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A first look at the effects of long inter-pregnancy interval and advanced maternal age on perinatal outcomes: A retrospective cohort study

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Abstract

Background: After China's One-child Policy was replaced with the Two-child Policy in 2013, the rate of second pregnancies with a longer inter-pregnancy interval (IPI) has suddenly increased in that country; however, the effect of long IPIs (≥49 months) on perinatal outcomes remains unreported.

Methods: This was a retrospective cohort study in China from July 2015 through June 2016. We used univariate and multivariate logistic regression models to test the associations among IPI, maternal age, and perinatal outcome (preterm delivery, term low birthweight, and small-for-gestational age). We included baseline factors and variables with biological plausibility as confounders.

Results: Our analytic sample included 3309 second pregnancies. The mean IPI was 75.36 months. Compared with second pregnancies with a short IPI of 7-24 months, those with long IPIs had higher adjusted odds ratios (ORs) of preterm delivery (1.70-2.00 [95% CI 1.20-3.33]) and term low birthweight (2.16-2.68 [1.10-6.17]), but not small-for-gestational age. The mean maternal age at current delivery was 32.0 years. Compared with the reference group (25-29 years), second pregnancies for the oldest maternal age group (≥35 years) showed no statistically significant increased ORs for adverse perinatal outcomes.

Conclusion: Long IPI is a significant contributor to preterm delivery and term low birthweight. Health care providers need to pay close attention to preterm delivery prevention and fetal growth during prenatal care for second pregnancies where the mothers have long IPIs.

KEYWORDS

Birth interval, China, maternal age, preterm delivery, small-for-gestational age, term low birthweight

1 | INTRODUCTION

Both short and long inter-pregnancy intervals (IPIs) have been reported to be associated with an increased risk of several adverse perinatal outcomes such as term low birthweight, small-for-gestational age, and preterm birth.[1–10] An IPI of 6-24 months was found to have a lower rate of adverse perinatal outcomes than either shorter or longer IPIs.[1] Several studies have compared short IPI (≤6 months) with typical IPI (12-23 months) and have found that births following short IPI had higher rates of adverse perinatal outcomes.[1,3,6,8,10] However, studies of the impact of long IPIs have been sparse.

Only a few articles included subgroups of IPIs longer than 60 months.[8-10] Given the limited research in this area, the effect of long IPI on perinatal outcomes has not been sufficiently studied. The recent change in China from a One-child to a Two-child Policy provides an ideal situation to study the effect of long IPIs on perinatal outcomes.

The One-child Policy was one of the first national policies to be promulgated in China after the Constitution of the People's Republic of China was adopted by the National People's Congress in December 1982.[11] According to the policy, each family was permitted to have only one child. The policy was meant to limit the population growth rate. The One-child Policy was changed to the Two-child Policy in November 2013. Under the new policy, couples in which either partner was from a single-child family were permitted to have two children.[12] In the latest update, known as the Universal Two-child Policy (November 2015), all couples are permitted to have two children.[13]

After the last policy change, many older couples of reproductive age who already had a child began planning to have a second one. The Chinese government estimates that 60% of the women who benefitted from the change to the Universal Two-child Policy are older than 35 years, and as many as half of them are over 40 years old.[13] Previous research has shown that high maternal age is a risk factor for adverse pregnancy outcomes such as fetal death, preterm delivery, term low birthweight, and small-for-gestational age.[1,14–16] Both the government and research scientists have stated that adverse perinatal outcomes will likely increase with advancing maternal ages,[1,13,17] but the specific effect of long IPI has not been determined.

Studies have shown that women sometimes request delivery by elective cesarean section without a valid medical indication because of the fear of episiotomy, long and painful labor, or pelvic floor trauma associated with vaginal birth.[18] This phenomenon seems to be particularly striking in China, where the prevalence of cesarean sections (with an average rate of 46.2% in the past 10 years) is significantly higher than the World Health Organization (WHO) recommended level.[19] Cesarean section has been linked to adverse perinatal outcomes,[20] and preexisting medical conditions have been shown to be exacerbated by both previous cesarean section and advanced maternal age.[21,22] Thus, advanced maternal age and previous cesarean section are both risk factors for adverse perinatal outcomes during second pregnancies in China.[17]

In the first 2 years after the change to the Two-child Policy in China, there have been many pregnancies with longer IPI and advanced age, but few with short IPI. In this paper, we examine the effects of long IPI and advanced age at second delivery on adverse perinatal outcomes, with emphasis on rates of preterm birth, term low birthweight, and small-for-gestational age. The study population comprised women who gave birth to their second singleton child at any of the three Xiangya hospitals of Central South University in Hunan province, China between July 2015 and June 2016.

