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A retrospective cohort study of risk factors and pregnancy outcomes in 14,014 Chinese pregnant women

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Abstract

This study aims to investigate major complications or symptoms of pregnant women, causes of maternal near-miss, and issues that are relevant to severe maternal disease.

A retrospective analysis was performed in the "maternal individual investigation form," which included all critical maternity patients admitted to the First Affiliated Hospital of Anhui Medical University from January 1, 2012 to September 31, 2015.

A total of 14,014 pregnant patients who delivered at 28 to 42 weeks of gestation were included. Eight thousand eighty-six patients experienced complications or symptoms, and top 7 of these were postpartum hemorrhage, hypertension during pregnancy, diabetes, anemia, hepatopathy, nephroma, and connective tissue disease, of which the morbidity were 11.92%, 10.15%, 9.34%, 8.57%, 3.13%. 0.56%, and 0.55%, respectively. Delivery times, gestational weeks, and informal pregnancy examinations had significant correlation with maternal near-miss (P < .05); nevertheless, the age at pregnancy, number of pregnancies, and education were not so significant (P > .05). Two hundred sixty-five patients had severe maternal diseases (maternal near miss), and the top 5 causes for severe maternal morbidity were massive blood transfusion, thrombocytopenia, clinical feature of shock, uterus removal induced by uterus infection or bleeding, and coagulation dysfunction, of which the morbidity were 24.15%, 18.87%, 13.58%, 9.43%, and 6.79%, respectively.

Delivery times, gestational weeks, and informal pregnancy examinations should be considered in maternal near miss patients. Moreover, hypertensive disorders during pregnancy, postpartum hemorrhage, anemia, thrombocytopenia, hepatopathy, and cardiopathy were the principal causes of maternal near miss. Therefore, the monitoring of these principal causes of severe maternity near miss is important for reducing the maternal morbidity and mortality.

Abbreviations: MMR = maternal mortality ratio, MNM = maternal near miss, WHO = World Health Organization.

Keywords: complication, maternal near miss, morbidity, mortality, pregnant

1. Introduction

Since the 1980s, the global health community has focused on reducing maternal mortality.^[1,2] The global maternal mortality

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Ethics approval and consent to participate: I confirm that I have read the Editorial Policy pages. This study was conducted with approval from the Ethics Committee of the First Affiliated Hospital of Anhui Medical University. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

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Received: 18 September 2017 / Accepted: 9 July 2018 http://dx.doi.org/10.1097/MD.000000000011748 ratio (MMR, number of maternal deaths per 100,000 live births) decreased by approximately 48.8% from 422 in 1980 to 216 in 2015.^[3-5] However, 89 countries with the highest MMR remained more than 100 per 100,000 live births in 1990, whereas 13 countries made no sufficient progress.^[6] Sustainable Development Goals have been proposed to reduce MMR to a global average of 70/100,000 live births by the year of 2030.^[5] In order to reduce MMR and improve the maternal health of women, many countries have made a set of programs to expand its access to effective interventions and high-quality reproductive health care. Many social and economic factors are associated with maternal mortality. The World Health Organization (WHO) statistics revealed that 99% of all maternal deaths occur in developing countries,^[7] and studies have found that MMR varied between countries, and >50% of all maternal deaths were in only 6 countries in 2008 (India, Nigeria, Pakistan, Afghanistan, Ethiopia, and the Democratic Republic of Congo).^[3] Furthermore, in 2013, there was a variation in MMR from 956.8 in South Sudan to 2.4 in Iceland.^[4] The data suggest that there is a big imbalance between developed countries and developing counties.

