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Incidence, trends and risk factors for obstetric massive blood transfusion in China from 2012 to 2019: an observational study

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ABSTRACT

Objectives This study aims to use the high-quality national monitoring data from the China's National Maternal Near Miss Surveillance System (NMNMSS) to ascertain the incidence, trends and risk factors of obstetric massive blood transfusion (MBT) from 2012 to 2019 in China and determine its clinical outcomes.

Settings Observational study of hospitalised pregnancies who had given birth or ended their pregnancy among member hospitals of NMNMSS.

Participants 11 667 406 women were included in this study.

Primary and secondary outcome measures We screened for the incidence, trends, risk factors and main reasons for obstetric MBT, and the outcomes after obstetric MBT. MBT was defined as the transfusion of ≥5 units of red blood cells or ≥1000 mL of whole blood. The incidence of MBT was defined as the MBT cases per 10 000 pregnancies.

Results Obstetric MBT occurred in 27 626 cases, corresponding to an incidence of 23.68 per 10 000 maternities, which exhibited an increasing trend in China during 2012–2019 (14.03–29.59 per 10 000 maternities, p for trend <0.001). Obstetric MBT was mainly associated with amniotic fluid embolism, uterine atony, abnormal placenta, severe anaemia, ectopic pregnancy, abortion, caesarean section, advanced maternal age and multiparous from biological effect. While from sociological effects, uterine atony, severe anaemia and placenta previa are the top three complications which more likely to undergo obstetric MBT in the Chinese population. Overall, the secular trends of hysterectomy incidence (25.07%–9.92%) and MMR during hospitalisation (21.41‰–7.48‰) among women who underwent MBT showed decreasing trends (p for trend <0.001).

Conclusion To minimise the incidence of obstetric MBT, more attention should be paid to education on the importance of the antenatal visit, evidence-based transfusion practice and females who are multiparous and have an advanced age, amniotic fluid embolism, uterine atony, severe anaemia and placenta previa.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Study was based on a national surveillance data covering 441 hospitals across 30 provinces.
⇒ This study first evaluated the incidence, trends, risk factors and main reasons of obstetric massive blood transfusion (MBT) at national level in China.
⇒ Limitation include the obstetric MBT is a binary variable, which does not allow us for additional analyses.
⇒ Our analysis was also limited to information presented in the National Maternal Near Miss Surveillance System record.

INTRODUCTION

Obstetric haemorrhage remains a common obstetric emergency and is the leading cause of maternal deaths worldwide,[1] similarly in China.[2] In addition to strengthening the patient's uterus contractions, drug haemostasis, surgery, etc, massive blood transfusion (MBT) also plays a key role in the treatment of obstetric haemorrhage.[3–6] MBT occurs when large volumes of blood products are administered over a short period of time, as a 'maternal near miss event', it signifies major obstetric haemorrhage and requires extensive coordination of the obstetric, anaesthesia and blood bank teams.[7 8]

The incidence of MBT in relation to delivery or postpartum haemorrhage (PPH) has been reported to be 2.3–10.0 per 10 000 maternities in high-resource countries,[9–13] and an increasing trend in the rate of MBT post partum has been reported in Sweden.[10] However, only two small studies focused on obstetric MBT in China.[14 15]. One study concluded that the incidence of MBT in relation to PPH was stable (25–27 per 10 000 maternities) during 2006–2015. Another reported that the MBT rate attributed to PPH was 0.31% in women undergoing caesarean delivery.[14] China's universal two-child policy was announced in October 2015.[16] Due to the new policy, the characteristics of mothers in China have changed greatly; for example, the

monthly percentage of multiparous mothers increased by 9.1% from a baseline mean level of 46.4%, and the monthly mean percentage of older women grew from 8.5% to 13.5%.[17] However, there is no research on obstetrics MBT after the policy was implemented in China. In addition, current studies on MBT are generally limited to PPH, caesarean section or maternal delivery after a certain gestational age.[10 11 13 14 18] There are many other obstetric diseases, such as abortion and ectopic pregnancy, that require MBT, and MBT is not performed only after a specific gestational age.[19 20] Emergency MBT is often needed to save these women. Therefore, it would be extremely helpful for establishing an emergency plan aims to prevent adverse outcomes by exploring the current status, characteristics and potential risk factors of obstetric MBT.

We aim to use the high-quality national monitoring data from the China's National Maternal Near Miss Surveillance System (NMNMSS) during 2012–2019 to determine the incidence and trends of obstetric MBT, the risk factors and main reasons for obstetric MBT, and the adverse outcomes after obstetric MBT.