2 | METHODS

This was a retrospective cohort study limited to singleton births for the second pregnancy, with a recorded IPI of over 6 months. The study included live births at ≥24 weeks' gestation delivered between July 1, 2015 and June 30, 2016 at Xiangya Hospital, the Second Xiangya Hospital, and the Third Xiangya Hospital of Central South University. Maternal and neonatal information was collected from electronic medical records at each hospital. Discharge diagnoses for deliveries were coded using the International Classification of Diseases, 10th Revision (ICD-10), Clinical Modification. Women without a known previous delivery date and women whose previous delivery date was not documented were excluded.

The data set was provided by the Department of Hospital Administration of Central South University. The study received approval by the Institutional Review Board of the Third Xiangya Hospital, Central South University.

The main variables of interest were IPI and maternal age at current delivery. For this study, IPI was defined as the time between a woman's previous delivery and the first day of the last menstrual period for the index pregnancy, which was calculated from electronic medical records. IPI was categorized by 24-month intervals (7-24, 25-48, 49-72, 73-96, and ≥97 months). We defined long IPI as two pregnancies at an interval of longer than 49 months. The births with IPI ≤6 months (N=25) were excluded as there were insufficient numbers of cases for detailed analysis. Maternal age categories were <25, 25-29, 30-34, and ≥35 years.

The adverse perinatal outcomes for this study were preterm delivery, term low birthweight, and small-for-gestational age. Gestational age was based on the last menstrual period and confirmed by ultrasound examination. Preterm delivery was defined as a delivery at <37 completed weeks of gestation. Term low birthweight was defined as birthweight <2500 g for full-term pregnancies. Small-for-gestational age was defined as the baby weighing less than the 10th percentile for a given gestational age.

Covariates were the maternal characteristics (marital status, educational level, BMI, number of prenatal care visits, current cesarean section) with significant differences in univariate comparisons, and variables with biological plausibility (previous cesarean section, and preexisting medical conditions that were considered to be the main risk factors of adverse perinatal outcomes after the change to the Two-child Policy).[17] The number of prenatal care visits ≥4 according to the doctor's suggestion was thought to be a normal prenatal care. Preexisting medical conditions included all diseases diagnosed by obstetricians and classified as endocrinal

(pregestational diabetes, hypothyroidism), circulatory/urological/respiratory (chronic hypertension, congenital heart disease, rheumatic heart disease, arrhythmia, nephritis, pulmonary tuberculosis, pneumonia, asthma, systemic lupus erythematosus), gynecological (pelvic inflammation, myoma of uterus, vaginitis, intrauterine adhesions, postintrauterine operation, ovarian cyst), hematological (anemia, thrombocytopenia), and digestive (hepatitis, intestinal neoplasm, appendicitis).

Frequency and mean (standard deviation) of participant demographics and characteristics for IPI and maternal age were described and compared, using one-way ANOVA, χ^2, or appropriate Fisher exact test for categorical variables. Probability values of <.05 were considered statistically significant. Uni- and multivariate logistic regression analysis were used to assess associations between IPI and maternal age categories and perinatal outcomes with an interval of 7-24 months as the reference category for IPI and 25-29 years as the reference category for maternal age. The influence of covariates was analyzed. First, prenatal care, maternal education level, previous cesarean section, current cesarean section, preexisting medical conditions, and body mass index (BMI) at admission were added as covariates. Then IPI and maternal age were added as each other's covariates to evaluate the interaction. Both crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Statistical analyses were performed using SPSS 21.0 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