The main causes of maternal mortality are severe maternal morbidity (maternal near miss [MNM]), which was defined by the WHO as "a woman who nearly died but survived a complication that occurred during pregnancy, childbirth, or within 42 days of termination of pregnancy."^[8,9] However, whether the terminology is "severe maternal morbidity," or "MNM," the main target is to identify women who have

complications that occur with organ system failure, which include hemorrhage, hypertension, sepsis, or infections, as well as indirect causes.^[10,11] Statistical data revealed that most maternal mortality cases are caused by hemorrhage (27%), hypertension during pregnancy (14%), sepsis (11%), or infections, as well as indirect causes (27.5%).^[6,12,13]

Studies have demonstrated that the cause patterns also vary substantially among region. A study reported that in 2008, MMR declined worldwide, but a noticeable change was the reduction in the number of births in East Asia, which resulted in an increase in the proportion of global maternal deaths from 23% (18-27) in 1980 to 52% (45-59) in 2008. Another surprising finding is that MMR rose in the USA, Canada, and Norway.^[3] In high-income regions in 2013, indirect and other direct causes were the main causes of maternal death. This was because abortion-related death, hemorrhage, hypertension, and maternal sepsis significantly decreased, which were the main causes of maternal death in 1990. By contrast, hemorrhage, hypertension, and maternal sepsis remain the most important causes in low-income countries.^[4] These data suggest that although MMR decreased in the past 30 years, the causes of maternal death changed especially in high-income countries.

In China, MMR was 165 in 1980, 98 in 1990, and decreased to 58 in 2000, and further decreased to 27 at present.^[3,4] MMR decreased approximately by 83.6% from 1980 to 2015. The causes of maternal death were related to biomedical, reproductive, health service, socioeconomic, and cultural factors.^[14] The 3 major direct causes of maternal death in China were postpartum hemorrhage (27.0%), amniotic embolism (12.9%), and heart disease (10.9%), which was followed by gestational hypertension (8.0%) in 2012.^[15] MMR varied between urban and rural areas. For example, MMR was 22.2 in the city and 25.6 in rural areas in 2012. Although China's progress in MMR survival for the past 40 years has been impressive, it is far higher than that in most developed countries, as MMR was only 3 in Finland, Iceland, Greece, and Poland.^[15,16] Thus, understanding the causes of deaths would be very helpful for making more effective policy and health program decisions for reducing maternal deaths. In the present study, a total of 14,014 pregnant patients received medical services in our hospital for the past 4 years. We studied the frequencies of the main causes of MMR for these patients, providing new insights into the causes of maternal mortality in China.

2. Materials and methods

2.1. Study participants

Table 1

A retrospective analysis was performed on all pregnant patents admitted to the First Affiliated Hospital of Anhui Medical University from January 1, 2012 to September 31, 2015, which included pregnant patients who labored at 28 to 42 weeks of gestation. The ages of the patients range within 14 to 50 years old. This hospital is a tertiary care teaching hospital in China. Patients who were admitted only to prevent miscarriage without any complications/symptoms were excluded. The classic WHO definition criterion in the year 2009 was used to identify MNM.^[8]

The definition of postpartum hemorrhage, hypertension during pregnancy, diabetes, anemia, hepatopathy, nephroma, connective tissue disease, advanced maternal age, multiple pregnancies, and multiparity were followed the William's Obstetrics 23rd Ed.^[17]

This study was conducted with approval from the Ethics Committee of the First Affiliated Hospital of Anhui Medical University and also was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

2.2. Study design

Data collection was conducted by the medical staff who had received special training. Monitoring and filling in the maternal individual investigation form was performed from the day of admission. Following protocol, the data were recorded into the national maternal surveillance system by a specialist, and statistical analysis was performed.

2.3. Statistical analysis

Data acquisition and sorting were performed using Microsoft Excel 2007. All statistical analysis was performed using the SAS system software version 9.2. Patient numbers were analyzed and presented as "n." The rates were expressed as percentage. Chi square was used to evaluate the differences in MNM and maternal death among groups. A *P* value <0.05 was used as a measure of statistical significance.