MATERIALS AND METHODS

Data sources

Individual-level data were collected from NMNMSS from 1 January 2012 to 31 December 2019. The NMNMSS system was first established in 2010 and covers 441 health facilities that treated more than 1000 deliveries annually. The included hospitals are located in 326 districts or counties throughout 30 provinces in mainland China, excluding Tibet. The detailed sample methods have been described elsewhere.[21–23] Within each hospital, sociodemographic and obstetric information were collected from all the pregnant or postpartum women admitted to the obstetric department. The doctors responsible for patient care collected the data, which included the date of delivery, the number of antenatal visits, the maternal education and marital statuses, the maternal age, the gestational age at delivery, the mode of delivery, the number of fetuses and the maternal complications (at any time during hospitalisation), and maternal near miss, including whether obstetric MBT have occurred. The inclusion criteria included the hospitalised pregnancies who had given birth or ended their pregnancy among member hospital of NMNMSS.

Institutional data were collected from each hospital through the NMNMSS in 2012, 2015 and 2018, including information on the hospital (hospital level, type), human resources (number, titles and degrees of the obstetricians) and service capability (whether there is safe blood storage in the hospital, etc).

Definitions

The usual definitions of maternal age, marital status, number of antenatal care visits, educational level, delivery method, history of caesarean section and parity were used, as detailed elsewhere.[22–24] Based on the hospital's location, we classified regions as eastern, central or western and the hospital level was defined based on the size of hospital (number of beds, number of doctors and number of equipment), medical service capacity (clinical service and clinical expert available, etc) and the management level of the hospital.[24] Level 1 represents the smallest hospitals and level 3 the largest.

We defined MBT as the transfusion of ≥5 units of red blood cells or ≥1000 mL of whole blood,[25 26] which is consistent with that used in the WHO multicountry survey on maternal and newborn health, listed in online supplemental appendix 1. Multiple blood component transfusions require transfusion volume conversion, the conversion standard is 200 mL of plasma/whole blood=1 units of red blood cells, while the other blood components were not included in the calculation of total blood transfusion.

Definition of pregnancy complications reference to obstetrics and gynaecology textbooks (eighth edition) used in China. Major complications associated with obstetric MBT were identified based on previously published studies, including obstetric haemorrhage-related conditions and complications that may cause obstetric haemorrhage.[9–11 15] Abortion, ectopic pregnancy, placenta previa, placenta accreta, placenta abruptio, placenta retained, uterine atony, uterine rupture and soft birth canal lacerations were included in the obstetric haemorrhage-related conditions, while hypertensive disorders in pregnancy, Hemolysis elevated liver enzymes and low platelets count syndrome(HELLP syndrome), puerperal infection, amniotic fluid embolism (AFE) and severe anaemia[3] were included in the complications. Severe anaemia was defined as haemoglobin concentration of <70 g/L and its definition excluded PPH.

In addition, the percentage of safe blood storage was defined as the amount of stored blood that can be guaranteed for general emergency blood use within the time period when the blood sent to the bank or delivered by the blood bank, is generally not less than that needed for 3 days of use.[27]

Statistical methods

In the study, multiple pregnancies were treated as one case. All statistical calculations were performed using Stata software, V.16.0 (StataCorp). A two-sided p<0.05 was considered statistically significant.

The discrete data were summarised as frequencies and percentages. The p for trends were determined by logistic regression. Then, we used the χ^2 test to examine the differences in distribution between the nulliparous and multiparous women.

Multivariable logistic regression was used to examine the associations between the maternal characteristics, relevant clinical factors and proportion of cases needing obstetric MBT. The findings from two models were reported. Model 1 presented the crude ORs and 95% CIs, considering the clustering of births within hospitals.

Model 2 further provided the adjusted ORs (aOR) and 95% CIs after the model was adjusted for (1) the clustering of births within hospitals; (2) the hospital region, birth location (urban/rural) and hospital level; (3) the mother's education level, marital status, age, parity, antenatal care, gestational week, multiple gestations, the presence of uterine scarring and the delivery method and (4) other major morbidities associated with obstetric MBT.

To identify the main causes of the obstetric MBT at the sociological level, we calculated the population aetiological fraction (PEF).

$$\text{Population etiologic fraction (PEF)} = \frac{P(aOR*1)}{[P(aOR-1)+1]} * 100\%$$

where P is the proportion of cases that are exposed to pregnancy complications and aOR is the aOR for the effect on obstetric MBT incidence.

Patient and public involvement

Patients and members of the public were not involved in the design of this study.

RESULTS

Overall incidence and trends of obstetric MBT

From 2012 to 2019, 11 667 406 women who had given birth or ended their pregnancy were included in this study. Obstetric MBT occurred in 27 626 cases, corresponding to an incidence of 23.68 per 10 000 maternities. As shown in figure 1, the incidence of obstetric MBT increased from 14.03 per 10 000 maternities in 2012 to 29.59 per 10 000 maternities in 2019 (p for trend <0.001). Similar trends were observed in the east, central and west of China. In addition, 350 health facilities had reported the institutional data for 2012, 2015 and 2018. The overall percentage of safe blood storage increased from 2012 to 2018 (77.71%–82.57%), and this increase remained after the data were stratified by hospital level (level 1: 30.61%–38.8%; level 2: 78.95%–84.74%; level 3: 96.40%–98.20%) (figure 2).