The total number of live births in the three Xiangya hospitals during the study period was 10 674. We excluded first pregnancies (N=7148), multiple gestations (N=27), births ≤6 months IPI (N=25), previous miscarriage (N=147), and records without a clear previous delivery date (N=18). Analyses were then limited to 3309 second pregnancies. For the 3309 second pregnancies, the mean IPI was 75.36 months (6.28 years). Among this group, the proportions of the various IPI categories were as follows: from 7 to 24 months, 9.1%; 25-48 months, 26.1%; 49-72 months, 23.9%, 73-96 months, 19.1%; and ≥97 months, 21.8%. The mean maternal age at current delivery was 32.0 years. The proportions of maternal age categories were: <25 years, 2.1%; 25-29 years, 26.9%; 30-34 years, 48.9%; and ≥35 years 22.0%.

TABLE 1 Maternal characteristics of second pregnancies by inter-pregnancy interval, Hunan, China, 2015-2016

		Inter-pregnancy interval, months *n* (%)					
	Total	7-24	25-48	49-72	73-96	≥97	
Characteristics	N=3309	N=300	N=863	N=791	N=632	N=723	*P*
Maternal age at delivery, y							<.01
<25	72 (2.1)	30 (10.0)	30 (3.5)	11 (1.4)	0	0	
25-29	891 (26.9)	186 (62.0)	407 (47.2)	178 (22.5)	108 (17.1)	12 (1.7)	
30-34	1618 (48.9)	84 (28.0)	402 (46.6)	484 (61.2)	402 (63.6)	246 (34.0)	
≥35	729 (22.0)	0	24 (2.8)	118 (14.9)	122 (19.3)	465 (64.3)	
Married	3299 (99.7)	300 (100)	856 (99.2)	789 (99.8)	631 (99.8)	723 (100)	.06
≤High school education	261 (7.9)	23 (7.7)	75 (8.7)	41 (5.2)	54 (8.5)	68 (9.4)	.12
Number of prenatal care visits ≥4	2917 (88.2)	270 (90.0)	737 (85.4)	720 (91.0)	566 (89.6)	624 (86.3)	<.01
Previous cesarean section	1555 (47.0)	78 (26.0)	408 (47.3)	352 (44.5)	331 (52.4)	386 (53.4)	<.01
Current cesarean section	1593 (48.1)	78 (26.0)	365 (42.3)	365 (46.1)	350 (55.4)	435 (60.2)	<.01
Preexisting medical conditions*	927 (28.0)	36 (12.0)	233 (27.0)	254 (32.1)	158 (25.0)	246 (34.0)	<.01
Endocrine disease	440 (13.3)	18 (6.0)	114 (13.2)	96 (12.1)	110 (17.4)	102 (14.1)	<.01
Circulatory, urological, respiratory disease	190 (5.7)	0	41 (4.8)	47 (5.9)	48 (7.6)	54 (7.5)	<.01
Gynecological disease	207 (6.3)	6 (2.0)	42 (4.9)	81 (10.2)	12 (1.9)	66 (9.1)	<.01
Hematological disease	101 (3.1)	18 (6.0)	30 (3.5)	17 (2.1)	6 (0.9)	30 (4.1)	<.01
Digestive disease	119 (3.6)	0	36 (4.2)	35 (4.4)	24 (3.8)	24 (3.3)	<.01
BMI at admission for delivery, mean [SD]	27.11 [2.90]	26.20 [3.00]	26.60 [2.76]	26.90 [2.90]	27.62 [2.74]	27.89 [2.89]	<.01

*Percentages may not add to totals as some women had more than one type of preexisting disease.

IPI and maternal age were associated with each other, and the prevalence of long IPIs showed a trend of increasing with maternal age (Table 1). The rate of previous cesarean section, current cesarean section, and BMI was higher with increasing IPI and maternal age. The rate of preexisting medical conditions was higher with increasing IPI except for the subgroup of 73-96 months. The percentage of women with ≥4 prenatal visits generally decreased with increasing IPI, except for the subgroup of 25-48 months. When examined by the maternal age group, the rate of preexisting medical conditions was higher and the rate of normal prenatal care was lower for women aged <25 years and ≥35 years (Table 2). Marital status and education level did not differ significantly by length of IPI, or by maternal age (Tables 1 and 2).