3. Results

3.1. Study participants

During the study period, a total of 14,105 pregnant patients were included, and then 91 patients were excluded without enough information and failed to contact. Finally 14,014 admitted patients were available for selection. When we defined complications/symptoms as pregnancy with internal diseases or postpartum hemorrhage, among all patients included, 8086 patients experienced complications/symptoms and 265 patients had severe maternal diseases (MNM), accounting for 57.7% and 1.89%, respectively. Furthermore, 10 patients died of MNM, and the mortality rate of MNM was 1.24% (Table 1). The top 7

| Maternal statistic data cohort 2012 to 2015. | | | | | | | | | |
|--|---------------------|---|--------------|-----------------|---|----------------------|------------------------------------|--|--|
| Year | Number of maternals | Number of maternals with complications/symptoms | MNM cases | Deaths cases | Complications/symptoms morbidity (%) | MNM morbidity (%) | Mortality rate (person/year, %) | | |
| 2012 | 3501 | 1902 | 69 | 2 | 54.3 | 1.97 | 0.57 | | |
| 2013 | 3296 | 2042 | 83 | 4 | 62 | 2.52 | 1.21 | | |
| 2014 | 4060 | 2477 | 73 | 2 | 61 | 1.8 | 0.49 | | |
| 2015 | 3157 | 1665 | 40 | 2 | 52.7 | 1.27 | 0.63 | | |
| Total | 14,014 | 8086 | 265 | 10 | 57.7 | 1.89 | 0.71 | | |

 Table 2

 Complications/symptoms in 14,014 pregnant patients.

| Events | Number | Percentage (%) |
|-------------------------------|--------|----------------|
| Postpartum hemorrhage | 1670 | 11.92 |
| Hypertension during pregnancy | 1422 | 10.15 |
| Diabetes | 1309 | 9.34 |
| Anemia | 1201 | 8.57 |
| Hepatopathy | 439 | 3.13 |
| Nephroma | 79 | 0.56 |
| Connective tissue disease | 77 | 0.55 |

MNM = maternal near miss.

complications/symptoms and distribution rates in the 14,014 pregnant patients are presented in Table 2.

3.2. Age, pregnant times, delivery times, and education were associated with severe maternal morbidity rates

MNM account for 265 of the 14,014 pregnant women, and the severe maternal morbidity rate in patients with the advanced age of 35 or above was 2.54%. The prevalence of MNM increased when pregnant times and delivery times increased. Moreover, the percentage of MNM was significantly increased if the pregnancy was terminated before 37 weeks of gestational or pregnancy examination times were <5 times. The incidence rate was strongly and significantly associated with pregnancy times and examination times (Table 3).

3.3. The distribution of the 265 maternal near miss and critical manifestations

According to the diagnosis criteria of the WHO for the identification of MNM cases, the clinical manifestations and signs, laboratory test, and management were analyzed in the 265 severe pregnant patients. After further investigating the case distribution and classification, it was found that in the top 10 causes (Table 4), the top 3 complications/symptoms were

hypertension during pregnancy (131 cases, account for 49.43%), postpartum hemorrhage (98 cases, account for 36.98%), and anemia (96 cases, account for 36.23%) (Table 5). The major approach used for terminating pregnancy was caesarean, which account for 80.75%. In the meantime, the major outcome was live birth, which account for 86.79% (Table 5).

4. Discussion

From this study, we found that hypertensive disorders during pregnancy, postpartum hemorrhage, anemia, thrombocytopenia, hepatopathy, and cardiopathy were the principal causes of MNM. Delivery times, gestational weeks, and informal pregnancy examinations should be considered in MNM patients. Therefore, the monitoring of these principal causes of severe MNM is important for decreasing the maternal morbidity and mortality.

Most maternal deaths were mainly caused by MNM such as hemorrhage, eclampsia, and sepsis. Most of these women died in low-income countries, and several countries in sub-Saharan Africa had very high MMR.^[2] Comprehensive studies have concluded that information on MNM is helpful for identifying health systems, providing estimates related to maternal health care.^[18] In the present study, we found that from January 1, 2012 to September 31, 2015, a total of 14,014 pregnant patients were included. Among them, *5*7.7% had complications/symptoms. The incidence of MNM was 1.89%, and MMR was 0.93%. The most frequent complications of MNM include hypertension, postpartum hemorrhage, anemia, thrombocytopenia, hepatopathy, and cardiopathy.

