Paternal Age and Adverse Birth Outcomes in Hong Kong Chinese

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Objective: To determine whether paternal age is associated with the risk of adverse birth outcomes in the Chinese population.
Methods: This was a retrospective study on 99,717 live singletons born to Chinese women aged 20 to 34 years between 1999 and 2008 in four regional hospitals in Hong Kong. Multiple logistic regressions were applied to estimate the independent effect of paternal age on adverse birth outcomes.
Results: Compared to infants born to fathers aged 25 to 29 years (the reference group), infants born to fathers aged 20 to 24 years had an increased risk of very preterm birth (odds ratio [OR]=1.70; 95% confidence interval [CI], 1.12-2.58), preterm birth (OR=1.42; 95% CI, 1.20-1.67), low birth weight (OR=1.26; 95% CI, 1.11-1.44), and low Apgar score at 1 minute (OR=1.33; 95% CI, 1.12-1.59). By contrast, such adverse outcomes were not associated with paternal ages of 30 years or more.
Conclusion: This is the first study on the impact of paternal age in the Chinese population. Younger fathers (aged 20-24 years) conferred an increased risk of adverse birth outcomes, whereas a paternal age of more than 30 years did not confer such a risk.
Hong Kong J Gynaecol Obstet Midwifery 2013; 13(1):33-9

Keywords: Birth weight; Paternal age; Pregnancy outcome; Premature birth

Introduction

Advancing maternal age has been shown to have increased risk of adverse pregnancy outcomes including miscarriage, fetal death, low birth weight, infant mortality, and Down syndrome[1-3]. However, less is known concerning the possible role of paternal age. Recently, the effects of paternal age on offspring has been addressed in the medical literature—the offspring of older fathers have long been postulated to be more susceptible to a wide range of problems, such as heart defects[4], acute lymphatic leukaemia[5], schizophrenia[6], and autism[7], but the exact degree of these associations with paternal age varies and is not well-defined.

Recent epidemiological studies have shown that paternal age may have a role on adverse birth outcomes, including miscarriage[8], fetal death[9], preterm birth[10], low birth weight[11], and low Apgar score[12], though the observed associations are somewhat inconsistent. Other studies found that advanced paternal age was not associated with an increased risk of preterm birth[3,13-15], low birth weight[3,13,14,16,17], and small-for-gestational-age birth[3,13].

Despite growing evidence on associations between paternal age and adverse birth outcomes in the literature, there was meager information on this topic in Asian

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populations. Thus whether there are any effects of paternal age on birth outcomes in Asians remains unknown. The objective of this study was to determine whether paternal age was associated with the risk of adverse birth outcomes, including low birth weight, preterm birth, and low Apgar score in a Chinese population.

Methods

Study Population

The electronic medical records of all women delivered during the period of 1 January 1999 to 31 December 2008 at Princess Margaret Hospital, Kwong Wah Hospital, Tuen Mun Hospital, and United Christian Hospital, in Hong Kong were retrospectively retrieved for analysis, through the hospital Obstetrics Specialty Clinical Information System and the Antenatal Record System. These systems were developed by the Hong Kong Hospital Authority to capture pregnancy information for women booked and delivered in Hong Kong public hospitals. Pregnancy information included the woman's date of birth, age, ethnic group, Hong Kong residency status, parity, age of husband, as well as neonatal outcomes, such as birth weight, gestational age at birth, and Apgar score. The data were obtained by attending doctors and nurses during outpatient antenatal visits for every pregnant woman and entered also by the attending midwives (in the labour ward) after the woman's delivery episode. Our study was restricted to live singletons born to Chinese women 20 to 34 years of age. Data from subjects with father's age of <20 years or missing, or missing maternal race, gestational age, and birth weight were excluded.

Definition

Paternal age was defined as the age of the father in completed years at the time of delivery, and categorised into seven groups: 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, and ≥50 years. The group aged 25-29 years of age was selected as the reference group for all the analyses.