Subgroup incidence and risk factors of obstetric MBT

Table 1 displays the incidence and risk of obstetric MBT according to maternal characteristics. Being elderly, a lower level of education, a history of fewer antenatal treatments, uterine scarring, multiparity, having a small gestational age delivery, caesarean section and multiple gestations were associated with a higher risk of needing obstetric MBT. Furthermore, the association between abortion and MBT was strong, with an aOR 1.77 (95% CI 1.42 to 2.21).

As table 2 shows, AFE, placenta accrete and HELLP syndrome had the three highest incidence values for obstetric MBT. The main risk factor for obstetric MBT was AFE, which led to a 127-fold increased risk, with an aOR 126.85 (95% CI 96.88 to 166.10). Women who had severe anaemia or uterine atony were nearly 36 times more likely to undergo obstetric MBT. We also found abnormal placenta to represent a major risk factor, with an aOR 6.93 (95% CI 6.05 to 7.94) for placenta previa, 11.65 (95% CI 9.48 to 14.31) for placenta accrete, 6.53 (95% CI 5.73 to 7.45) for placenta abruptio and 3.01 (95% CI 2.48 to 3.65) for placenta retained. In addition, compared with non-HELLP syndrome, maternal HELLP syndrome led to a higher risk of needing obstetric MBT. Furthermore, the association between ectopic pregnancy

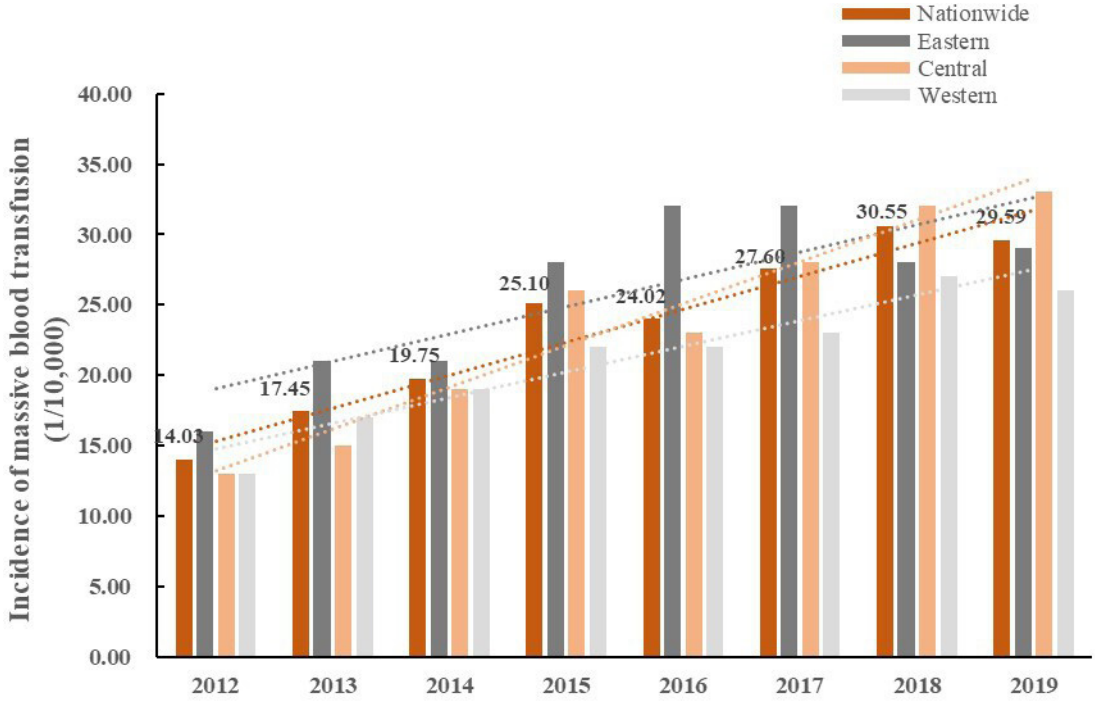

Figure 1 The secular trends and incidence of massive blood transfusion (1/10 000) during 2012–2019.