In China, total prevalence of MMR was 27 in 2015.^[5] However, in our hospital, MMR was 93 from 2012 to 2015. It is far higher than the average level, and also far exceeds the level in rural areas in China.^[15] The analysis of the 14,014 pregnant patients revealed that 57.7% of them had complications/symptoms, and the incidence of MNM was 1.89%. However, approximately 15% of all pregnant women develop a potentially life-threatening

Table 3

Demographic characteristics among 265 case of maternal near miss.

| | | | Maternal r | near miss | | | Maternal | nal deaths | |
|----------------------------|---------------|---------------|------------|-----------|--------|---------------|----------|------------|-------|
| Characteristics | No. maternals | No. maternals | % | χ^2 | Р | No. maternals | % | χ^2 | Р |
| Age | | | | | | | | | |
| <35 | 12,242 | 220 | 1.8 | 4.599 | <.05 | 10 | 0.82 | 1.449 | .2288 |
| ≥35 | 1772 | 45 | 2.54 | | | 0 | 0 | | |
| Pregnancy times | | | | | | | | | |
| <3 | 69,70 | 169 | 2.42 | 19.509 | <.0001 | 7 | 1 | 0.154 | .6942 |
| ≥3 | 3459 | 96 | 2.78 | | | 3 | 0.87 | | |
| Delivery times | | | | | | | | | |
| 0–1 | 9809 | 229 | 2.33 | 67.282 | <.0001 | 8 | 0.82 | 6.895 | .0086 |
| ≥2 | 555 | 36 | 6.49 | | | 2 | 3.6 | | |
| Gestational weeks | | | | | | | | | |
| <37 | 2801 | 150 | 5.36 | 1471.47 | <.0001 | 8 | 2.86 | 14.31 | <.001 |
| ≥37 | 10,230 | 115 | 1.12 | | | 2 | 0.2 | | |
| Examination times | | | | | | | | | |
| <5 | 2970 | 129 | 4.34 | 122.182 | <.0001 | 9 | 3.03 | 19.937 | <.001 |
| ≥5 | 11,044 | 136 | 1.23 | | | 1 | 0.09 | | |
| Education | | | | | | | | | |
| Bachelor's degree or above | 6994 | 41 | 0.59 | 128.119 | <.0001 | 3 | 0.43 | 3.58 | .0585 |
| High school or below | 3281 | 224 | 6.83 | | | 7 | 2.13 | | |

 Table 4

 The critical manifestations of 265 maternal near miss.

| Classify | No maternals | Percentage (%) |
|---|--------------|----------------|
| Massive blood transfusion | 64 | 24.15 |
| Platelet transfusion | 50 | 18.87 |
| Clinical manifestation of shock | 36 | 13.58 |
| Uterus removal induced by infection or bleeding | 25 | 9.43 |
| Blood coagulation disorder | 18 | 6.79 |
| Use of vasoactive drugs | 16 | 6.04 |
| Severe hypoxia | 15 | 5.66 |
| Severe shortness of breath | 14 | 5.28 |
| Cardiopulmonary resuscitation | 14 | 5.28 |
| Eclampsia | 12 | 4.5 |

complication worldwide. The MNM incidence rate was 0.05% to 14.98% in Africa, and 0.02% to 5.07% in Asia.^[19–21] It might because that the normal childbirth of healthy delivery women stayed in local hospitals, and most women with complications/ symptoms were transferred into our hospital. Another reason might be the increase in MNM incidence itself. In China, the increase in MNM incidence was caused by many factors, including increase in maternal age, prepregnancy obesity, pre-existing chronic medical conditions, and cesarean delivery.^[14,22]