Hong Kong residency status was categorised into two groups: Hong Kong resident and non–Hong Kong resident. Residents holding a valid Hong Kong Identification Card were classified as Hong Kong residents. Women who entered Hong Kong legally on temporary permits and those who either overstayed or were without valid documentation to enter Hong Kong were classified as non–Hong Kong residents.

The gestational age was calculated (in complete weeks) by the expected date of confinement (EDC), which was entered by attending doctors or midwives during initial maternal visits. The EDC was calculated from the last menstrual period (LMP), or adjusted accordingly by the attending doctors if a woman had a dating ultrasound done which showed an EDC discrepancy from the LMP or if the LMP was not available.

Adverse birth outcomes considered in this study included very preterm delivery (live infant delivered at <32 weeks' gestation), preterm delivery (live infant delivered at <37 weeks' gestation); very low birth weight (live infant weighing <1500 g at birth), low birth weight (live infant weighing <2500 g at birth); very low Apgar score at 1 min (<4), low Apgar score at 1 min (<7), very low Apgar score at 5 min (<4), and low Apgar score at 5 min (<7).

Statistical Analysis

Descriptive statistics collated in this study included maternal age, maternal Hong Kong residency status, parity, and infant gender—all stratified by the paternal age. Rates of adverse birth outcomes were calculated for each paternal age-group. The adjusted odds ratios for these adverse birth outcomes along with their 95% confidence intervals were derived for each of the seven paternal age categories, using the 25-29 years' age-group as the reference category. They entailed multiple logistic regressions with adjustment for potential confounding variables, including maternal age, parity (nulliparous, multiparous) with nulliparous as the reference, Hong Kong residency status (resident, non-resident) with Hong Kong resident as the reference, and infant gender (male, female) with male as the reference. Analyses with exclusion of data from those with infants with birth defects were also performed. All analyses were performed with statistical software (StatLab, SPSS for Windows, version 16.0; SPSS, Inc., Chicago [IL], US). Statistical significance was concluded for p values of less than 0.05.

Results

There were 195,919 live births during the study period in the designated hospitals, of which 188,686 singleton infants were born to Chinese women. After excluding cases involving women aged ≥35 years, parents less than 20 years, missing data on birth weights and gestational age, we had 148,981 eligible births. However, 49,264 records were excluded as the father's age was missing, which left 99,717 cases for the final analysis (Figure).

Table 1 summarises the maternal and infant characteristics associated with different paternal age-groups. In general, the mother's age correlated with the father's age.

Children born to fathers of younger age were more likely to have had a mother of similar age, while those born to fathers who were older (age >35 years) were more likely to have mothers who were older (age 30-34 years). The proportion of mothers being non–Hong Kong residents (over Hong Kong residents) increased for children with fathers of older age-groups (≥45 years) compared with younger age-groups (<45 years). The last column in Table 1 shows the characteristics of the group with missing paternal age, which was excluded from later analysis.

