared with those with a third labour stage of normal duration. Meta-analysis showed that the incidence of PPH in these two groups

was 52.1% and 20.9%, respectively, and the difference was statistically significant ($RR = 3.53$; 95% CI 2.75, 4.52; $p < 0.01$). The heterogeneity test result was $I^2 = 26\%$; $p = 0.23$ (Fig. 5).

Correlation analysis between uterine inertia and prolongation of the third stage of labour

Three studies [20, 22, 23] were enlisted to compare the risk of a prolonged third stage of labour in pregnant women with uterine inertia to the risk in those with normal contractions. Meta-analysis showed that the difference in the incidence of a prolonged third stage of labour between these two groups was 72.3% and 15.5%, respectively, and the results were statistically significant ($RR = 0.47$; 95% CI 0.35, 0.60; $p < 0.01$). The heterogeneity test result was $I^2 = 42\%$; $p = 0.18$ (Fig. 6).

DISCUSSION

Postpartum haemorrhage due to prolonged duration of labour is an important public health problem, both nationally

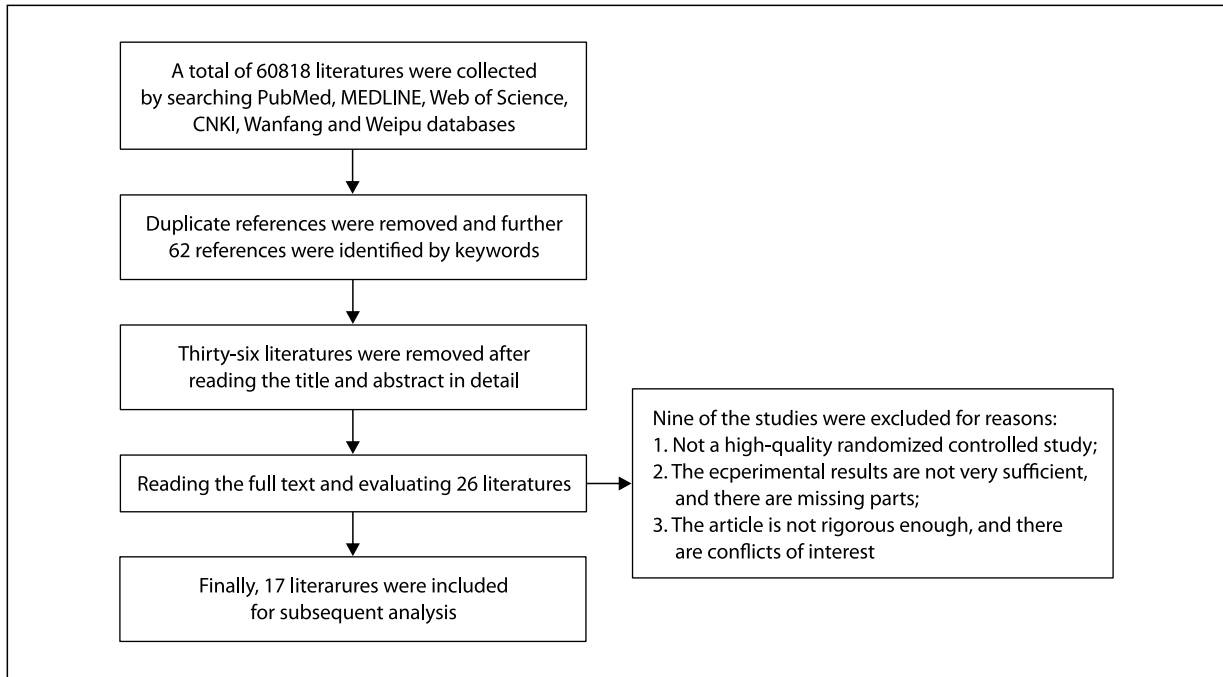


Figure 1. Literature search and screening process

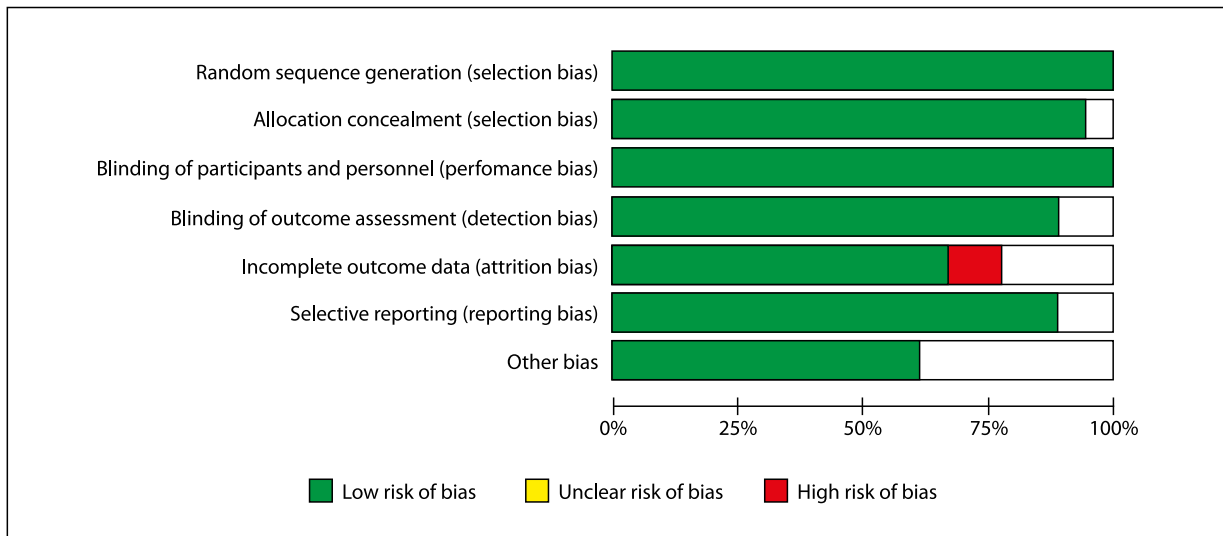


Figure 2. Quality evaluation of related literature