Overall rates of adverse perinatal outcomes for these second pregnancies were 9.6% for preterm delivery, 4.7% for term low birthweight, and 8.6% for small-for-gestational age. The rate of preterm delivery, term low birthweight, and small-for-gestational age for the group with an IPI of 7-24 months was lower than that for longer IPIs (see Figure 1). The rate of term low birthweight and small-for-gestational age with an IPI of 49-72 months was the highest and the rate of preterm delivery with an IPI of 73-96 months was the highest.

Logistic regression analysis was performed to assess the influence of IPI on perinatal outcomes (Table 3). Compared with an IPI of 7-24 months (the reference group), long IPIs had higher adjusted ORs for preterm delivery: 2.00 (1.20-3.33) for 73-96 months, and 1.70 (1.43-2.03) for ≥97 months. Patterns were similar for term low birthweight, with adjusted ORs of 2.68 (1.16-6.17) for 49-72 months, 2.26 (1.18-4.32) for 73-96 months, and 2.16 (1.10-4.21) for ≥97 months. In contrast, there were no significant differences by small-for-gestational age (Table 3).

The occurrence of adverse perinatal outcomes across maternal age categories is shown in Figure 2 as a U-shaped curve. The lowest rate of preterm delivery, term low birthweight, and small-for-gestational age was for the maternal age group of 30-34 years. Compared with the maternal age group of 25-29 years, no statistically significant increase in ORs was shown for adverse perinatal outcomes in the higher maternal-age category in unadjusted logistic regression models. Meanwhile, the maternal age group 30-34 years

TABLE 2 Maternal characteristics of second pregnancies by maternal age at second delivery in Hunan, China, 2015-2016

	Maternal age at delivery, y *n* (%)				
	<25	25-29	30-34	≥35	
	N=71	N=891	N=1618	N=729	*P*
Inter-pregnancy interval, months					<.01
7-24	30 (42.3)	186 (20.9)	84 (5.2)	0	
25-48	30 (42.3)	407 (45.7)	402 (24.8)	24 (3.3)	
49-72	11 (15.5)	178 (20.0)	484 (29.9)	118 (16.2)	
73-96	0	108 (11.8)	402 (24.8)	122 (16.7)	
≥97	0	12 (1.3)	258 (15.6)	465 (63.8)	
Married	71 (100)	887 (99.6)	1613 (99.7)	728 (99.9)	.68
≤High school education	5 (7.0)	68 (7.6)	126 (7.8)	62 (8.5)	.98
Number of prenatal care visits ≥4	53 (74.6)	789 (88.6)	1439 (88.9)	636 (87.2)	<.01
Previous cesarean section	24 (33.8)	369 (41.4)	776 (48.0)	386 (52.9)	<.01
Current cesarean section	23 (32.4)	357 (40.1)	754 (46.6)	459 (63.0)	<.01
Preexisting medical conditions*	29 (40.8)	245 (27.5)	437 (27.0)	216 (29.6)	.05
Endocrine disease	24 (33.8)	120 (13.5)	204 (12.6)	92 (12.6)	<.01
Circulatory, urological, respiratory, disease	6 (8.5)	47 (5.3)	89 (5.5)	48 (6.6)	.48
Gynecological disease	5 (7.0)	36 (4.0)	114 (7.0)	52 (7.1)	.01
Hematological disease	6 (8.5)	30 (3.4)	41 (2.5)	24 (3.3)	.03
Digestive disease	0	36 (4.0)	47 (2.9)	36 (4.9)	.02
BMI at admission, mean [SD]	26.94 [5.74]	26.43 [2.91]	27.06 [2.51]	28.09 [3.04]	<.01

*Percentages may not add to totals as some women had more than one type of preexisting disease.