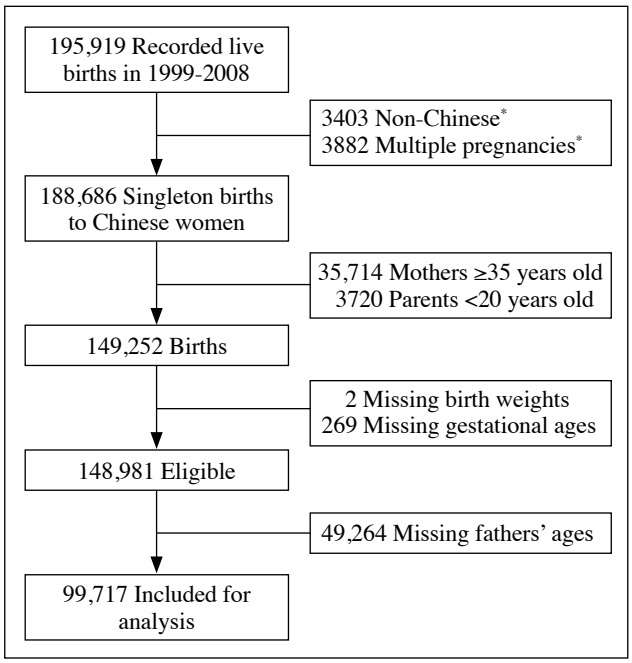

Figure. Steps to select the sample to be analysed

* Some subjects are both non-Chinese and with multiple pregnancies

Table 2 summarises the rates of adverse birth outcomes in infants born to fathers in different age-groups. The rates of very preterm births, preterm births, and low birth weight were higher in infants born to fathers 20-24 years of age than those with fathers in older age-groups.

Table 3 summarises the odds ratios for adverse birth outcomes in infants born to fathers in different age-groups. After adjustment for maternal age, maternal Hong Kong residency status, parity and infant gender, there were significantly increased risks of very preterm births, preterm births, low birth weights, and low Apgar scores at 1 min among infants born to fathers 20-24 years of age as compared to those of fathers aged 25-29 years.

Odds ratios obtained after exclusion of data if infants had congenital abnormalities are shown in Table 4, and yield similar results as Table 3. Paternal age-groups of older than 30 years were not associated with an increased

Table 1. Maternal and infant characteristics in different paternal age-groups

Characteristics	Paternal age (years)							Missing paternal age
	20-24	25-29	30-34	35-39	40-44	45-49	≥50	
No. of births	5560	21,659	34,292	22,171	10,225	4010	1800	49,264
Maternal age (years) [%]								
20-24	78.4	31.5	10.3	7.8	8.4	7.6	7.5	22.5
25-29	19.3	57.4	40.2	30.1	32.3	31.8	30.6	40.1
30-34	2.3	11.2	49.5	62.1	59.3	60.5	61.9	37.4
HK residency status (%)								
HK resident	67.4	68.6	76.7	74.3	64.2	52.4	41.9	63.4
Non–HK resident	32.6	31.4	23.3	25.7	35.8	47.6	58.1	36.6
Parity (%)								
Nulliparous	81.4	70.6	58.2	48.6	43.7	42.6	46.0	50.1
multiparous	18.6	29.4	41.8	51.4	56.3	57.4	54.0	49.9
Infant sex (%)								
Male	52.7	51.6	51.7	51.6	52.7	52.4	50.3	52.5
Female	47.3	48.4	48.3	48.4	47.3	47.6	49.7	47.5
Birth defects (%)								
No	99.2	99.1	99.0	99.0	99.1	98.8	99.4	99.8
Yes	0.8	0.9	1.0	1.0	0.9	1.2	0.6	0.2

Table 2. Rates of adverse birth outcomes in singleton infants born to fathers in different age-groups with mothers 20-34 years of age

Birth outcome	Paternal age (years)							Missing paternal age
	20-24	25-29	30-34	35-39	40-44	45-49	≥50	
No. of births	5560	21,659	34,292	22,171	10,225	4010	1800	49,264
Median (range) gestational age (weeks)	40 (23-42)	40 (23-42)	40 (23-42)	40 (23-42)	40 (23-42)	40 (23-42)	40 (26-42)	40 (23-42)
Gestational age <32 weeks (%)	0.6	0.4	0.5	0.5	0.5	0.5	0.3	0.7
Gestational age <37 weeks (%)	3.6	2.9	3.0	3.1	2.9	2.9	2.8	3.4
Mean (± SD) birth weight (g)	3146.96 ± 460.02	3185.73 ± 444.25	3209.57 ± 460.82	3230.41 ± 465.70	3261.27 ± 468.97	3276.60 ± 477.00	3265.56 ± 460.36	3200.42 ± 470.79
Birth weight <1500 g (%)	0.6	0.4	0.5	0.6	0.5	0.4	0.5	0.6
Birth weight <2500 g (%)	6.0	4.9	5.0	4.7	4.2	4.1	3.4	5.2
Apgar score at 1 min <4 (%)	0.4	0.3	0.3	0.4	0.3	0.4	0.3	0.5
Apgar score at 1 min <7 (%)	3.0	2.5	2.5	2.5	2.5	3.1	2.2	3.0
Apgar score at 5 mins <4 (%)	0.2	0.1	0.1	0.2	0.1	0.3	0.1	0.3
Apgar score at 5 mins <7 (%)	0.4	0.3	0.3	04	0.3	0.5	0.2	0.5

