

Original article

Maternal and neonatal outcomes in multiple pregnancy: A multicentre study in the Beijing population

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Received 12 August 2015

Available online 26 September 2015

Abstract

Objective: To compare the adverse maternal and neonatal outcomes of multiple pregnancy and singleton pregnancy from multiple medical centers in Beijing.

Methods: Data concerning maternal and neonatal adverse outcomes in multiple and singleton pregnancies were collected from 15 hospitals in Beijing by a systemic cluster sampling survey conducted from 20 June to 30 November 2013. The SPSS software (version 20.0) was used for data analysis. The χ^2 test was used for statistical analyses.

Results: The rate of caesarean deliveries was much higher in women with multiple pregnancies (85.8%) than that in women with singleton pregnancies (42.6%, $\chi^2 = 190.8$, $P < 0.001$). The incidences of anemia ($\chi^2 = 40.023$, $P < 0.001$), preterm labor ($\chi^2 = 1021.172$, $P < 0.001$), gestational diabetes mellitus ($\chi^2 = 9.311$, $P < 0.01$), hypertensive disorders ($\chi^2 = 122.708$, $P < 0.001$) and post-partum hemorrhage ($\chi^2 = 48.550$, $P < 0.001$) was significantly increased with multiple pregnancy. In addition, multiple pregnancy was associated with a significantly higher rate of small-for-gestational-age infants ($\chi^2 = 92.602$, $P < 0.001$), low birth weight ($\chi^2 = 1141.713$, $P < 0.001$), and neonatal intensive care unit (NICU) admission ($\chi^2 = 340.129$, $P < 0.001$).

Conclusions: Multiple pregnancy is a significant risk factor for adverse maternal and neonatal outcomes in Beijing. Improving obstetric care for multiple pregnancy, particularly in reducing preterm labor, is required to reduce the risk to mothers and infants.

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Keywords: Multiple pregnancy; Perinatal outcomes; Systemic cluster sampling survey; Multicenter; Beijing

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Peer review under responsibility of Chinese Medical Association.



Introduction

A number of previous studies have shown that multiple pregnancy is associated with a higher risk of maternal and neonatal complications compared to singleton pregnancy.^{1–4} The increased risk of preterm delivery, post-partum hemorrhage and hypertensive disorders in multiple pregnancy is a well-known issue.^{1,4–6} Additionally, low birth weight and small-for-gestational-age (SGA) status were reported at higher rates in infants conceived in multiple pregnancy than with singleton pregnancy, and these are known risk factors for prenatal mortality and morbidity.^{7–9} Because multiple pregnancy can contribute significantly to adverse maternal and perinatal outcomes, it is important to comprehensively investigate the risks involved in multiple pregnancy in China. The adverse outcomes of multiple pregnancy across medical centers in China have not been extensively investigated. Clarifying the perinatal consequences of multiple pregnancy becomes increasingly helpful in facilitating resource allocation and closer developmental surveillance for infants at risk of dysplasia. Thus, in this study we performed a multi-centre analysis to determine the severity of maternal and neonatal complications of multiple pregnancy in comparison to those of singleton pregnancy in the Beijing population.

Methods

Study population and variables

The study was based on the data obtained from a system sampling survey conducted in 15 hospitals in Beijing. Medical records of 15,194 pregnant women who delivered between 20 June 2013 and 30 November 2013 were collected. Sorted by the number of fetuses, there were 253 multiple pregnancies and 14,941 singleton pregnancies.

Independent variables included maternal characteristics, such as maternal age (<25, 25–35, and >35 years), maternal height (centimeters), pre-pregnancy weight (grams), parity (primiparous vs. multiparous), gestational age (weeks) and mode of delivery (vaginal vs. caesarean); in addition to maternal complications, which included anemia, preterm labor (<37 completed weeks of gestation), gestational diabetes mellitus (GDM), hypertensive disorders (including preeclampsia, eclampsia, pregnancy-induced hypertension, and hemolysis, elevated liver enzymes and low platelet syndrome, HELLP), post-partum hemorrhage, and premature rupture of membrane (PROM, including

preterm premature rupture of membranes, PPRM); and infant complications, such as low birth weight (<2500 g), SGA, neonatal intensive care unit (NICU) admission and congenital malformations. The whole study was approved by the ethics review board of Peking University First Hospital (resolution 2013, 578). Informed written consent was obtained from the pregnant women before enrollment.

