Maternal age, not BMI influences the increased trends in gestational diabetes mellitus in a Chinese population

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ABSTRACT

Maternal age and obesity have significantly increased worldwide. The global incidence of gestational diabetes mellitus (GDM) has significantly increased and Asian have higher incidence of GDM. It is unclear as to whether maternal age and obese contribute to the increased trend of GDM in Chinese women or not. In this study, we analysed the trend in the incidence of GDM from 97,580 pregnant women between 2011 and 2017 and the potential associated risk factors. During the study period, there were 12,842 cases of GDM. The incidence of GDM significantly increased from 8.6% in 2011 to 15.1% in 2017 after age-standardisation rate analysis. The proportion of pregnancies with advanced age (over 35 years) was significantly increased from 7.7% in 2011 to 17.5% in 2017. The maternal age in women with GDM also significantly increased from 30.2 years in 2011 to 31.9 years in 2017. The incidence of GDM in women with advanced age doubled in women who were under 35 years. However, the trends of body mass index (BMI) in women with GDM were unchanged between 2011 and 2017 regardless of maternal age and sub-groups of BMI. Our study demonstrates an increased trend of GDM with increased maternal age but not maternal BMI.

Key words: GDM, advanced maternal age, BMI, Chinese population.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a major complication of pregnancy which affects 10-15% healthy pregnancies dependent on the ethnicities and regions (Donovan and McIntyre, 2010; Carolan et al., 2012). It increases the risk of developing other complications associated with pregnancy such as preeclampsia (Yoge et al., 2004; Weissgerber and Mudd, 2015) and increases the need for a caesarean section (Song et al., 2017; Langer et al., 2005). GDM also increases the risk of developing type 2 diabetes in adulthood (Donovan and McIntyre, 2010; Ferrara et al., 2004). Over the last decade, the prenatal cares including prenatal nutrition (e.g., Vitamin D supplementation) (Jelsma et al., 2013), intervention and early screening tests for women with high risk factor(s) or for prediction of clinical outcomes have significantly improved worldwide in order to prevent GDM. However, recent data showed that the incidence of GDM has significantly increased in an ethnicity dependent manner over the last decades (Jovanovic and Pettitt, 2001; Ferrara, 2007) and the causes of this increase may vary based on the ethnicity.

GDM is caused by a lack of insulin in the setting of insulin resistance during pregnancy. In addition to the risk factor of being overweight or obese, advanced maternal age (maternal age over 35 years) is also a well-known risk factor for developing GDM (Carolan et al., 2012). Moreover, it has previously been reported that 13% of GDM are over the age of 44 years (Donovan and McIntyre, 2010). Another study has shown a trend of age related GDM increasing in women who were living in Australia and found that 35% of GDM occurred in women with advanced maternal age, which was approximately four times higher than women under 35 years (Carolan et al., 2012). The maternal age at birth has progressively increased worldwide over the past few decades, in particular in developed countries (Mathews...
and Hamilton, 2002). We recently also reported that the average maternal age significantly increased from 28.1 years in 2003 to 29.4 years in 2013 in a Chinese population (Li et al., 2016). In addition, the proportion of advanced maternal age at birth has also significantly increased over the last decade in many developed countries, including the United States, United Kingdom and Norway (Wang et al., 2011; Kenny et al., 2013; Martin et al., 2015). All these studies suggest a clear trend in increased maternal age at birth worldwide.

Investigations regarding the trends in the incidence of GDM are limited, particularly in Asian populations where there is a higher prevalence of GDM as compared with other ethnicities (Carolan et al., 2012). Whether the increase in the incidence of GDM is associated with increasing maternal age or obesity is unclear. China is currently moving towards industrialisation and undergoing a nutritional transition that incorporates many western dietary patterns including fast food. As a direct consequence of these changes, obesity is becoming a major health issue in China, where there is a strong positive correlation between fast food consumption and the incidence of GDM (Dominguez et al., 2014). The few studies that have investigated GDM in Chinese populations have shown that between 1999-2012, there was an increase in cases of GDM from 7 to 20%, respectively (Hirst et al., 2012; Leng et al., 2015; Zhu et al., 2017), but these studies did not investigate the trends in the incidence of GDM.

The objective of this retrospective study was to investigate the trends in the incidence of GDM and whether maternal age and obese are associated with the changes in the incidence of GDM between 2011 and 2017 or not. All the data were collected from the largest women’s hospital in the largest city (Shanghai) in China.