Abbreviation: SD = standard deviation

Table 3. Odds ratios for adverse birth outcome in singleton infants born to fathers in different age-groups and mothers 20-34 years of age (with adjustment for maternal age, maternal Hong Kong residency status, parity, and sex)

Birth outcome	Paternal age (years)						
	20-24	25-29	30-34	35-39	40-44	45-49	≥50
No. of births	5560	21,659	34,292	22,171	10,225	4010	1800
	Odds ratio (95% confidence interval)						
Gestational age <32 weeks	1.70* (1.12 - 2.58)	1.00	1.00 (0.76 - 1.33)	1.07 (0.78 - 1.47)	1.17 (0.81 - 1.69)	1.07 (0.64 - 1.85)	0.73 (0.29 - 1.83)
Gestational age <37 weeks	1.42* (1.20 - 1.67)	1.00	0.92 (0.83 - 1.03)	0.93 (0.82 - 1.05)	0.89 (0.77 - 1.04)	0.95 (0.77 - 1.17)	0.96 (0.72 - 1.30)
Birth weight <1500 g	1.47 (0.97 - 2.22)	1.00	0.91 (0.70 - 1.20)	1.04 (0.77 - 1.40)	1.00 (0.70 - 1.44)	0.82 (0.47 - 1.42)	1.09 (0.54 - 2.21)
Birth weight <2500 g	1.26* (1.11 - 1.44)	1.00	1.00 (0.92 - 1.09)	0.94 (0.86 - 1.04)	0.90 (0.80 - 1.02)	0.93 (0.78 - 1.11)	0.82 (0.63 - 1.07)
Apgar score at 1 min <4	1.23 (0.75 - 2.02)	1.00	0.87 (0.64 - 1.19)	1.09 (0.78 - 1.53)	0.90 (0.59 - 1.39)	1.09 (0.63 - 1.90)	0.83 (0.36 - 1.95)
Apgar score at 1 min <7	1.33* (1.12 - 1.59)	1.00	0.95 (0.84 - 1.06)	0.97 (0.85 - 1.11)	1.03 (0.88 - 1.21)	1.25* (1.01 - 1.54)	0.88 (0.63 - 1.28)
Apgar score at 5 mins <4	1.45 (0.70 - 3.02)	1.00	0.72 (0.44 - 1.17)	1.07 (0.65 - 1.78)	0.63 (0.31 - 1.27)	1.30 (0.61 - 2.76)	0.56 (0.13 - 2.41)
Apgar score at 5 mins <7	1.42 (0.85 - 2.38)	1.00	0.93 (0.67 - 1.28)	1.08 (0.76 - 1.53)	0.86 (0.57 - 1.38)	1.32 (0.78 - 2.25)	0.57 (0.20 - 1.59)

* $p<0.05$

risk of adverse birth outcomes when compared with the reference group (age 25-29 years).

Discussion

Our study indicated that younger fathers (20-24 years old) had an increased risk of adverse birth outcomes (preterm birth, low birth weight, and low Apgar score at 1 min), whereas paternal age of older than 30 years was not associated with adverse birth outcomes.