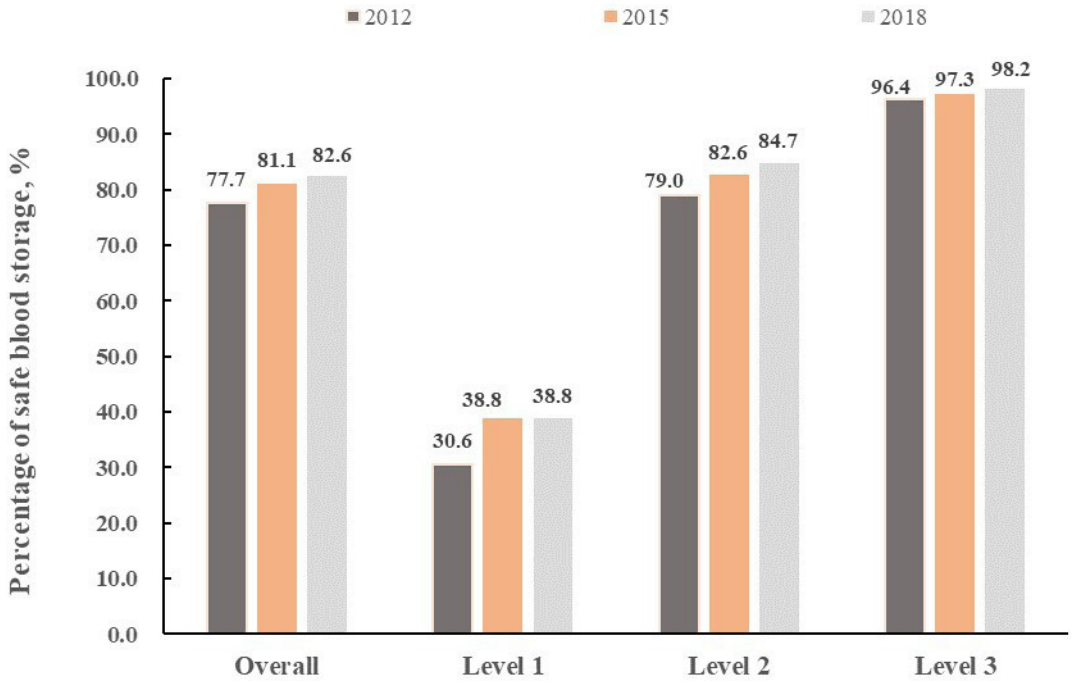

Figure 2 Changes in the proportion of safe blood storage (%) in different health facilities (level 1, level 2 and level 3).

and uterine rupture and obstetric MBT was strong. Moreover, pre-eclampsia or eclampsia, soft birth canal lacerations and puerperal infection were also associated with the incidence of obstetric MBT.

Characteristics of multiparous women

We further compared the differences in obstetric MBT-related risk factors in addition hysterectomy and MMR during the hospitalisation between the nulliparous and multiparous women. An advanced maternal age, a lower education level, less antenatal care, abortion, ectopic pregnancy, placental abnormalities, severe anaemia, uterine rupture, AFE, hysterectomy and mortality during hospitalisation were more likely to occur in women who were multiparous (online supplemental appendix table).

Population aetiological fraction for complications

We calculated the PEF for the different complications to identify the main reasons for obstetric MBT at the population perspective. As table 3 presents, the three highest PEFs were 42.28% for uterine atony, 12.33% for severe anaemia and 6.08% for placenta previa.

Clinical outcomes and trends in the MBT population

Of the 27 626 women, 4010 underwent hysterectomy, and 376 died during the hospitalisation. As shows in figure 3, the trends of hysterectomy (25.07%–9.92%) and MMR during hospitalisation (21.41‰–7.48‰) from 2012 to 2019 among women who underwent MBT was decrease (p for trend <0.001). A decrease trend in hysterectomy and the MMR during the hospitalisation in level 1 and level 2 hospitals as well as in level 3 hospitals were also observed. As online supplemental appendix figure shows, a greater decline in level hospital and level 2 hospitals for hysterectomy, and a greater decline in level 2 hospitals for maternal mortality rate was observed.

DISCUSSION

The incidence of obstetric MBT during 2012–2019 was 23.66 per 10 000 maternities, and there was an increasing trend in China. An advanced maternal age, uterine scarring, a multiparous status and multiple gestations were associated with a higher risk of needing obstetric MBT. AFE, uterine atony and severe anaemia were major complications associated with obstetric MBT. The top three PEFs were 42.28% for uterine atony, 12.33% for severe anaemia and 6.08% for placenta previa.

Obstetric MBT has been internationally reported in recent years.[9 11–13] However, due to differences in the definition of MBT, the incidence of MBT varies greatly across countries; for example, the incidence is 5.3 per 10 000 maternities in Sweden,[10] 10.0 per 10 000 maternities in New York,[9] 6.5 per 10 000 births in the Netherlands[13] and 2.3 per 10 000 maternities in the UK.[11] The definition of MBT is generally limited to 24 hours after giving birth. However, different amounts of blood, typically 5–10 units of red blood cells, have been used. MBT involves ≥10 units of red blood cells in Sweden and New York[9 10] and ≥8 units of red blood cells in the UK and Netherlands.[11 13] In our study, obstetric MBT was defined as the transfusion of ≥5 units of red blood cells or ≥1000 mL of whole blood.[28] Despite these differences in the incidence of MBT, the increasing trend is consistent across countries, except in the Netherlands.[10 13] The incidence of obstetric MBT also showed an increasing trend from 2012 to 2019 in China (14.03 per 10 000 maternities to 29.59

Table 1 The incidence and risk of massive blood transfusion (MBT) among different maternal characteristics (N=11 667 406)