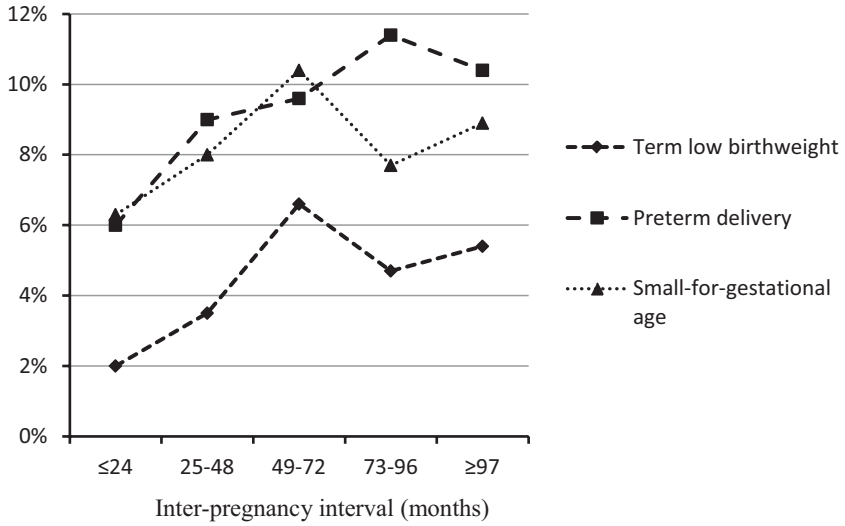

FIGURE 1 Adverse perinatal outcomes by inter-pregnancy interval, Hunan, China, 2015-2016

showed decreased ORs. There were no changes after adjusting for prenatal care, maternal education level, previous cesarean section, current cesarean section, preexisting medical conditions, BMI at admission, and IPI. Low maternal age (<25 years) showed an increased risk of preterm delivery and small-for-gestational age compared with 25-29 years; but there was no significant difference for term low birthweight (Table 4).

4 | DISCUSSION

In this study, we examined the period after China's One-child Policy was updated to a Two-child Policy. We assessed the association of long IPI and advanced maternal age on adverse perinatal outcomes and found that longer IPI was a significant risk factor for preterm delivery and term low birthweight, independent of maternal age, previous cesarean section, preexisting medical conditions, and BMI at admission. The association between long IPIs and adverse perinatal outcomes has been supported by other research.[3,8,10,23] In this paper, we have shown that long IPI (49-72, 73-96, and ≥97 months) is linked to an increased risk of preterm delivery and term low birthweight with adjusted ORs higher than in a previous study.[8] No increased risk was observed between long IPI and small-for-gestational age, which is at variance with two other studies.[3,10] The small-for-gestational age rate is similar to that found in de Weger's study, which showed no relationship between IPI and small-for-gestational age.[1]

As in previous studies[17,20] previous cesarean section and preexisting medical conditions were important risk factors for adverse perinatal outcomes. A recent WHO study of 24 Asian countries found that China had the highest cesarean rate (46.2%) among the countries studied. Our study confirms the very high cesarean rate (47.0%) among first births in China. The total rate of preexisting medical conditions was 28.0%, which showed an increase with longer IPI in this study. The preexisting medical conditions rate in this study (28.8%) was higher than Timofeev's result (0.1-10.3%).[21] This might be because we have included a large number of possible co-morbidities, whereas other studies included only pregestational diabetes and chronic hypertension.[2,3,8,9]

The rate of adverse perinatal outcomes (preterm delivery, term low birthweight, and small-for-gestational age) decreased with maternal age from <25 years to 30-34 years and then increased in the >35 years group, which was similar to de Weger's findings[1] but in contrast to the results of another study.[9] We did not find that advanced maternal age was a high-risk factor for adverse perinatal outcomes in this study. The risk of preterm delivery even decreased in the 30-34 year maternal age group (adjusted OR 0.70 [95% CI 0.55-0.90]). This might be the result of a self-selection process by healthier women who were taking advantage of the new Two-child Policy. Previous studies have shown that the level of ovarian aging influenced in vitro fertilization outcomes more than did the level of chronologic aging.[24] Therefore, the time interval from intention to conception could be considered among pregnancy risk factors.