MATERIALS AND METHODS

This study was approved by the ethic committees of the Hospital of Obstetrics and Gynaecology, Fudan University, China.

Study population

Body mass index (BMI) in women with GDM and data on maternal age at birth with a live birth after 28 weeks of gestation used in this retrospective study (n=97,580) was collected from The Hospital of Obstetrics and Gynaecology of Fudan University, Shanghai, China from January 2011 to October 2017. All data were collected from hospital electronic based database. The Hospital of Obstetrics and Gynaecology of Fudan University is located in Shanghai and is the largest university teaching hospital specialized in Obstetrics and Gynaecology in China, with more than 10,000 births a year. Shanghai is the largest and wealthiest city with a total population of 25 million in China and has an advanced maternal care system. Of 97,580 pregnancies, there were 12,842 women who developed GDM during the study period.

GDM was defined as any degree of glucose intolerance with onset or first recognition during pregnancy. In 2011, the World Health Organization (WHO) revised and formulated a new set of diagnostic criteria for gestational diabetes (http://www.who.int/iris/handle/10665/85975). Our study has used the new WHO guidelines to assess GDM. Specifically, oral glucose tolerance tests (OGTT) were measured by a 1 step approach. A 75 g glucose load was administrated after fasting glucose and plasma glucose levels were measured after 1 and 2 h. GDM was diagnosed if either of the glucose values fell at or above the specific glucose threshold (≥5.1 mmol/L for fasting, ≥10.0 mmol/L at 1 h, and ≥8.5 mmol/L at 2 h).

BMI was measured and calculated as the ratio of maternal weight and height (kg/m2) at first time booking. The WHO classification of BMI for Asian/Indian women (underweight (18.4 kg/m2), normal weight (18.5-22.99 kg/m2), overweight (23-27.49 kg/m2) and obese (over 27.50 kg/m2)) were used to classify women cohorts based on BMI.

Statistical analysis

Data on maternal age were expressed as mean and standard deviation (SD). The statistical difference in the trend of maternal age over the study period was performed by ANOVA linear trend analysis. The statistical difference in proportion of women with advanced maternal age over the study period was performed by Chi-square test for linear trends. Analysis was conducted in GraphPad Prism software (Version 7). P<0.05 was considered as a statistical difference.

RESULTS

The maternal age in all pregnancies including women with GDM was significantly increased

We first investigated the trends of maternal age in all pregnancies over the study period and found that the mean maternal age in all pregnancies had significantly increased from 28.8 years in 2011 to 30.7 years in 2017 (p<0.0001, ANOVA test for linear trend). In addition, the proportion of all pregnant women with advanced maternal age (over 35 years) was significantly increased from 7.7% in 2011 to 17.5% in 2017 over the study period (Figure 1, p=0.0001, Chi-square test for linear trend). We then analysed the trends of maternal age in women with GDM. The mean maternal age in women with GDM also significantly increased from 30.2 years in 2011 to 31.9 years in 2017 (Figure 2, p<0.0001, ANOVA test for linear trend). We also found that the trend of the proportion of GDM women with advanced maternal age was significantly increased in total
The incidence of GDM was significantly increased during the study period

We then analysed the trend in the incidence of GDM. Of 97,580 pregnancies, there were 12,842 cases with GDM over 7 years of study period. The overall incidence of GDM was 13.1% during the study period. The trend of the incidence of GDM was significantly increased (Table 1, p=0.0001, Chi-square test for linear trend) from 8.6% in 2011 to 16.2% in 2017. We next performed an age-standardization rate analysis to correct the incidence of GDM. After age-standardization rate analysis, which referred
The trend of GDM with advanced age (%)

Figure 3: The trend of GDM with advanced age in all cases (p=0.0001, Chi-square test for linear trend).