Age of procreation depends on both fecundity and family planning[18]. Some couples have children at an

Table 4. Odds ratios for adverse birth outcomes in singleton infants without birth defects born to fathers in different age-groups and mothers 20-34 years of age (with adjustment for maternal age, maternal Hong Kong residency status, parity, and sex)

Birth outcome	Paternal age (years)						
	20-24	25-29	30-34	35-39	40-44	45-49	≥50
No. of births	5515	21,462	33,957	21,953	10,135	3959	1790
	Odds ratio (95% confidence interval)						
Gestational age <32 weeks	1.72* (1.13 - 2.61)	1.00	1.00 (0.75 - 1.33)	1.07 (0.78 - 1.47)	1.19 (0.82 - 1.73)	1.05 (0.61 - 1.81)	0.75 (0.30 - 1.87)
Gestational age <37 weeks	1.39* (1.17 - 1.64)	1.00	0.92 (0.82 - 1.02)	0.91 (0.81 - 1.03)	0.88 (0.76 - 1.03)	0.92 (0.74 - 1.14)	0.97 (0.72 - 1.31)
Birth weight <1500 g	1.39 (0.91 - 2.11)	1.00	0.90 (0.69 - 1.18)	1.02 (0.75 - 1.37)	1.03 (0.71 - 1.47)	0.74 (0.41 - 1.32)	1.13 (0.56 - 2.28)
Birth weight <2500 g	1.23* (1.10 - 1.43)	1.00	1.00 (0.92 - 1.09)	0.94 (0.85 - 1.04)	0.91 (0.81 - 1.03)	0.92 (0.77 - 1.09)	0.82 (0.63 - 1.07)
Apgar score at 1 min <4	1.10 (0.65 - 1.87)	1.00	0.86 (0.62 - 1.19)	1.07 (0.75 - 1.51)	0.95 (0.62 - 1.48)	0.92 (0.50 - 1.71)	0.92 (0.39 - 2.17)
Apgar score at 1 min <7	1.32* (1.10 - 1.58)	1.00	0.96 (0.85 - 1.08)	0.98 (0.86 - 1.12)	1.05 (0.90 - 1.24)	1.21 (0.98 - 1.51)	0.92 (0.66 - 1.29)
Apgar score at 5 mins <4	1.21 (0.54 - 2.69)	1.00	0.67 (0.40 - 1.12)	0.97 (0.57 - 1.66)	0.71 (0.35 - 1.44)	1.19 (0.52 - 2.73)	0.65 (0.15 - 2.80)
Apgar score at 5 mins <7	1.22 (0.69 - 2.14)	1.00	0.91 (0.65 - 1.27)	1.01 (0.70 - 1.46)	0.92 (0.58 - 1.45)	0.94 (0.50 - 1.75)	0.62 (0.22 - 1.73)

* $p<0.05$

advanced age because they are not able to conceive at a younger age. Because subfecundity might be associated with the risk of adverse birth outcomes[19], we restricted our study to women 20-34 years of age who have the lowest incidence of subfecundity, thereby minimising the potential confounding effect of maternal fecundity, and other conditions related to advanced maternal age. Like previous studies in the literature[10,15,20], we excluded parents younger than 20 years of age because of peculiar risk factors associated with pregnancy in teenagers[20]. We restricted our study to singleton infants because multiple births are important risk factors for adverse birth outcomes. As congenital abnormalities may affect the results of preterm birth and low birth weight, those cases were also excluded for analyses as shown in Table 4.

We adjusted the results of adverse birth outcomes for potential confounders including maternal age, parity, Hong Kong residency status, and infant gender, as nulliparity is associated with higher risks of adverse birth outcomes, and mothers with non–Hong Kong residency status were also shown to have higher risks of pregnancy complications[21].

