Pregnancy outcomes in Chinese urban women at a very advanced maternal age

Haili Jiang, Xin Wang

Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Chaoyang District, Beijing (P.R.China)

Summary

Aim: To compare the maternal-fetal outcomes in Chinese urban women at the maternal age of ≥ 40 years with those aged between 35 and 39 years. *Materials and Methods:* In this retrospective study, women in a single-center that delivered from January 1 to December 31, 2013, were included. The authors divided the subjects into two groups according to the age, and evaluated the obstetric history, delivery mode, incidence of obstetric diseases, and neonatal outcomes of each group. *Results:* They enrolled 1,965 pregnant women in total. The women between 35 to 39 years of age reached 1,727 (87.9%), and the remaining 238 (12.1%) were women ≥ 40-years-old. The incidence rates of in vitro fertilization (IVF, $p < 0.01$), gestational diabetes mellitus (GDM) ($p < 0.05$), and hypertension ($p < 0.05$) for the elder group were higher than the younger group. Furthermore, women ≥ 40-years-old were associated with a higher rate of cesarean section (84.0% *vs.* 67.6%, $p < 0.001$) compared with the younger group, varying significantly on intrauterine infection (1.5% *vs.* 0.5%, $p < 0.05$), IVF (6.5% *vs.* 3.2%, $p < 0.01$), and maternal request (41.0% *vs.* 30.6%, $p < 0.001$). No significant differences in neonatal outcomes were found and no neonatal deaths were recorded for the two groups. *Conclusions:* These results showed an increase risk of pregnancy complications for the women giving birth at ≥ 40 years of age, yet most of them still carried a favorable pregnancy and neonatal outcome, similar to the younger women.

Key words: Advanced maternal age; Cesarean section; Chinese urban women; Perinatal outcomes; Pregnancy complications.

Introduction

In the past three decades, delaying child bearing to a later reproductive age has become increasingly common, especially in some high-income developed countries [1, 2]. In some parts of the world, the percentage of women commencing childbearing at 35 years and beyond is stable at about 20% [3-5]. Well-educated, demanding professional career, higher socio-economic status, and development in assisted reproductive technology are contributed to this trend [6].

With the economic, technological, and social changes, the rate of giving birth at advanced maternal age (AMA, $\geq$ 35 years) has also significantly increased in China, especially in urban areas. As the national census data showed, the mean maternal age at first birth of Chinese women rose by 1.4 years, from 24.8 to 26.2 years between 2000 and 2010 [7]. Furthermore, a population-based study, which including all deliveries performed after 28 completed weeks of gestation within 2011 in 39 hospitals of 14 provinces in China, indicated the mean age for urban women childbirth was 28.18 years [8]. In addition, 10.1% of the urban women in that study were considered with AMA, which was near to the status of the western developed countries at the beginning of 20th century [9, 10].

Many studies have shown that AMA is associated with increased incidence of maternal and fetal complications, including pregnancy-induced hypertension, gestational diabetes mellitus (GDM), amniotic fluid embolisms, as well as higher rates of elective cesarean section (CS) [8, 11-13]. In addition, perinatal morbidity and mortality, intrauterine fetal death (IUFD), and premature labor have also increased significantly for childbearing at AMA [8, 14, 15].

In previous studies, most have declared age 35 years as the cutoff for childbirth, after which the risk of adverse perinatal outcomes (stillbirth, perinatal and neonatal loss, low birth weight, and preterm birth) would increase. Meanwhile, some authors suggested that the association only becomes significant at the age greater than 40 years [16, 17]. Prior studies have however mainly focused on European and American populations investigation. The figures of childbearing delay for Asians are deficient [18]. So in this study, the authors carried out a retrospective research, to investigate the associations between adverse pregnancy outcomes and delivery age ($\geq$35 years) in Chinese urban women and to compare the pregnancy outcomes for the women at very AMA of $\geq$ 40 years old with those aged between 35 and 39 years.