Characteristics	Case/total deliveries	Incidence of MBT (1/10 000)	Crude OR* (95% CI)	Adjusted OR† (95% CI)
Age (years)				
<20	473/287 790	16.44	1.15 (1.03 to 1.28)	1.09 (0.97 to 1.21)
20–24	3030/2 114 730	14.33	reference	reference
25–29	8024/4 642 235	17.28	1.21 (1.12 to 1.30)	0.99 (0.94 to 1.06)
30–34	8116/2 900 510	27.98	1.96 (1.77 to 2.16)	1.05 (0.97 to 1.13)
35–39	5151/1 125 337	45.77	3.20 (2.89 to 3.55)	1.13 (1.03 to 1.24)
≥40	1860/278 675	66.74	4.68 (4.23 to 5.19)	1.24 (1.10 to 1.40)
Missing	972/318 129	30.55	2.14 (1.62 to 2.81)	1.30 (1.07 to 1.56)
Education				
College or higher	7977/4 315 935	18.48	reference	reference
High school	7264/3 118 196	23.30	1.26 (1.08 to 1.48)	1.25 (1.11 to 1.40)
Middle school	9186/3 581 050	25.65	1.39 (1.07 to 1.80)	1.59 (1.33 to 1.91)
Primary school	1552/344 874	45.00	2.44 (1.97 to 3.02)	1.59 (1.38 to 1.84)
Illiteracy	412/60 294	68.33	3.72 (2.76 to 5.01)	1.94 (1.56 to 2.40)
Missing	1235/247 057	49.99	2.71 (1.24 to 5.95)	1.27 (0.76 to 2.12)
Marital status				
Unmarried	639/196 743	32.48	1.38 (1.17 to 1.63)	1.15 (0.95 to 1.39)
Married	26 979/11 468 023	23.53	reference	reference
Missing	8/2640	30.30	1.29 (0.58 to 2.86)	1.07 (0.50 to 2.30)
Parity				
Nulliparous	9788/6 400 896	15.29	reference	reference
1	12 628/4 438 595	28.45	1.86 (1.72 to 2.02)	1.19 (1.12 to 1.26)
2	5142/810 139	63.47	4.17 (3.64 to 4.78)	1.83 (1.65 to 2.03)
Missing	68/17 776	38.25	2.51 (0.53 to 11.91)	0.66 (0.13 to 3.48)
Antenatal care				
None	1802/253 698	71.03	4.45 (3.00 to 6.61)	1.99 (1.40 to 2.82)
1–3	3512/947 952	37.05	2.32 (1.75 to 3.06)	1.49 (1.18 to 1.88)
4–6	7217/3 193 661	22.60	1.41 (1.14 to 1.74)	1.44 (1.23 to 1.69)
7–9	7038/3 390 343	20.76	1.30 (1.06 to 1.58)	1.31 (1.11 to 1.54)
≥10	5621/3 504 970	16.04	reference	reference
Missing	2436/376 782	64.65	4.05 (2.91 to 5.64)	1.55 (1.22 to 1.96)
Birth location				
City	20 316/6 985 253	29.08	1.87 (1.43 to 2.43)	1.36 (1.04 to 1.78)
Rural	7310/4 682 153	15.61	reference	reference
Previous scar				
No	17 804/9 736 123	18.29	reference	reference
Yes	9719/1 908 222	50.93	2.79 (2.54 to 3.08)	1.35 (1.24 to 1.46)
Missing	103/23 061	44.66	2.45 (0.75 to 8.00)	1.30 (0.74 to 2.27)
Region				
East	8762/3 366 371	26.03	1.23 (0.85 to 1.79)	1.75 (1.29 to 2.37)
Central	11 075/4 621 694	23.96	1.13 (0.84 to 1.53)	1.75 (1.31 to 2.33)
West	7789/3 679 341	21.17	reference	reference
Hospital level				
Level 1	1225/1 297 341	9.44	reference	reference

Continued

Table 1 Continued

Characteristics	Case/total deliveries	Incidence of MBT (1/10 000)	Crude OR* (95% CI)	Adjusted OR† (95% CI)
Level 2	8940/5 298 378	16.87	1.79 (1.31 to 2.44)	1.22 (0.85 to 1.73)
Level 3	17 461/5 071 687	34.43	3.66 (2.66 to 5.02)	1.86 (1.29 to 2.70)
Multiple gestations				
No	24 973/11 422 786	21.86	reference	reference
Yes	2261/215 694	104.82	4.83 (4.31 to 5.43)	1.54 (1.35 to 1.75)
Missing	392/28 926	135.52	6.27 (3.93 to 10.01)	1.34 (0.86 to 2.08)
Gestational week				
<28	3048/490 420	62.15	4.25 (3.57 to 5.06)	2.06 (1.59 to 2.66)
28–32	2313/167 840	137.81	9.49 (8.44 to 10.67)	2.21 (1.94 to 2.51)
33–36	6413/655 802	97.79	6.71 (6.04 to 7.45)	1.78 (1.64 to 1.93)
37–41	15 037/10 228 278	14.70	reference	reference
≥42	114/75 265	15.15	1.03 (0.84 to 1.26)	1.22 (1.01 to 1.47)
Missing	701/49 801	140.76	9.70 (6.52 to 14.42)	4.83 (3.67 to 6.36)
Mode of delivery				
Vaginal	5676/6 167 464	9.20	reference	reference
CS	18551/4 998 004	37.12	4.04 (3.93 to 4.17)	2.08 (1.89 to 2.28)
Abortion	3349/498 143	67.23	7.35 (7.04 to 7.67)	1.77 (1.42 to 2.21)
Missing	50/3795	131.75	14.49 (10.95 to 19.18)	0.73 (0.34 to 1.57)