We found that 22% of the women with second births were aged 35 and older. This information was in contrast to an analysis from the Chinese government indicating that the percentage of pregnancies to women 35 and older might be 60% for several years after the change to the Two-child Policy.[13]

Strengths of our study include large sample sizes for long IPIs with three subcategories (49-72, 73-96, and ≥97 months) while controlling for a large number of covariates. Limitations included the lack of information on alcohol or substance-use. However, studies have shown that usage rates for these substances among Chinese women are very low.[25] Data were also not available on the details of the first pregnancy, type of contraception used, or in vitro fertilization.[4,6-8] Also, data

TABLE 3 Crude and adjusted odds ratios for adverse perinatal outcomes by IPI, Hunan, China, 2015-2016

Variable	Percentage	Crude OR (95% CI)	Model 1 Adj OR (95% CI)	Model 2 Adj OR (95% CI)
Preterm delivery				
7-24	6.0	Reference	Reference	Reference
25-48	9.0	1.56 (0.94-2.58)	1.34 (0.81-2.24)	1.37 (0.82-2.30)
49-72	9.6	1.67 (1.01-2.73)	1.51 (0.91-2.50)	1.58 (0.95-2.64)
73-96	11.4	2.01 (1.23-3.29)	1.91 (1.16-3.15)	2.00 (1.20-3.33)
≥97	10.4	1.81 (1.11-2.96)	1.72 (1.44-2.05)	1.70 (1.43-2.03)
Term low birthweight				
7-24	2.0	Reference	Reference	Reference
25-48	3.5	1.77 (0.76-4.12)	1.74 (0.75-4.04)	1.66 (0.71-3.87)
49-72	6.6	3.45 (1.51-7.86)	2.94 (1.29-6.73)	2.68 (1.16-6.17)
73-96	4.7	2.44 (1.07-5.59)	2.06 (0.89-4.73)	2.26 (1.18-4.32)
≥97	5.4	2.79 (1.23-6.35)	2.15 (0.94-4.91)	2.16 (1.10-4.21)
Small-for-gestational age				
7-24	6.3	Reference	Reference	Reference
25-48	8.0	2.10 (0.49-8.94)	1.51 (0.35-6.55)	1.89 (0.43-8.22)
49-72	10.4	2.84 (0.92-8.81)	2.48 (0.73-8.43)	3.09 (0.99-9.56)
73-96	7.7	1.43 (0.34-6.07)	0.92 (0.20-4.21)	1.42 (0.32-6.34)
≥97	8.9	2.16 (0.51-9.14)	1.43 (0.38-5.44)	1.59 (0.39-6.57)

Model 1: Adjusted for number of prenatal visits, maternal education level, previous cesarean section, current cesarean section, preexisting medical conditions, and BMI at admission.

Model 2: Adjusted for number of prenatal visits, maternal education level, previous cesarean section, current cesarean section, preexisting medical conditions, BMI at admission, and advanced maternal age.

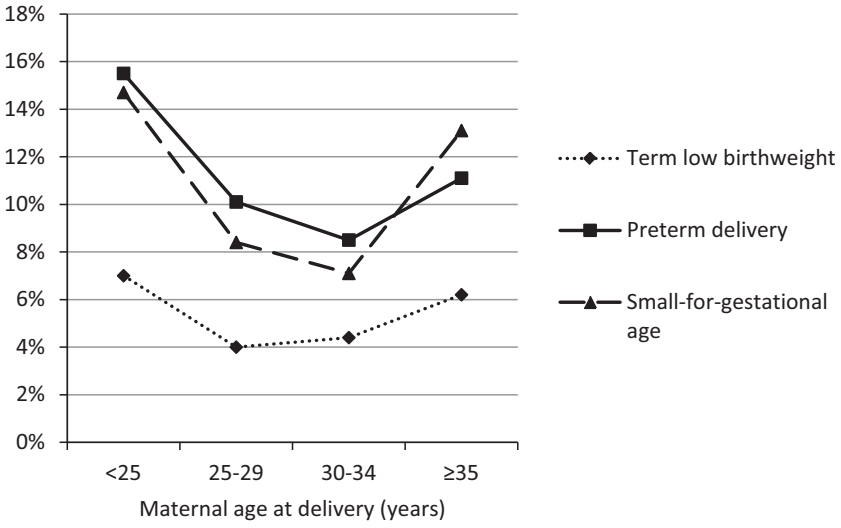

FIGURE 2 Adverse perinatal outcomes by maternal age at second delivery, Hunan, China, 2015-2016

were collected from three provincial hospitals, thus results may not be generalizable to China as a whole. Although we excluded data for women with a previous miscarriage, previous miscarriages might have been underreported, leading to possible bias. Finally, sample data were collected just 2 years after the One-child Policy was updated; future studies should observe longer-term effects of the updated policy.