Definitions

Multiple pregnancy was defined as twins or triplets. Anemia was defined by hemoglobin levels <110 g/L during pregnancy. Gestational age was based on the number of days between the first day of an expectant mothers' last menstrual period (LMP) and date of delivery and was expressed in completed weeks after the LMP. The SGA was defined as a birth weight below the 10th percentile for gestational age. The GDM was diagnosed by a diagnostic 2-h 75 g OGTT at the 24th–28th week of gestation by the Chinese MOH 2011 criteria when one of the following plasma glucose values was met or exceeded: 0 h, 5.1 mmol/L; 1 h, 10.0 mmol/L; and 2 h, 8.5 mmol/L.

Statistical analysis

The SPSS software version 20.0 (SPSS Inc. Chicago, IL) was used for all statistical analyses. Univariate associations between multiple pregnancy and maternal and neonatal complications were explored with Pearson's χ^2 . Categorical variables were expressed as frequencies and percentages. Continuous variables are presented as the mean \pm standard deviation (SD), and two groups were compared using a one-way analysis of variance (ANOVA). A *P*-value less than 0.05 was considered statistically significant.

Results

We reviewed the medical records of 253 multiple deliveries and 14,941 singletons from 15 hospitals in Beijing. **Table 1** shows the maternal characteristics of multiple versus singleton pregnancies. Mothers with multiple pregnancy were significantly more likely to be age 35 years or older ($\chi^2 = 31.557$, $P < 0.001$). Pre-pregnancy weight ($F = 15.958$, $P < 0.001$) and the rate of caesarean delivery ($\chi^2 = 190.80$, $P < 0.001$) significantly increased in these cases and gestational age was observed to significantly decrease ($F = 1043.28$, $P < 0.001$). There were no significant

Table 1
Maternal characteristics of singleton and multiple pregnancy in 15 hospitals in Beijing.

| Variables | Singletons (n = 14941) | Multiple pregnancy (n = 253) | χ^2/F | P-value |
|---------------------------|---------------------------|---------------------------------|------------|---------|
| Maternal age (year) | 28.4 ± 16.5 | 29.6 ± 5.0 | 1.158 | 0.28 |
| <25 (n,%) | 3985 (26.7) | 47 (21.3) | | |
| 25–35 (n,%) | 9761 (65.4) | 134 (60.6) | 31.557 | <0.001* |
| ≥35 (n,%) | 1175 (7.9) | 40 (18.1) | | |
| Maternal height (cm) | 162.0 ± 4.9 | 162.3 ± 4.8 | 0.415 | 0.52 |
| Pre-pregnancy weight (kg) | 56.96 ± 9.36 | 59.36 ± 10.63 | 15.958 | <0.001* |
| Parity | | | | |
| Primiparous (n,%) | 10,671 (71.4) | 153 (60.5) | 14.550 | <0.001* |
| Multiparous (n,%) | 4270 (28.6) | 100 (39.5) | | |
| Gestational age (weeks) | 39.0 ± 1.6 | 35.6 ± 2.5 | 1043.28 | <0.001* |
| Delivery mode | | | | |
| Vaginal delivery (n,%) | 8241 (55.2) | 33 (13.0) | 190.800 | <0.001* |
| Caesarean delivery (n,%) | 6350 (42.6) | 217 (85.8) | | |

The results are reported as the mean ± standard deviation (SD) and frequency (percentage), and * $P < 0.05$ is statistically significant.

differences in the mean maternal height between multiple and singleton pregnancies.

Multiple pregnancy was significantly more likely to be associated with GDM ($\chi^2 = 9.311$, $P = 0.01$) and hypertensive disorders ($\chi^2 = 122.708$, $P < 0.001$) than was singleton pregnancy, but less likely to be associated with PROM ($\chi^2 = 1.301$, $P = 0.52$) (Table 2). The prevalence of anemia ($\chi^2 = 40.023$, $P < 0.001$), preterm labor ($\chi^2 = 1021.172$, $P < 0.001$) and postpartum hemorrhage ($\chi^2 = 48.550$, $P < 0.001$) was much higher for mothers with multiple pregnancy than for those with singleton pregnancy (Table 2).