Materials and Methods

Data Collection

The data for this study were obtained from Beijing Obstetrics and Gynecology Hospital, Capital Medical University between January 1 and December 31, 2013. The study population included the women of pregnancies aged 35 years and beyond, with preg-

Table 1. — *Demographic and obstetric characteristics of the two groups.*

Variable	Group 1: 35-39 y	Group 2: ≥ 40 y	*p* value
N	1727	238	
Maternal age, years [a]	36.4 ± 1.3	41.2 ±1.5	< 0.001
Gravidity [a]	1.4 ± 1.3	2.0 ± 1.6	< 0.001
Parity [a]	0.3 ± 0.5	0.4 ± 0.7	< 0.001
Nulliparity, n (%)	1251 (72.4)	149 (62.6)	0.002
In vitro fertilization, n (%)	165 (9.6)	36 (15.1)	0.008
Adverse pregnancy history	203 (11.8)	38 (16.0)	0.06
Previous caesarean history, n (%)	245 (14.2)	39 (16.4)	0.37
Previous hysteromyomectomy history, n (%)	40 (2.3)	7 (2.9)	0.55
Pregnancy complications			
- Gestational diabetes mellitus, n (%)	272 (15.7)	62 (26.1)	0.001
- Gestational hypertension, n (%)	122 (7.1)	28 (11.8)	0.011
- Hysteromyoma	203 (11.4)	38 (16.0)	0.063

[a] Data are presented as mean ± SD.

nancies that have reached at least 24 weeks of gestation. Abortions and maternal transport were excluded. The study was approved by the Institutional Review Boards.

In total, 1,997 cases were collected, of which 1,965 had complete medical records and were enrolled in the study (at a rate of 98.4%). All subjects with complete information were divided into two groups according to the maternal age: the younger group of pregnant women aged 35–39 years and the elder group of women aged 40-44 years. Only eight cases were ≥ 45 years of age and they were included in the elder group. The younger group was composed of 1,727 cases (1,727 / 1,965: 87.9%), while the elder one had 238 cases (238 / 1,965: 12.1%).

Outcome definition

Data of maternal characteristics, obstetrical complications, and perinatal outcomes was recorded in this study, including gestational age, assisted reproduction technologies (ART), mode of delivery, amount of puerperal bleeding, postpartum hemorrhage, birth weight, neonatal gender, Apgar scores at one and five minutes, admission to the neonatal intensive care unit (NICU), and fetal death. Gestational hypertension was defined as blood pressure equal to or more than 140/90, without the features of chronic hypertension or significant proteinuria. Patients with gestational hypertension as well as significant proteinuria (more than 300 mg per 24-hour urine collection) were diagnosed as preeclamptic. GDM was confirmed when 75 g oral glucose tolerance tests (OGTT) were abnormal, characterized by fasting blood glucose levels above 5.1 mmol/L, one-hour postprandial blood sugar levels above 10.0 mmol/L, and two-hour postprandial blood sugar levels above 8.5 mmol/L. Postpartum hemorrhage was defined as uterine bleeding ≥ 500 ml within 24 hours. Polyhydramnios was defined as the amniotic fluid volume > 2,000 ml, amniotic fluid index > 20 cm, or amniotic fluid volume > seven cm on ultrasonography during pregnancy. Preterm birth was defined as birth at a gestational age of < 37 weeks, and very preterm birth was defined as birth at a gestational age of < 32 weeks. Low birth weight and very low birth weight was defined as birth weight < 2,500 and < 1,500 grams, respectively.