It is worthy to mention that in our hospital, the main causes of maternal mortality are hypertension, postpartum hemorrhage, anemia, thrombocytopenia, hepatopathy, and cardiopathy. Maternal mortality is caused by direct and indirect factors. In developed countries, it is attributed to indirect factors, otherwise in China direct factors remain the main cause of maternal deaths.^[4,23] Recent statistical data revealed that the 3 major direct causes of maternal death in China were postpartum hemorrhage (27.0%), amniotic embolism (12.9%), and heart disease (10.9%), these were followed by gestational hypertension (8.0%) in 2012 ^[17]. However, in our hospital, the main causes were hypertension, postpartum hemorrhage, anemia, and thrombocytopenia. There were great differences with the ones in whole country. This bias

| Та | Ы | e | 5 |
|----|---|---|----------|
| | | - | . |

| Distribution of 265 maternal near-miss cases and outcomes | Distribution of 265 | maternal | near-miss | cases | and | outcomes. |
|---|---------------------|----------|-----------|-------|-----|-----------|
|---|---------------------|----------|-----------|-------|-----|-----------|

| Outcomes | Number of maternals | Percentage (%) |
|---------------------------------------|---------------------|-------------------|
| Complications/symptoms | | |
| Hypertension during pregnancy | 131 | 49.43 |
| Eclampsia | 58 | 21.89 |
| Severe pre-eclampsia | 44 | 16.6 |
| Hemolysis, elevated liver enzymes, | 15 | 5.66 |
| and low platelets syndrome | | |
| Postpartum hemorrhage | 98 | 36.98 |
| Uterine inertia | 39 | 14.72 |
| Placenta previa | 29 | 10.94 |
| Anemia | 96 | 36.23 |
| Pregnancy associated thrombocytopenia | 66 | 24.91 |
| Hepatopathy | 26 | 9.81 |
| Cardiopathy | 17 | 6.42 |
| Terminal pregnancy | | |
| Vaginal delivery | 33 | 12.45 |
| Cesarean | 214 | 80.75 |
| Others | 18 | 6.79 |
| Perinatal child outcome | | |
| Live births | 230 | 86.79 |
| Dead births | 7 | 2.64 |
| Stillbirths | 28 | 10.57 |

might be that most women with complications/symptoms chose to undergo childbirth in our hospital. The proportion of patients with complications/symptoms was approximately 57% in the present study, whereas globally it was approximately 15% in all pregnant women.^[24] In 2012, the main cause of maternal deaths was complications/symptoms, and no patient died of postpartum hemorrhage in Beijing. In our area, maternal deaths were mainly attributed to postpartum hemorrhage (26.7%), complications/ symptoms (26.7%), and other indirect factors (26.7%). In the West-North areas of China, the leading cause of maternal deaths was postpartum hemorrhage (nearly >30%, and >50% in some provinces).^[15] These results suggested that there were significant differences in causes among different regions in China, which might be attributed to the imbalance of medical condition and the level of clinical treatment in different regions.

Other studies had demonstrated many social and economic factors, including maternal age, pre-existing chronic medical conditions, and cesarean delivery, which also increased the risk of MNM. Maternal race and ethnicity were associated with inconsistent outcomes. For example, African American women demonstrated a 4-fold higher MMR incidence than white women in the United States.^[25,26] Our study indicated that the high prevalence of MNM was probably correlated to advanced ages, multiple pregnancy and delivery, small gestational weeks, informal examinations, and low educational attainment, which also had significant difference among groups. The present study also showed that lower educational attainment and awareness regarding prenatal and postnatal health protection, as well as less informal examinations, also associated with MNM. Therefore, it is important to strengthen maternal awareness campaigns and health care, especially in low-income rural areas. Empowering medical staff with health education and improving the diagnosis of critically pregnant women would decrease the risk and prevalence of complications/symptoms, and achieve early detection and treatment. MNM patients should be admitted into the ICU, to improve the quality of life of patients and decrease mortality,^[26,27] which was named "life rescue procedure" and 1 reform of modern obstetric management policy.

Moreover, in this study retrospective cohort analysis was carried out. Exposure status may be not clear when it is necessary to go back to explain the MNM outcomes.

In conclusion, the highly frequent disorders in the women who died were hemorrhage, hypertension, infections, and indirect causes. Because of the higher MMR incidence in our hospital and many factors may take effects, more improvements should be done, such as a perinatal stage health care and emergency treatment, to decrease maternal mortality. The present information was only from 1 hospital; more multicenter studies should be done in the future.

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