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Incidence of down syndrome by maternal age in an Asian population

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Abstract

Objective: This study aims to estimate the maternal age-related risk of Down syndrome in an Asian population.

Methods: We performed a retrospective data analysis including a total of 206295 pregnant women who presented for second-trimester maternal serum screening for Down syndrome at Hubei Maternal and Child Health Hospital for the years 2008 to 2017.

Cases were assigned to three groups: ≤26 years of age, 27-33 years of age, and ≥34 years of age. The incidence of Down Syndrome was calculated for each age group. The differences between groups were tested using the chi-square ($\chi 2$) test.

Results: The incidence of Down syndrome in women ≤26 years of age, 27-33 years of age, and ≥34 years of age was 0.67 ‰, 0.29 ‰, and 2.07 ‰ respectively. Statistically significant difference was found between the three age groups ($\chi 2 = 79.748$, $P < 0.05$).

Conclusion: Down syndrome rate was significantly higher in women ≥34 years of age. Younger women (≤26 years of age) had a significantly higher risk for Down's syndrome, compared to women aged 27-33.

Introduction

Down Syndrome (DS) is the most recognized genetic cause of mental retardation, which occurs in 3.05 per 10,000 live births in China [1]. Since there is no medical cure for DS, it imposes an enormous financial burden on affected families and the health care system [2]. The average lifetime economic burden of a new DS case from the family perspective and the societal perspective amounted to US$47,000 and US$55,000, respectively [2].

Advanced maternal age (AMA) is a well-established risk factor for DS and an essential determinant in all prenatal screening strategies [3]. The association between maternal age distribution and the live birth prevalence of DS has been well documented in American and Europe [4]. However, racial-ethnic differences exist in prenatal diagnostic test use and associated outcomes of AMA [5]. In this study, we estimated the maternal age-related risk of Down syndrome in an Asian population.

Materials and Methods

Subjects

We performed a retrospective data analysis including a total of 206295 pregnant women who presented for second-trimester maternal serum screening for Down syndrome at Hubei Maternal and Child Health Hospital for the years 2008 to 2017.

Maternal serum screening

For each pregnant woman, 2 ml of maternal peripheral blood was collected and conserved at 4°C after separation of serum. The serum biomarkers, AFP, μE3, and β-HCG were detected by chemiluminescent immunoassay. The TCsoft prenatal screening software was used to calculate the screening risk. Risk = Age-specific Risk*LR(AFP)*LR(β-HCG) *LR(μE3). The initial MOM value was corrected by body weight, race, multiple births, diabetes, and other factors. The cut-off value for DS risk was set at 1:380

DS diagnosis

Before 2014, pregnant women with a positive screening result were diagnosed with amniocentesis. After 2014, pregnant women with a positive screening result were diagnosed by non-invasive prenatal screening (NIPS) and/or amniocentesis.

Statistical analysis

All cases were assigned to three groups: ≤ 26 years of age, 27-33 years of age, and ≥ 34 years of age. The incidence of Down's Syndrome was calculated for each age group. The differences between groups were tested using the $\chi 2$ test. All the analyses were performed by SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA). A P value of < 0.05 was considered statistically significant.

Results

The incidence of DS by maternal age.

The incidence of DS by maternal age was summarized in Table 1. In a total of 206295 cases, 13100 (6.35%) had positive screening tests (DS

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Table 1. Incidence of DS by maternal age.

Maternal age	Diagnosed cases			Total cases	Incidence (‰)
	Diagnosed antenatally	Diagnosed postnatally	Total		
18-21	1	0	1	3061	0.33
22	2	0	2	3294	0.61
23	5	0	5	5985	0.84
24	3	2	5	9876	0.51
25	8	3	11	14560	0.76
26	12	2	14	19955	0.70
27	6	1	7	26409	0.27
28	10	1	11	28267	0.39
29	6	1	7	26517	0.26
30	2	0	2	20152	0.10
31	6	0	6	14753	0.41
32	2	0	2	11259	0.18
33	4	0	4	9194	0.44
34	5	0	5	6726	0.74
35	4	0	4	3602	1.11
36	3	1	4	1203	3.33
37	4	0	4	623	6.42
38	1	0	1	364	2.75
39	1	0	1	203	4.93
≥40	8	0	8	292	27.40
Total	93	11	104	206295	0.50

risk > or = 1:380). 93 (89.4%) fetuses were diagnosed with DS prenatally and 11 (10.6%) fetuses were diagnosed postnatally (Table 1).