Table 1: The trend in the incidence of GDM according to the years.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total pregnancies (number)</th>
<th>Incidence of GDM (number, %)</th>
<th>Incidence of GDM after age standardization (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>11775</td>
<td>1024 (8.6%)</td>
<td>8.6%</td>
</tr>
<tr>
<td>2012</td>
<td>11673</td>
<td>2165 (18.5%)</td>
<td>18.67%</td>
</tr>
<tr>
<td>2013</td>
<td>14283</td>
<td>1930 (13.5%)</td>
<td>13.38%</td>
</tr>
<tr>
<td>2014</td>
<td>16947</td>
<td>1897 (11.2%)</td>
<td>10.94%</td>
</tr>
<tr>
<td>2015</td>
<td>14223</td>
<td>1391 (9.7%)</td>
<td>9.22%</td>
</tr>
<tr>
<td>2016</td>
<td>16439</td>
<td>2473 (15.0%)</td>
<td>14.29%</td>
</tr>
<tr>
<td>2017</td>
<td>12240</td>
<td>1962 (16.2%)</td>
<td>15.12%</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>&lt;0.0001</td>
<td>&lt;0.0003</td>
</tr>
</tbody>
</table>

GDM: gestational diabetes mellitus.
*: 2011 was the reference population.

age distribution (under 35 and over 35 years) in 2011, the trend of the incidence of GDM was significantly increased from 8.6% in 2011 to 15.1% in 2017 (Table 1, p=0.0003). In addition, we found that the odds of GDM in women with advanced age was 2.044 (95%CI: 1.99 to 3.63) times the odds of GDM in women who were under 30 years.

We further analysed the maternal age distribution in GDM women over the study period. The trend of the incidence of GDM in pregnant women who were under 25 years was significantly increased from 3.93% in 2011 to 8.6% in 2017 (Table 2). The trend of the incidence of GDM in pregnant women who were over 35 years was also significantly increased from 13.77% in 2011 to 23.72% in 2017 (Table 2). However, the trend of the incidence of GDM in pregnant women who were between 25 and 34 years was not changed (data not shown).

The proportion of women with obese in GDM was not significantly increased in 2017 compared to 2011.

A traditional risk factor for the development of GDM is maternal BMI. We then compared the maternal BMI in GDM women in 2017 with that in 2011 based on four categories of BMI. The proportion of GDM women who were underweight, normal weight, over-weight or obese was unchanged between the 2017 and 2011 cohorts (Table 3, p=0.252).

Because advanced maternal age is a risk factor for developing GDM, we further analysed the BMI in women with GDM who were under 35 years or over 35 years in 2011 and 2017. In GDM women who were under 35 years, there was no difference in the proportion of GDM women who were under-weight, normal weight, over-weight or
Table 2: Age distribution on GDM according to the years.

<table>
<thead>
<tr>
<th>Under 25 years</th>
<th>GDM (number, %)</th>
<th>Total pregnancies who were under 25 years (number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>50 (3.93%)</td>
<td>1272</td>
</tr>
<tr>
<td>2012</td>
<td>85 (10.3%)</td>
<td>826</td>
</tr>
<tr>
<td>2013</td>
<td>46 (4.28%)</td>
<td>1074</td>
</tr>
<tr>
<td>2014</td>
<td>42 (3.66%)</td>
<td>1146</td>
</tr>
<tr>
<td>2015</td>
<td>43 (4.51%)</td>
<td>954</td>
</tr>
<tr>
<td>2016</td>
<td>62 (7.87%)</td>
<td>788</td>
</tr>
<tr>
<td>2017</td>
<td>48 (8.6%)</td>
<td>542</td>
</tr>
</tbody>
</table>

P value 0.024

<table>
<thead>
<tr>
<th>Over 35 years</th>
<th>GDM (number, %)</th>
<th>Total pregnancies who were over 35 years (number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>126 (13.77%)</td>
<td>915</td>
</tr>
<tr>
<td>2012</td>
<td>250 (31.25%)</td>
<td>800</td>
</tr>
<tr>
<td>2013</td>
<td>292 (14.92%)</td>
<td>1953</td>
</tr>
<tr>
<td>2014</td>
<td>353 (20.15%)</td>
<td>1752</td>
</tr>
<tr>
<td>2015</td>
<td>352 (18.59%)</td>
<td>1894</td>
</tr>
<tr>
<td>2016</td>
<td>587 (25.19%)</td>
<td>2330</td>
</tr>
<tr>
<td>2017</td>
<td>509 (23.72%)</td>
<td>2146</td>
</tr>
</tbody>
</table>

P value 0.0128

Table 3: The proportion of GDM women in different BMI categories between 2011 and 2017.