and globally. Liu et al. and others [26–28] have found that a prolonged duration of labour can increase the risk of PPH. The primary mechanism for this is a reduction in both the gap connection of smooth uterine muscle cells and calcium ion cell influx, which lead to the contraction of smooth muscle cells in the uterus, eventually causing PPH due to uterine contractions. However, at present, a meta-analysis does not exist confirming the link between the duration of labour and the risk of PPH, and relevant literature is highly controversial. The correlation between duration of labour

and the risk of PPH was analysed here based on current study data [5–25, 29–31].

The second stage of labour plays a pivotal role in the process of delivery and is also the most dangerous phase of labour. Studies have shown that a prolongation of the second stage of labour can result in abnormal childbirth, which can lead to the occurrence of PPH, infection, renal failure and other adverse consequences [30, 32, 33]. A second labour stage of extended duration is linked to significant increases in the rates of PPH and maternal vaginal

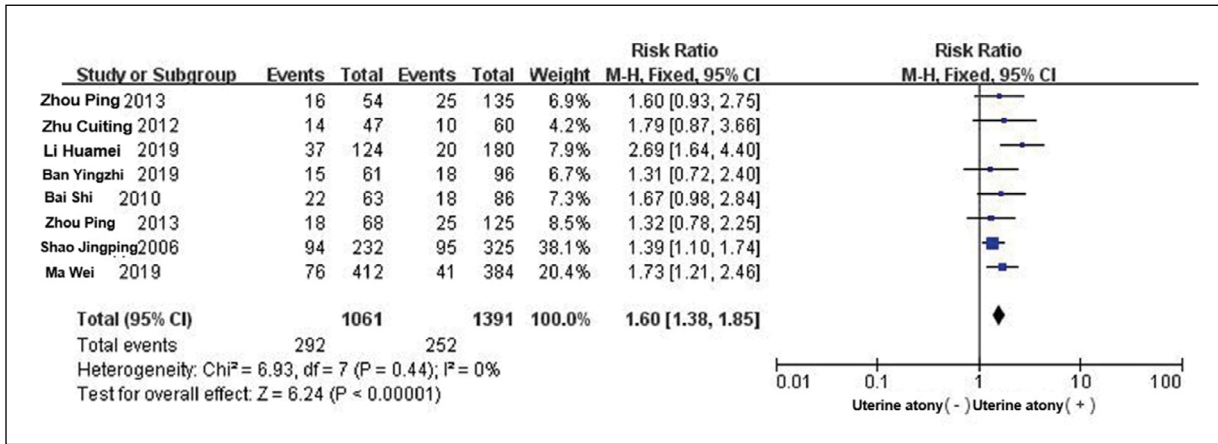


Figure 3. Assessment associated with uterine inertia and postpartum hemorrhage risk; CI — confidence interval