*Adjusted for the clustering of births within hospitals.
†Adjusted for: the clustering of births within hospitals; region; hospital level; antenatal care; birth location; multiple gestations; gestational week; mother's education, marital status, age and parity; the delivery method and other factors thought to be associated with massive blood transfusion, such as a placenta previa; placenta accrete; placenta abruptio; placenta retained; all hypertensive disorders in pregnancy; hemolysis elevated liver enzymes and low platelets count syndrome (HELLP syndrome); severe anaemia; uterine atony; ruptured uterus; soft birth canal lacerations; puerperal infection and amniotic fluid embolism.
CI, confidence interval; CS, caesarean section; OR, odds ratio.

per 10 000 maternities). Regarding excessive maternal bleeding, if there are no adequate blood resources, it is difficult to save the mother's life.[29] Our results showed that the percentage of safe blood storage at level 3 hospitals in 2012 was 96.4%, while that at level 1 hospitals was 30.6%. In recent years, primary medical institutions have been increasingly constructed in China.[30] In addition, the rate of blood supply in China showed a steadily increasing trend (from 1.23 to 1.74 units per 1000 population) from 2012 to 2014.[31] As a result, the percentage of safe blood storage increased the most in level 1 hospitals increasing from 30.6% to 38.8% during 2012–2018. In addition, educational awareness to patients and clinicians on optimal blood utilisation practices, and relatively better access to blood products or implementation of a protocol for the management of massive obstetric haemorrhage both contributed to the rising trend of MBT.

The increased incidence of MBT plays a key role in reducing adverse outcomes in pregnancies. On the one hand, it is possible to prevent the occurrence of maternal deaths. From 2012 to 2019, the MMR due to obstetric haemorrhage with MBT in nationwide hospitals showed a decreasing trend (decreased by 68.8%), and the magnitude of decrease was larger than that in the population-based obstetric haemorrhage MMR reported by National Maternal Death Monitoring during the same period (54.6%).[32] On the other hand, the uterus can be saved by timely MBT. When severe obstetric haemorrhage fails to respond to other treatments, hysterectomy is usually performed. Although an increased hysterectomy rate was found among the MBT women in Sweden, we found a decreasing trend in Chinese women. Retaining the uterus can not only realise their dream of becoming a mother but also preserve their quality of life. This trend was observed at all three levels(level 1–level 3).

Every woman who needs obstetric MBT might have a fatal obstetric haemorrhage, and the slightest error in treatment can kill them before they undergo blood transfusion. Therefore, recognising the possible risk factors for MBT and preventing their occurrence are effective strategies to ensure the safety of women. We found that higher parity is associated with an increased risk of needing obstetric MBT. In our study, advanced maternal age, lower education level, less antenatal care and obstetric haemorrhage-related conditions were more likely to occur in women who were multiparous. Of course, these factors are also positively associated with obstetric MBT. Due to the new fertility policy, the characteristics of

Table 2 The incidence and risk of mass transfusion (MBT) among different complications (N=11 667 406)

Characteristics	Cases	Incidence of MBT (1/1000)	Crude OR* (95% CI)	Adjusted OR† (95% CI)
Ectopic pregnancy‡	45 648	33.52	15.41 (12.02 to 19.76)	9.70 (7.57 to 12.42)
Placenta abnormal				
Placenta praevia‡	126 105	61.56	38.054 (33.79 to 42.85)	6.93 (6.05 to 7.94)
Placenta accreta‡	21 545	157.53	89.68 (70.31 to 114.39)	11.65 (9.48 to 14.31)
Placenta abruptio‡	54 460	47.26	22.95 (19.45 to 27.07)	6.53 (5.73 to 7.45)
Placenta retained§	141 113	24.83	12.14 (9.93 to 14.85)	3.01 (2.48 to 3.65)
Hypertensive disorders				
Chronic hypertension‡	37 732	4.51	1.91 (1.59 to 2.29)	1.27 (1.04 to 1.55)
Gestational hypertension‡	158 526	4.88	2.10 (1.89 to 2.32)	1.62 (1.46 to 1.79)
Superimposed pre-eclampsia‡	11 951	8.53	3.64 (2.90 to 4.56)	1.32 (0.99 to 1.74)
Pre-eclampsia or eclampsia‡	257 096	10.53	4.86 (4.43 to 5.33)	2.23 (2.05 to 2.43)
HELLP syndrome‡	6702	92.36	43.83 (36.12 to 53.19)	13.02 (10.58 to 16.02)
Severe anaemia‡	46 898	76.17	39.75 (35.30 to 44.75)	36.00 (32.09 to 40.41)
Uterine atony§	240 063	49.65	37.95 (31.97 to 45.05)	36.45 (30.88 to 43.04)
Uterine rupture§	22 748	36.09	16.23 (11.76 to 22.39)	5.05 (3.67 to 6.95)
Soft birth canal lacerations§	127 320	7.61	3.31 (2.36 to 4.65)	4.28 (3.31 to 5.54)
Puerperal infection§	13 468	33.71	14.93 (12.25 to 18.20)	3.47 (2.78 to 4.34)
Amniotic fluid embolism§	1558	411.42	301.49 (245.43 to 370.37)	126.85 (96.88 to 166.10)