Some studies have found older paternal age to be linked to preterm birth[10,20], low birth weight[11], and low Apgar score[12]. A possible 'U-shaped' effect of paternal age on preterm birth and low birth weight was observed[3]. In our study, however, a significant association between older paternal age and adverse birth outcomes was not found, which was consistent with most other studies in the USA[3,13,15-17] and Canada[14]. On the other hand, the absence of socioeconomic data for adjustment may have affected our results. Older-aged fathers in our population may have higher socioeconomic status[22], which may confer a protective effect from adverse outcomes.

The association between younger paternal age and adverse birth outcomes is less well-documented. Both Chen et al[18] and Abel et al[3] found that younger paternal age (<20 years) was associated with a higher risk of adverse birth outcomes. Olshan et al[13] and Tough et al[14] also found that younger paternal age (<20 years) was associated with an increased risk of preterm birth. In our study, we excluded teenage parents (<20 years old) because of the peculiar risks of teenage pregnancy and complex socioeconomic issues confounding this age effect. Our study showed that there were significantly increased risks of preterm birth, low birth weight, and low Apgar score at 1 min in infants born to fathers aged 20-24 years, when compared with those with fathers aged 25-29 years.

An important strength of this study was the large variation in paternal age and the limited age range of the mothers. This study was specifically designed to assess the effects of paternal age among women who were at the lowest risk of adverse birth outcomes. Our study is the first to explore the paternal age effect in Chinese subjects. While the effect of paternal age on birth outcome is gaining attention in the western literatures, its effect on subjects of Chinese ethnicity is relatively unknown.

The most important limitation of our study was the small number of covariates we were able to include in the analysis. Socioeconomic status, lifestyle, smoking status, reproductive history, and management of pregnancy also influence the risk of adverse birth outcomes, but, regrettably such information was not routinely included in our database. We also lacked the information on paternal race. However, in Hong Kong Chinese culture, more than 99.5% of Chinese women marry Chinese men[23]. Thus we assumed the effect of paternal race was minimal after excluding all women of non-Chinese origin. Around 25% of subjects were excluded because of missing information on paternal age, as this entry was not compulsory in our electronic system. Data on the group of missing paternal age in Tables 1 and 2 showed that this group of patients tended to have more adverse outcomes, and may contribute to a selection bias. One of the possible explanations is that infants with missing paternal data may have been from unmarried mothers, of younger age, and of lower socioeconomic status. However, this cannot be confirmed from our current data set, because socioeconomic status was not recorded. It may be possible that had we included cases with missing paternal data in our study, the younger age-groups may have had shown even more prominent adverse risks. Besides, the preterm and very preterm rates in our study were lower than those in the local reported statistics, which may be due to the exclusion of cases with maternal age of 35 years or older, and those with missing paternal data (with a higher risk of preterm and very preterm births).

The mechanisms by which being a young father may contribute to an increased risk of adverse birth outcomes have been postulated by Chen et al[18]. First, younger men (age <25 years) had lower sperm counts, semen volumes, total number of spermatozoa and percentage of motile spermatozoa, all of which might be associated with an increased risk of adverse birth outcomes and result in abnormal placentation[18]. Second, young fathers are more likely to come from economically disadvantaged families and to have lower educational attainment[24]. Socioeconomic factors such as educational and occupation are known to be associated with a number of health outcomes[25]. Chen et al[18] and our present study, however, were unable to include socioeconomic factors for adjustment in our analysis. Third, the dynamics of the parent's relationships among young couples may contribute to adverse birth outcomes. Young fathers tend to provide less financial and emotional support, which in turn affect the mother's physical, emotional, and reproductive health[18]. Other potential factors such as illicit drug use, smoking, and alcohol intake among teenage fathers may be less prominent in our study, as we excluded infants of those aged <20 years.

This study demonstrated that in our Chinese population, being a young father (aged 20-24 years) was a possible risk factor for adverse birth outcomes while older fathers are not. This adds further information on current concerns regarding paternal age as a risk factor for adverse pregnancy outcomes.

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