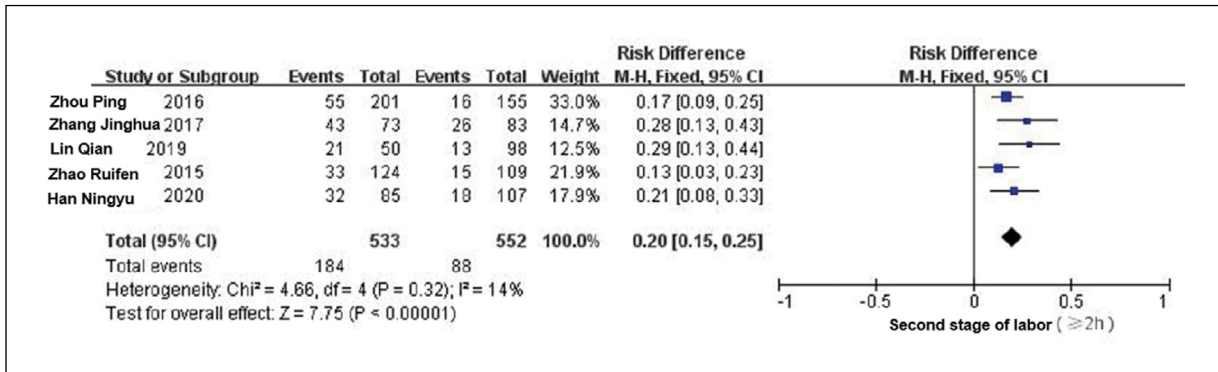


Figure 4. Assessment associated with the second stage of labor and postpartum hemorrhage risk; CI — confidence interval

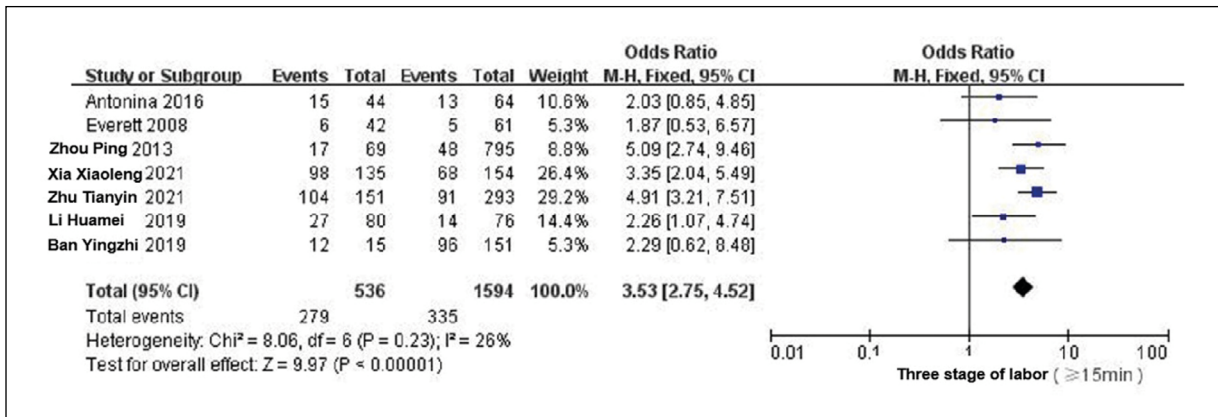


Figure 5. Assessment associated with the third stage of labor and postpartum hemorrhage risk; CI — confidence interval

dystocia. In addition, an extended labour duration delays the exposure of the foetus, compressing the pelvic floor and causing local perineal tissue ischemia and oedema. Any accompanying vaginal midwifery can increase the chance of maternal puerperal infection. Brun et al. [34] showed that, when the second stage of labour exceeds 2.5 h, the occurrence of PPH and the rates of forceps mid-

wifery increase. As early as 2013, Wetta and Hayman et al. [35, 36] conducted clinical trials on the second stage of labour and maternal PPH. A total of 587 primipara were included, and the results showed that when the second stage of labour exceeded 2 h, the incidence of PPH increased significantly. This is consistent with the conclusion of this meta-analysis — namely, that the probability of