Table 2. — *Delivery outcomes of the two groups.*

Variable	Group 1: 35-39 y	Group 2: ≥ 40 y	*p* value
N	1727	238	
Gestational age, weeks [a]	38.0 ± 2.3	37.7 ± 2.2	0.06
< 37, n (%)	169 (9.8)	28 (10.6)	0.34
< 32, n (%)	44 (2.5)	7 (3.0)	0.72
Delivery mode, n (%)			
Vaginal delivery	560 (32.4)	38 (15.9)	0.001
- Spontaneous	520 (30.1)	36 (15.1)	0.001
- Forceps delivery	40 (2.3)	2 (0.8)	0.14
Cesarean section	1167 (67.6)	200 (84.0)	0.001
Indication for cesarean delivery, n (%)			
Abnormal fetal position	101 (8.7)	14 (7.0)	0.98
Dystocia	10 (0.9)	2 (1.0)	0.63
Fetal distress	43 (3.7)	3 (1.5)	0.24
Intrauterine infection	5 (0.5)	3 (1.5)	0.027
IVF	38 (3.2)	13 (6.5)	0.003
Multifetal gestation	61 (5.2)	9 (4.5)	0.85
Macrosomia	48 (4.1)	3 (1.5)	0.17
Nonreassuring fetal heart rate	5 (0.4)	0 (0.0)	0.41
Oligohydramnios	31 (2.7)	6 (3.0)	0.44
Pelvic stenosis or deformity	54 (4.6)	6 (3.0)	0.61
Placental abruption	6 (0.5)	1 (0.5)	0.86
Placenta previa	51 (4.3)	9 (4.5)	0.49
Preeclampsia	29 (2.5)	5 (2.5)	0.64
Pregnancy complications	14 (1.2)	3 (1.5)	0.48
Previous cesarean delivery	31 (2.7)	6 (3.0)	0.44
Scarred uterus	22 (1.9)	2 (1.0)	0.57
Stillbirth	23 (1.9)	4 (2.0)	0.66
Maternal request	357 (30.6)	82 (41.0)	0.00
Other	238 (20.4)	29 (14.5)	0.61
Placental abruption	6 (0.3)	2 (0.8)	0.26
Preeclampsia	32 (1.9)	5 (2.1)	0.79
Fetal distress	193 (11.2)	18 (7.6)	0.09
Postpartum hemorrhage, n (%)	311 (18.0)	54 (22.7)	0.08
Postpartum hemorrhage, ml [a]	362.5 ± 215.2	381.1 ± 185.5	0.21
Vaginal delivery, ml [a]	270.5 ± 139.5	276.8 ± 145.3	0.74
Cesarean section, ml [a]	386.0 ± 234.3	400.9 ± 185.9	0.96
Prolonged hospitalization [b]	284 (16.4)	30 (15.0)	0.13

[a] Data are presented as mean ± SD. [b] Hospitalization for more than 4 or 7 days after vaginal or cesarean delivery, respectively.

Statistical analysis

Statistical analysis, applying SPSS package, was performed to compare outcomes using the Chi-square test, Fisher exact two-tailed test, and Spearman bivariate correlation. The confidence interval (CI) at 95% was calculated. Level of significance was set at *p* value < 0.05, indicating a difference exists.

Results

In the study, 1,965 women were investigated, of which 1,727 (87.9%) women were aged 35-39 years, and 238 women (12.1%) were aged ≥ 40 years. The demographic and obstetric characteristics for each group are given in Table 1. The average age of the younger group was 36.4 ± 1.3 (mean ± SD) years, while the value was 41.2 ± 1.5 years

Table 3. — *Neonatal outcomes for the two groups.*

Variable	Group 1: 35-39 y	Group 2: ≥ 40 y	p value
N	1727	238	
Birth weight, grams [a]	3292.2 ± 618.6	3222.5 ± 619.5	0.13
> 4000, n (%)	138 (8.0)	12 (5.0)	0.21
< 2500, n (%)	127 (7.4)	21 (8.8)	0.97
< 1500, n (%)	43 (2.5)	7 (2.9)	0.99
Small for gestational age: 10th percentile, n (%)	169 (9.8)	21 (8.8)	0.64
1-min. Apgar score <7, n (%)	3 (0.2)	1 (0.4)	0.22
5-min. Apgar score <7, n (%)	0 (0.0)	0 (0.0)	/
Male sex, n (%)	898 (50.0)	118 (47.4)	0.48
Twin	68 (3.9)	11 (4.6)	0.61
Hospitalization, d	5.2 ± 2.9	5.0 ± 2.2	0.71
Neonatal intensive care unit admission, n (%)	139 (8.0)	18 (7.5)	0.80
Neonatal malformation or anomalies, n (%)	44 (2.5)	5 (2.1)	0.68
Neonatal death	0 (0.0)	0 (0.0)	/

[a] Data are presented as mean ± SD.

for the older group. The proportion of primipara was 72.4% in the younger group and 62.6% in the elder group. The elder group was more likely characterized by a significantly higher rates of in vitro fertilization (IVF, $p < 0.01$), GDM ($p < 0.05$), and hypertension ($p < 0.05$).