Infants from multiple pregnancies had a significantly higher rate of SGA ($\chi^2 = 48.550$, $P < 0.001$), low birth weight ($\chi^2 = 1141.713$, $P < 0.001$) and NICU admission ($\chi^2 = 340.129$, $P < 0.001$) than infants from a singleton pregnancy. However, the prevalence of congenital malformations was 0.8% for infants from a multiple pregnancy and 0.6% for infants

from a singleton pregnancy, there was no significant difference between the multiple and singleton pregnancies ($\chi^2 = 0.124$, $P = 0.725$) (Table 2).

Discussion

Our study showed a high rate of approximately 1.7% of multiple pregnancies in the Beijing population. Multiple pregnancy was significantly associated with older maternal age, caesarean delivery, preterm labor, GDM, hypertensive disorders, SGA, low birth weight (<2500 g) and NICU admission but was not associated with maternal height, PROM, and congenital malformations. This suggested that in Beijing, multiple pregnancy still confers an intrinsic risk of maternal and neonatal adverse outcome.

The prevalence of multiple pregnancy in Beijing was higher than the rate of 6.7%–16.8% measured in other regions of China.¹⁰ In recent years, with the

Table 2
Maternal and neonatal complications in singleton and multiple pregnancies, n (%).

| Variables | Singletons (n = 14941) | Multiple pregnancy (n = 253) | χ^2 | P-value |
|----------------------------|---------------------------|---------------------------------|----------|---------|
| Anemia | 2272 (16.0) | 73 (31.5) | 40.023 | <0.001* |
| Preterm labor | 790 (5.3) | 136 (53.8) | 1021.172 | <0.001* |
| Hypertensive disorders | 625 (4.3) | 47 (19.0) | 122.708 | <0.001* |
| GDM | 2927 (19.6) | 60 (23.7) | 9.311 | 0.010* |
| Post-partum hemorrhage | 927 (6.2) | 43 (17) | 48.550 | <0.001* |
| PROM | 2907 (19.5) | 46 (18.2) | 1.301 | 0.520 |
| SGA | 738 (4.9) | 45 (17.8) | 92.602 | <0.001* |
| Low birth weight (<2500 g) | 525 (3.5) | 118 (46.6) | 1141.713 | <0.001* |
| NICU admission | 973 (6.5) | 92 (36.4) | 340.129 | <0.001* |
| Congenital malformations | 92 (0.6) | 2 (0.8) | 0.124 | 0.725 |

PROM: premature rupture of membranes; GDM: gestational diabetes mellitus; NICU: neonatal intensive care unit; SGA: small-for-gestational-age. * $P < 0.05$ is statistically significant.

development of assisted reproductive technology (ART), the incidence of multiple pregnancy has increased rapidly world-wide, most notably in developing countries.¹¹ Yang X et al.¹² demonstrated that the proportion of births from ART in mainland China was approximately 1.0% in 2011, and that multiple gestations had significantly increased in these pregnancies. The high rate of multiple pregnancy in Beijing might be attributable to an increase in the age of pregnant women and the increased availability of ART.

The increased risks to maternal outcomes from multiple pregnancies, such as anemia, preterm labor, hypertensive disorders and caesarean delivery were consistent with previous findings.^{13–15} Preterm labor emerged as the most serious maternal complication in multiple pregnancy and was much more common in multiple pregnancy than in singleton pregnancy (53.8% vs. 5.3%). The rate of preterm labor in this study was higher than the rate of 12%–13% found in the USA and other developed countries, where reported rates were generally 5%–9%.^{16,17} Goldenberg RL et al.¹⁸ showed that 40% of the surveyed population delivered spontaneously before 37 weeks of gestation, and Kazemier BM et al.¹⁹ found 57% of twin pregnancies occurring after a previous preterm singleton birth might be associated with a risk of recurrence of preterm birth. These results were somewhat in accordance with our findings.