Incidence of DS by maternal age groups

All cases were assigned to three groups: ≤26 years of age, 27-33 years of age, and ≥34 years of age. The incidence of DS in women ≤26-years of age, 27-33 years of age, and ≥34 years of age was 0.67 ‰ (38/56731), 0.29 ‰ (39/136551), and 2.07 ‰ (27/13013) respectively (Table 2). Statistically significant difference was found between the three age groups ($\chi 2 = 79.748$, $P < 0.05$) (Table 2). Remarkably, the proportion of pregnant women ≤26-years of age was 27.5% (56731/206295) and the incidence of DS in this age group is significantly higher than women 27-33 years of age (Table 2).

Discussion

Down syndrome (DS) can occur at any maternal age but the chance of having a child with DS increases over time. It has been well accepted that women over age 35 at delivery are at higher risk for giving birth to a child with DS. In fact, for a long time, advanced maternal age (AMA) has been considered as a sole indication for genetic amniocentesis for definitive prenatal diagnosis [6]. In our study, the incidence of DS in women over age 34 was significantly higher than in other age groups (Table 2). These data are consistent with previous research [7,8]. Fortunately, women in this age group are usually well informed about the age-associated risk and treated as if they need the level of care necessary for any high-risk pregnancy. Our data showed all diagnoses in this age group were made prenatally except one (Table 1).

A trend has developed worldwide for women to delay childbearing into their late 30s or early 40s. In China, at end of October 2015, the one-child policy was replaced by a universal two-child policy. As a result, the proportion of women with AMA at delivery increased by 85.68%, from 8.52% in 2013 to 15.82% in 2017 in Zhejiang province [9]. The results of our study, which analyze a population of pregnant women in Hubei province, showed the proportion of women over age 34 was only 6.3% between 2008 and 2017 suggesting that there are considerable variations in the prevalence of AMA across the county (Table 2). Future studies are required to confirm the trend and understand the demographic differences.

Previous studies conclude there is no association between younger maternal age and the risk of DS. However, we found that women under age 26 (18-26) account for nearly 27% of all pregnant women and are more likely to have babies with DS than women aged 26-34 ($\chi 2$-14.858 $P < 0.01$) (Table 2). This is partly due to the increasing availability of more powerful tests, which significantly increased the overall detection rate. Another explanation could be that young mothers lack all awareness of pregnancy and therefore are more likely to engage in risk behaviors such as smoking, drinking, and using illicit drugs that can induce chromosomal non-disjunction [10]. They are also more likely to be sleep-deprived, have an imbalanced diet to control body weight. In our study, 18.4% (7/38) of DS in women ≤26 years of age are diagnosed postnatally, compared to 7.7 (3/39) in the women aged 26-34 and 3.7% (1/27) in the woman ≥34 years of age (Tables 1 and 2). In an early study, it predicts that with continued use of prenatal diagnosis among older women, upward of 80% of DS births will occur to younger mothers [11]. Our study shows high occurrence of DS in women younger than 26 years. Therefore, much more attention needs to be given to younger mothers. Maternal serum screening for DS should be routinely performed to all pregnant women. Healthcare professionals need to help them to understand the importance of this screening test and make informed decisions.

Conclusion

The incidence of DS was significantly higher in women ≥34 years of age. Younger women (≤26 years of age) had a significantly higher risk for DS, compared to women aged 27-33.

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Table 2. Incidence of DS by maternal age groups.

Maternal age	Total cases	Diagnosed cases	Incidence (‰) *
≤26	56731	38	0.67
27-33	136551	39	0.29
≥34	13013	27	2.07

*The incidence of DS was significantly different among the groups ($\chi^2 = 79.748$, $P < 0.05$)

Ethics approval and consent to participate

The research was approved by the Ethics Committee of Maternal and Child Health Hospital of Xiaogan(Approval number: 2019-yc-0919) All patient guardians gave informed consent to the study.

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