Delivery outcomes of the two groups are summarized in Table 2. No significant difference was discovered between the two groups with regards to fetal distress, postpartum hemorrhage, and prolonged hospitalization, while the women of elder group were significantly associated with higher rate for cesarean section (CS, $p < 0.001$), reaching 84.0%. Accordingly, the rates of vaginal delivery in this group, particularly in case of spontaneous vaginal delivery, were significantly lower ($p < 0.001$) compared to the group aged of 35- 39 years. The main indications for cesarean section were intrauterine infection, IVF, and maternal request, with the ratio of 1.5% *vs.* 0.5% ($p < 0.05$), 6.5% *vs.* 3.2% ($p < 0.01$), and 41.0% *vs.* 30.6% ($p < 0.001$) for the two groups, respectively.

Neonatal outcomes are presented in Table 3. The results did not show a great difference for the two groups. The index of birth weight, gender, Apgar score, and the rate of admission to NICU was at similar level. In addition, no neonatal deaths were recorded in either group.

Discussion

In China, postponement of childbearing has become more and more prevalent, particularly in large modern cities, such as Beijing. The data of 1% population-sampling survey in Beijing at early 2005 showed, the average childbearing age of women had reached 28.8 years [19], similar to the average level for urban China women in 2011 [8].

Despite there is no more current data, it is reasonable to infer that the value has increased in recent years, which could be supported indirectly by the high proportion (71.2%) of the primiparas in the present study. Chinese urban women, especially for the first-time parents, usually pursue high-quality maternity care in spite of a higher fee. The present research institution is a high-level special hospital in Beijing providing professional women-children healthcare, with the registered patients of relatively advanced age and high income level. This could explain why the rate of primipara at advanced age in the present study was higher than other countries, with a rate of 22-48% [20-22].

Previous studies have shown that compared to younger women, AMA women possess an increasing risk of hypertension and GDM. The present study corroborates these findings and further revealed that the risk of developing these morbidities increases with the age, which is also consistent with the previous studies [21, 23]. In this research, the rates of gestational hypertension (26.1%) and diabetes (11.8%) in ≥ 40-year-old group were obviously higher than the younger group (15.7% and 7.1%, respectively). Nevertheless, the rates exceeded other domestic studies on advanced maternal age pregnancy. For example, Zhang *et al.* [24] found the rates of 14.7% for hypertension and 9.6% for diabetes among women aged more than 35 years in Xi'an city, Shanxi province, and Zhu *et al.* [25] found the corresponding rates of 11.9% and 7.0% respectively in Beijing in 2005. Meanwhile, the incidences rate for hypertension and GDM in the ≥ 40-year-old group were similar to the high-income developing countries such as United Arab Emirates [26], but higher than the developed countries such as Australia [27], Israel [21], and USA [28]. This might relate to the more advanced healthcare conditions and the circumstances as the AMA women are usually associated with higher socio-economic status and healthier life style in the developed countries.

Cesarean section (CS) rates of 84.0% in the elder group and 67.6% in the younger group were reported in the present study. Of the contributing factors for cesarean section, maternal request was the major one resulting in the differences. The proportions (41.0% and 30.6% for the two groups, respectively) of maternal request CS in the present study were apparently higher than the values for the AMA women in other countries, ranging from 0% to 20% [20, 21, 29]. This reflected Chinese women's unusual preference for CS. In China, shifting from an estimated low rate of 3.4% in 1988 to the high percentage of 39% in 2008, overuse of CS has been a public health concern [30]. Because of pain suffering, insecurity about natural delivery, timing consuming, and lack for pregnancy knowledge, Chinese pregnancy women are more likely to request a cesarean birth. Furthermore, the AMA women's worries about birth safety for fetus increase with the age, therefore resulting the strengthened desire for the cesarean birth [30-32]. Meanwhile, the present study

found that the known contributing factors for cesarean rates, such as dystocia, abnormal fetal position, oligohydramnios, placental abruption, placenta previa, and preeclampsia, have no significant difference between the two groups, except for the higher rate of macrosomia in the younger group and more common IVF in the elder group. It appears that maternal request contributes the most for the higher rates of CS in the AMA women than other contributing factors.