*Adjusted for the clustering of births within hospitals.
†Adjusted for: the clustering of births within hospitals; region; hospital level; antenatal care; birth location; multiple gestations; gestational week; mother's education, marital status, age and parity; the delivery method and other factors thought to be associated with massive blood transfusion, such as a placenta previa; placenta accrete; placenta abruptio; placenta retained; all hypertensive disorders in pregnancy; HELLP syndrome; severe anaemia; uterine atony; ruptured uterus; soft birth canal lacerations; puerperal infection and amniotic fluid embolism.
‡Prenatal factors were included in model 2
§Prenatal and postnatal factors were included in model 2
CI, confidence interval; HELLP syndrome, Hemolysis elevated liver enzymes and low platelets count syndrome; OR, odds ratio.

Chinese maternal population have changed greatly.[16 17] In our study, 44.99% of women were multiparous, among whom 36.35% had uterine scars, which may be related to the high caesarean section rate during the one-child policy (46.2%).[33] Uterine scarring is associated with an increase in the risk of abnormal placenta, infection and uterine rupture.[34 35] Women with these complications may experience extremely large volumes of blood loss during or soon after delivery, ranging from 2000 mL to 6000 mL[36 37]

In agreement with previous studies, we found that uterine atony, abnormal placenta, uterine rupture and pre-eclampsia were strongly associated with obstetric MBT.[9 10] However, we also found that AFE was the main risk factor for obstetric MBT (aOR 126.85, 95% CI 96.88 to 166.10). AFE, although rare, remains one of the leading direct causes of maternal mortality in high-income countries, and its management principles include the active correction of coagulation disorders, the aggressive treatment of uterine atony and the use of high-dose glucocorticoids as early as possible.[38 39] The total incidence of AFE was 13.4 per 100 000 maternities in our study, which was higher than that previously reported (1.7–7.7 per 100 000 maternities).[38 40] This finding may explain why AFE is considered the primary risk factor for obstetric MBT in our study.

Our study also showed that women with severe anaemia, abortion or ectopic pregnancy were at a higher risk of needing obstetric MBT. Severe anaemia has been associated with an increased prevalence of PPH.[41 42] Similarly, our study showed that severe anaemia increases the risk of needing obstetric MBT by 36-fold (OR 36.00, 95% CI 32.09 to 40.41). No studies have focused on ectopic pregnancy, abortion. We found that the association between ectopic pregnancy and MBT was strong, with an aOR of 9.70 (95% CI 7.57 to 12.42), and maternal abortion showed a relatively weaker association with the risk of needing obstetric MBT (aOR 1.77, 95% CI 1.42 to 2.21). Both of them often occur at young gestational ages and may put the woman at risk of intraperitoneal bleeding or related complications in the short term and can even lead to death.[43]

However, the OR reflects only the biological effect of a certain disease, while PEF integrates information about the effect estimate's magnitude with information about the prevalence of the disease and can reflect sociological

Table 3 Population aetiological fraction (PEF) for complications

	No	Prevalence (1/10 000)	PEF (95% CI)
Abortion	498 143	426.95	3.18% (1.76 to 4.91%)
Ectopic pregnancy	45 648	39.12	3.29% (2.51% to 4.28%)
Placenta praevia	126 105	108.08	6.08% (5.18% to 6.98%)
Placenta accreta	21 545	18.47	1.93% (1.54% to 2.41%)
Placenta abruptio	54 460	46.68	2.52% (2.16% to 2.92%)
Placenta retained	141 113	120.95	2.37% (1.76% to 3.09%)
Chronic hypertension	37 732	32.34	0.09% (0.01% to 0.18%)
Gestational hypertension	158 526	135.87	0.84% (0.62% to 1.06%)
Superimposed pre-eclampsia	11 951	10.24	0.03% (0% to 0.08%)
Pre-eclampsia or eclampsia	257 096	220.35	2.64% (2.26% to 3.05%)
HELLP syndrome	6702	5.74	0.69% (0.55% to 0.86%)
Severe anaemia	46 898	40.20	12.33% (11.11% to 13.67%)
Uterine atony	240 063	205.76	42.28% (38.07% to 46.38%)
Uterine rupture	22 748	19.50	0.78% (0.52% to 1.15%)
Soft birth canal lacerations	127 320	109.12	3.46% (2.46% to 4.72%)
Puerperal infection	13 468	11.54	0.28% (0.21% to 0.38%)
Amniotic fluid embolism	1558	1.34	1.65% (1.26% to 2.16%)