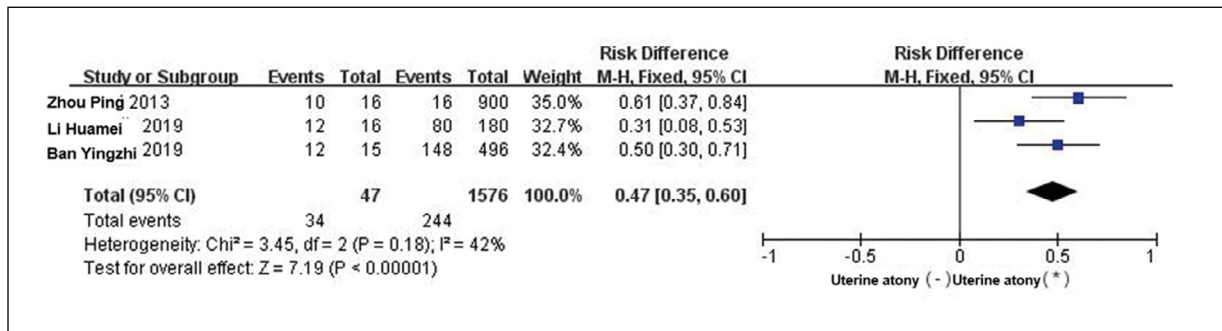


Figure 6. Evaluation of the correlation between uterine inertia and prolongation of the third stage of labor; CI — confidence interval

PPH in pregnant women with a prolonged second stage of labour (≥ 2 h) is significantly higher than that in those with a second stage of labour of normal duration.

It is generally accepted that the third stage of labour begins with the completion of foetal delivery and ends with the complete delivery of the placenta, and its duration is related to the risk of PPH. Placental delivery is an important, yet often ignored, stage of labour management [8, 18, 30]. In 2012, Zhao Xiangjuan et al. [37] demonstrated that when the third stage of labour exceeds 30 min, the risk of PPH is significantly increased. To some extent, a safe duration for the third stage of labour was limited to 30 min, and any prolongation was regarded as an extended third stage requiring intervention to reduce the risk of PPH. This is consistent with the results herein. Also, from the perspective of pathology, chronic inflammation leads to cervical polyps, the symptoms of this disease will directly lead to the phenomenon of hyperplasia of the local mucous membrane of the cervix, which will eventually cause the occurrence of uterine bleeding.

However, some studies have reported that even a third stage of labour >15 min can trigger uterine muscle oedema and inertia in primipara, causing the uterus to be unable to undergo normal contractions to effectively shed and deliver the placenta.

In addition, a delay in the closure of the uterine wall sinus can lead to uterine inertia-related PPH [38]. This is consistent with the conclusions of this meta-analysis — namely, that the probability of PPH in pregnant women with a prolonged third stage of labour (≥ 15 min) is significantly higher than that in women with a third stage of labour of normal duration.

This study has several limitations. For example, some of the articles included in this study were observational. The lack of large-sample, multi-centre randomised controlled studies herein could cause publication bias. Additionally, due to language restrictions, only publicly published Chinese and English articles were searched, and there was an incomplete final literature search of other languages, meaning

the results may not be rigorous enough. Furthermore, the literature involved in this study is mainly concentrated in China, and relevant studies from other countries were rarely included. Therefore, considering that differences in race, geographical region and regional living habits may have an impact on some diseases, the conclusions of this meta-analysis would benefit from being further confirmed by additional sample data and more multi-centre, randomised controlled studies.

CONCLUSIONS

In conclusion, the risk of PPH increases as the duration of labour extends. The prolongation of the second and third stages of labour is closely associated with the occurrence of PPH. And the mechanism might be explained by the disruptions of terine muscle function or energetic exhaustion of the muscle. Once a normal time frame for the second or third stage of labour has been exceeded, bleeding should be closely monitored to facilitate intervention in the early stage of haemorrhage, and attention should be paid to uterine inertia.

Article information and declarations

Data availability statement

All data generated or analyzed during this study are included in this article.

Ethics statement

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Beijing Obstetrics and Gynecology Hospital. Written informed consent was obtained from all participants.

Author contributions

Conception and design: Cai Y.
Administrative support: Li K.

Provision of study materials or patients: Shi QY.

Collection and assembly of data: Shi QY.

Data analysis and interpretation: Li K.

Manuscript writing: All authors.

Final approval of manuscript: All authors.

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Conflict of interest

None of the authors had any personal, financial, commercial, or academic conflicts of interest separately.

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