5 | CONCLUSION

This study demonstrates that long IPI (≥49 months) is a risk factor for preterm delivery and term low birthweight. Our outcomes can inform health care policy and encourage Chinese prenatal care providers to pay more attention to preterm

TABLE 4 Crude and adjusted odds ratios for adverse perinatal outcomes by maternal age, Hunan, China, 2015-2016

Variable	Percentage	Crude OR (95% CI)	Model 1 Adj OR(95% CI)	Model 2 Adj OR (95% CI)
Preterm delivery				
<25	15.5	1.62 (0.99-2.70)	1.59 (0.97-2.61)	1.73 (1.05-2.84)
25-29	10.1	Reference	Reference	Reference
30-34	8.5	0.83 (0.65-1.05)	0.81 (0.64-1.03)	0.70 (0.55-0.90)
≥35	11.1	1.11 (0.87-1.42)	1.17 (0.91-1.50)	0.79 (0.59-1.05)
Term low birthweight				
<25	7.0	1.80 (0.87-3.71)	1.76 (0.90-3.44)	1.94 (0.99-3.80)
25-29	4.0	Reference	Reference	Reference
30-34	4.4	1.09 (0.76-1.56)	0.97 (0.69-1.36)	0.82 (0.58-1.16)
≥35	6.2	1.56 (1.08-2.25)	1.39 (0.98-1.98)	0.88 (0.59-1.32)
Small-for-gestational age				
<25	14.7	3.74 (1.54-9.08)	3.57 (1.46-8.73)	3.28 (1.33-8.10)
25-29	8.4	Reference	Reference	Reference
30-34	7.1	0.74 (0.41-1.34)	0.72 (0.40-1.30)	0.79 (0.43-1.45)
≥35	12.8	1.59 (0.89-2.83)	1.16 (0.64-2.08)	1.50 (0.78-2.92)

Model 1: Adjusted for number of prenatal visits, maternal education level, previous cesarean section, current cesarean section, preexisting medical conditions, and BMI at admission.

Model 2: Adjusted for number of prenatal visits, maternal education level, previous cesarean section, current cesarean section, preexisting medical conditions, BMI at admission, and inter-pregnancy interval.

delivery prevention and to potential fetal growth problems when they are working with women experiencing a second pregnancy and a longer IPI. In addition, Chinese policy makers should plan accordingly for the care of second babies with adverse perinatal outcomes. The government should train health care providers on how to deal with the specific issues of second pregnancies and should provide economic support for professional second pregnancy care, especially for those cases where the pregnancy involves a longer IPI.