HELLP syndrome, Hemolysis elevated liver enzymes and low platelets count syndrome.

effects. Our data were retrieved from a facility-based surveillance system, which covered almost all of China, excluding Tibet. Routinely calculating complication-specific PEFs will allow us to identify the populations most affected for targeted interventions. The top three complications according to the PEFs were uterine atony, severe anaemia and placenta previa in the Chinese population. Women with such complications should be highly concerned because these complications have a high prevalence in Chinese mothers, and they also lead to a high risk of needing obstetric MBT. Although AFE leads to the highest risk of obstetric MBT, its PEF was low due to its relatively low maternal incidence. Our findings indicated that it is necessary to focus on the tertiary prevention of uterine atony, severe anaemia, and placenta previa to reduce the risk of needing obstetric MBT in China and minimise the occurrence of adverse maternal outcomes.

The main strength is that we included all women who had given birth or ended their pregnancy during 2012–2019 from a large nationwide data in China. However, the retrospective nature of the study by itself is a limiting factor as access to all clinical and transfusion variables

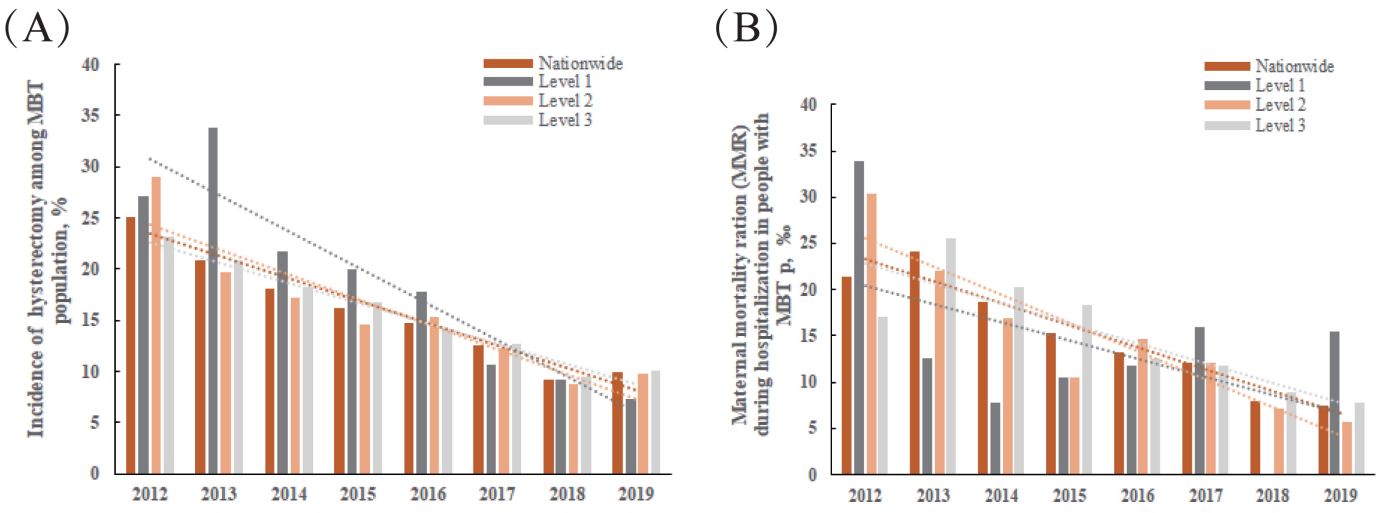

Figure 3 The secular trends and incidence of hysterectomy (%) (A) and maternal mortality ratio during hospitalisation (‰) (B) among MBT population during 2012–2019. MBT, massive blood transfusion.

are not possible. The major limitation is the lack of availability of data on many confounding variables that may influence the MBT or adverse outcomes, and the lack of a specific blood transfusion volume limits our ability to conduct additional analyses. In addition, although we recorded the types of blood transfusions performed, we could not use the data for analysis due to the lack of quantitative information.

CONCLUSION

The incidence of obstetric MBT is increasing in China, but the hysterectomy rate and MMR are decreasing among women undergoing MBT. To minimise the incidence of obstetric MBT, more attention should be paid to education on the importance of the antenatal visit, evidence-based transfusion practice, multiparous women with an advanced age, AFE, uterine atony, severe anaemia and placenta previa. Appropriate blood transfusion preparations and the antenatal early identification for high-risk women might improve the outcomes and reduce the adverse outcomes.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Ethical approval for the NMNMSS was provided by the Ethics Committee of West China Second University Hospital, Sichuan University, China. Informed consent from the patient was waived from the Ethics Committee, as the data used in this study were obtained from a national routine surveillance system established by the government. Data use was authorised by the National Health Commission, and data provided to us were de-identified.

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