The association between GDM and multiple pregnancy has rarely been reported. A previous study showed that the risk of GDM might be similar between singleton and twin pregnancies.²⁰ The significantly higher risk of GDM in multiple pregnancy in our study was found to be in accordance with the statement from the American College of Obstetricians and Gynecologists (ACOG) practice bulletin.²¹ In this bulletin, mothers with a multiple pregnancy were found to be slightly older than mothers with a singleton pregnancy, which might partially explain the higher rate of GDM, whereas, GDM was associated with a lower risk of pregnancy-related complications in multiple pregnancy in the case of hypertensive disorders. These results validated a study in which patients with a twin pregnancy did not have a higher rate of GDM but did have a higher rate of pregnancy-induced hypertension (PIH) (GDM 3.4% vs. 3.4%, $P = 0.63$; PIH 2.8% vs. 9.0%, $P = 0.036$).²²

Because of the higher rate of caesarean delivery and primiparity in multiple pregnancy, the prevalence of

severe adverse maternal outcomes, such as post-partum hemorrhage, was found to be more pronounced in multiple pregnancy. Regulations to lower elective caesarean delivery might reduce the preterm birth rate.²³ Recently, a consensus has been reached by the ACOG regarding the appropriate mode of twin delivery.²⁴ In China, caesarean delivery is more widespread, and it is recommended that vaginal delivery be attempted for women with twin gestations when the first twin is in cephalic presentation, especially for nulliparous woman.²⁵

The findings of the present study also corroborate the extensive evidence that low birth weight and SGA are the common neonatal complications of multiple pregnancy worldwide.^{5,9} Infants born with low birth weight and SGA have an increased risk of fetal death, and these conditions contribute significantly to adult-onset disorders, including type 2 diabetes, hypertension and metabolic syndrome.^{26–28} The increased risk of NICU admission (36.4%) was also in agreement with the findings of a multicentre, randomized controlled trial of multiple gestations conducted by Refuerzo et al.⁹ in the USA. Arianne C. Lim's study determined that approximately 30% of all preterm infants admitted to the NICU were from twin pregnancies.¹⁷

To the best of our knowledge, this is the largest study on the topic of multiple pregnancy using a systemic cluster sampling survey that contributes to the current data on the issue of multiple pregnancy in Beijing. The study also complements the existing evidence concerning the risk of multiple pregnancy through a multicentre study that surpasses the previously reported studies from single institutions.

This study has limitations that should be noted. We lacked sufficient data on several maternal and neonatal outcomes, such as neonatal jaundice, hypoglycemia, and fetal death. The medical records were obtained from 15 hospitals operating at different levels of quality; therefore, despite the involvement of individuals specifically trained for this study, some information was missing. In addition, some of the medical documentation was suboptimal, which might have affected the data quality. We had no information on the use of ART, which has been verified to have a significant impact on maternal and neonatal outcomes.^{29,30}

Our findings suggest that the maternal and neonatal outcomes associated with multiple pregnancy are significant, and there is an immediate need for efforts to reduce adverse perinatal outcomes. Because primary

prevention for the risks associated with multiple pregnancy, such as prematurity, hypertension, low birth weight, and SGA are often unattainable, mothers with multiple gestations should seek increased obstetric care and be educated on the importance of timely intervention and developmental surveillance for optimal child growth and development.

Acknowledgments

The author acknowledges the support of the entire management of the fifteen hospitals surveyed in Beijing in the data retrieval efforts for the study, including Tongzhou Maternal and Child Health Hospital of Beijing, Beijing, China; General Hospital of Beijing Military Region; Center Hospital of Aviation Industry; Pinggu Maternal and Child Health Hospital of Beijing, Beijing, China; Beijing Hospital of Miyun City; Navy General Hospital; Beijing Daxing District Hongxing Hospital; Beijing Chui Yang Liu Hospital; Peking University Shougang Hospital; Combined with Traditional Chinese and Western Medicine Hospital of Beijing City; Beijing No.6 Hospital; Beijing Changping Hospital of Traditional Chinese Medicine; General Hospital of Jingmei Group. We declare that we have no conflicts of interest.

This study was supported by the World Diabetes Foundation (WDF 10-517).

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Edited by Yang Pan