The present authors have also found that the rates of some specific obstetric complications, such as placental abruption, preeclampsia, and postpartum hemorrhage, were relatively higher in the ≥ 40-year-old group, but with no significant difference in two groups. Similar conclusion was described by previous research, that the rates of these obstetric complications did not increase with age in the AMA women less than 45 years old, while the risks dramatically increased when the age ≥ 45 years [21]. By contrast, nationwide data from the USA showed the risk of preeclampsia is unrelated to the age before 35 years but increases thereafter by 30% per year [33]. Furthermore, data from a large cohort study indicated the risk for preeclampsia increases by 4% for every year over the age of 32 years old [34]. The differences can be explained by the limited sample size in the present study, especially for the elder group, resulting in the disability to find the potential risk.

Adverse neonatal outcomes such as preterm, very preterm birth, low birth-weight, and stillbirths have slightly risen for women ≥ 40-years-old in this study, compared to the women aged 35-39 years. These results are consistent with the conclusions reported in other studies. For pre-term births, the rate (10.6%) in the present study of births < 37 weeks gestation were higher than that reported by Kenny *et al.* [20] and Schimmel *et al.* [23], while similar to rates revealed by Ludford *et al.* [29], Yogev *et al.* [21], and Favilli *et al.* [22], ranging from 10.4% to 15.4%. Yogev *et al.* has also reported the rates of pre-term birth at less than 32 weeks gestation (2.0%) and low birth-weight (12.7%) for the AMA women [21], which are slightly different with the present study of 3.0% and 8.8%, respectively. Regarding macrosomia, the present authors defined the fetal weights over 4.0 kg at birth in this study, compared to other research to consider macrosomia as ≥ 4.5 kg [20, 35]. The overall proportion of macrosomia in the present study was very low, with a percentage of 5.0% in the elder group and the higher rate of 8.0% in the younger group. It is worthwhile to note that there were no maternal or neonatal deaths in this study. The reason for the relatively benign outcomes can be explained by good prenatal care and consistent monitoring provided by the study institute.

There were, however, several limitations in this study. Firstly, the study was performed in a single hospital. The limitation of the sample size and the possibility of selection bias cannot be excluded. Secondly, the dataset did not include socio-demographic details such as income, educational level, lifestyle, and body mass index, and these variables may have an impact on the outcomes for the women giving birth at very AMA. Thirdly, the authors excluded pregnancies that ended before viability (< 24 weeks of gestation) because they aimed to evaluate the pregnancy outcome. They speculate that early and late abortions might be more prevalent in the ≥ 40-year-old group, who are more likely afflicted by pregnancy complications.

Conclusion

The present study firstly focused on the group of Chinese urban pregnant women aged greater than 40 years. The authors demonstrate that the AMA women greater than 40-years-old are more likely to have chronic maternal diseases (such as chronic hypertension, diabetes mellitus, hysteromyoma), and the rate of cesarean delivery also increased substantially due to maternal request. Despite the present data showed an increase risk of pregnancy complications for the women giving birth at ≥ 40-years-old, most of them still carried a favorable pregnancy and neonatal outcome, similar to the younger women. Further studies with larger cohorts and greater statistical power are desirable, which may accurately clarify the risk of adverse maternal-fetal outcomes in Chinese women at more elderly age.

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Corresponding Author:
XIN WANG, M.D.
Department of Obstetrics
Beijing Obstetrics and Gynecology Hospital
Capital Medical University
251 Yaojia Yuan Road, Chaoyang District
Beijing 100026 (China)
e-mail: clbfish@sina.com