REFERENCES

1. de Weger FJ, Hukkelhoven CW, Serroyen J, Te VE, Smits LJ. Advanced maternal age, short interpregnancy interval, and perinatal outcome. *Am J Obstet Gynecol*, 2011;204:421.e1-421.e9.
2. Chen I, Jhangri GS, Lacasse M, Kumar M, Chandra S. Relationship between interpregnancy interval and adverse perinatal and neonatal outcomes in Northern Alberta. *J Obstet Gynaecol Can*. 2015;37:598-605.
3. Conde-Agudelo A, Belizan JM, Norton MH, Rosas-Bermudez A. Effect of the interpregnancy interval on perinatal outcomes in Latin America. *Obstet Gynecol*. 2005;106:359-366.
4. DeFranco EA, Stamilio DM, Boslaugh SE, Gross GA, Muglia LJ. A short interpregnancy interval is a risk factor for preterm birth and its recurrence. *Am J Obstet Gynecol*, 2007;197:264.e1-264.e6.
5. Ekin A, Gezer C, Taner CE, Ozeren M, Mat E, Solmaz U. Impact of interpregnancy interval on the subsequent risk of adverse perinatal outcomes. *J Obstet Gynaecol Res*. 2015;41:1744-1751.
6. Grisaru-Granovsky S, Gordon ES, Haklai Z, Samueloff A, Schimmel MM. Effect of interpregnancy interval on adverse perinatal outcomes—A national study. *Contraception*. 2009;80:512-518.
7. Mahande MJ, Obure J. Effect of interpregnancy interval on adverse pregnancy outcomes in northern Tanzania: A registry-based retrospective cohort study. *BMC Pregnancy Childbirth*. 2016;16:140.
8. Mignini LE, Carroli G, Betran AP, et al. Interpregnancy interval and perinatal outcomes across Latin America from 1990 to 2009: A large multi-country study. *BJOG*. 2016;123:730-737.
9. Nabukera SK, Wingate MS, Kirby RS, et al. Interpregnancy interval and subsequent perinatal outcomes among women delaying initiation of childbearing. *J Obstet Gynaecol Res*. 2008;34:941-947.
10. Zhu BP, Rolfs RT, Nangle BE, Horan JM. Effect of the interval between pregnancies on perinatal outcomes. *N Engl J Med*. 1999;340:589-594.
11. Wen Xin. The history of population planning in China. News China. 2015. http://news.china.com.cn/txt/2015-10/29/content_36929413.htm. Accessed July 14, 2016.
12. Yangcheng Ou. Insight China: Little effect of the Two-child Policy for couples where either the husband or the wife is from a single-child family. BBC World Service. 2014. http://www.bbc.com/zhongwen/simp/china/2014/12/141210_china_watch_one_china. Accessed July 14, 2016.
13. Xiaofei Peng. The unification of the time to implement the universal Two-child Policy. Beijing Youth Daily. 2015. http://epaper.ynet.com/html/2015-11/05/content_164050.htm?div=-1. Accessed July 14, 2016.
14. Kenny LC, Lavender T, McNamee R, O'Neill SM, Mills T, Khashan AS. Advanced maternal age and adverse pregnancy

outcome: Evidence from a large contemporary cohort. *PLoS ONE*. 2013;8:e56583.
15. Laopaiboon M, Lumbiganon P, Intarut N, et al. Advanced maternal age and pregnancy outcomes: A multicountry assessment. *BJOG*. 2014;121(Suppl 1):49-56.
16. Zapata-Masias Y, Marqueta B, Gomez RM, Gonzalez-Bosquet E. Obstetric and perinatal outcomes in women >/=40 years of age: Associations with fetal growth disorders. *Early Hum Dev*. 2016;100:17-20.
17. Chen S, Zhang C, Chen Y, Cheng W. Analysis of factors influencing safety of department of obstetrics based on "the second child" policy and investigation of countermeasures. *J Shanghai Jiaotong University (Medical Science)*. 2016;36:742-746.
18. Wang CPY, Tan WC, Kanagalingam D, Tan HK. Why we do caesars: A comparison of the trends in cesarean section delivery over a decade. *Ann Acad Med Singapore*. 2013;42:408-412.
19. Lumbiganon P, Laopaiboon M, Gulmezoglu AM, et al. Method of delivery and pregnancy outcomes in Asia: The WHO global survey on maternal and perinatal health 2007-08. *Lancet*. 2010;375:490-499.
20. Ye F, Huang J. Antenatal care for women in their second pregnancies in China. *Lancet Glob Health*. 2016;4:e303.
21. Timofeev J, Reddy UM, Huang CC, Driggers RW, Landy HJ, Laughon SK. Obstetric complications, neonatal morbidity, and indications for cesarean delivery by maternal age. *Obstet Gynecol*. 2013;122:1184-1195.
22. Daltveit AK, Tollanes MC, Pihlstrom R, Irgens LM. Cesarean delivery and subsequent pregnancies. *Obstet Gynecol*. 2008;111:1327-1334.
23. DeFranco EA, Seske LM, Greenberg JM, Muglia LJ. Influence of interpregnancy interval on neonatal morbidity. *Am J Obstet Gynecol*, 2015. 212: 386. e1-9.
24. Te VE, Pearson PL. The variability of female reproductive ageing. *Hum Reprod Update*. 2002;8:141-154.
25. Chen Z, Peto R, Zhou M, et al. Contrasting male and female trends in tobacco-attributed mortality in China: Evidence from successive nationwide prospective cohort studies. *Lancet*. 2015;386:1447-1456.

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