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>2011 (n=1000)*</th>
<th>2017 (n=1496)*</th>
<th>Chi-square test</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>36 (3.6%)</td>
<td>59 (3.9%)</td>
<td>P=0.252</td>
</tr>
<tr>
<td>18.5-22.9</td>
<td>469 (47%)</td>
<td>648 (43.3%)</td>
<td></td>
</tr>
<tr>
<td>23-27.4</td>
<td>365 (35%)</td>
<td>601 (40.2%)</td>
<td></td>
</tr>
<tr>
<td>≥27.5</td>
<td>130 (13%)</td>
<td>188 (12.6%)</td>
<td></td>
</tr>
</tbody>
</table>

* Data on BMI in 24 cases in 2011 and 466 cases in 2017 were not available.

obese between 2011 and 2017 (Table 6, p=0.201). In women with GDM with advanced maternal age, there was also no statistical difference in the proportion of women who were under-weight, normal weight, over-weight or obese between 2011 and 2017 (Table 4, p=0.168).

DISCUSSION

The global incidence of GDM has significantly increased within one or two decades in a number of countries including developing countries (reviewed in Zhu and Zhang (2016)). Although the incidence of GDM is ethnicity and region dependent (Donovan and McIntyre, 2010; Carolan et al, 2012), Asian have a higher incidence of GDM as compared with the western counties. For example, a recent study reported that the trend in the incidence of GDM was significantly increased from 3.86% in 2007 to 11.86% in 2010 in Korean (Cho et al, 2015). The incidence of GDM in Tianjin, a second line city in China has also increased since 1999 from 2.3 to 6.8% in 2008 (Leng et al, 2015; Zhang et al, 2011). In our current study, after age-standardization rate analysis, we found that the trend in the incidence of GDM was significantly increased over the study period, from 8.6% in 2011 to 15.1% in 2017 in Shanghai, the largest city in China. The higher incidence of GDM seen in Shanghai as compared with other cities in China could reflect the fact that Shanghai is an international city and the lifestyle is largely different to other cities in China as lifestyle may be also a risk factor for GDM (Chasan-Taber, 2015).

Maternal age is one of the most common and important risk factors for the development of GDM (Jovanovic and Pettitt, 2001; Ferrara, 2007). In the present study, we found that the risk for developing GDM in women with advanced maternal age was two times that of women who were under 35 years, which was lower than that of Australian counterparts (Carolan et al, 2012). It is well reported that the proportion of women who delay childbearing beyond the age of 35 years has significantly increased worldwide. In the present study, in line with our previously published data
which identified that the average maternal age significantly increased during the study period, from 28.8 years to 31.3 years and the proportion of pregnancies with advanced maternal age also significantly increased from 7.7% in 2011 to 17.5% in 2017. Furthermore, we also found that the maternal age in women with GDM significantly increased over the study period. However, in our current study, we interestingly found that in addition to the increased trend of GDM in women with advanced maternal age, the trend in the incidence of GDM in women who were under 25 years was also significantly increased. When our age-standardization rate analysis data was combined, our study suggests that in addition to increased maternal age, other factors also significantly contributed to the increase in the incidence of GDM.

High BMI is one of the strongest risk factors for developing GDM. However, studies investigating the trend of BMI in pregnant women, in particular in Asian population, are limited and inconsistent. The higher incidence of GDM found in this study may result from the fact that Shanghai is an international city and many western dietary patterns including fast food have been incorporated into daily life over last decade. These changes consequently result in increased obesity among the population. Similarly, in the USA, the incidence of maternal obesity was increased between 1993 and 2003 (Kim et al., 2007). While in the United Kingdom (between 2002 and 2009) (Davenport et al., 2010) and Korea (between 2007 and 2010) (Cho et al., 2015), the incidence of maternal obese was not significantly increased. In our current study, we also found that the incidence of maternal obesity was not significantly increased in women with GDM between 2011 and 2017 regardless of the maternal age (above or below 35 years). The WHO ethnic-specific BMI distribution data show that 10–12% of Chinese women are underweight, around 70% are normal weight, 10–15% are overweight, and only 2–3% are obese (WHO Expert Consultation, 2004). Taken together, our data may suggest that although half of GDM (48% to 52%) cases reported were in overweight or obese women, the increased trend in the incidence of GDM in Chinese women may not be explained by maternal obesity.

Other factors such as parity (Cho et al., 2015), physical inactivity (Dempsey et al., 2004) and smoking (England et al., 2004) have been reported to be associated with the development of GDM. Due to one child policy in China that ended in early 2016, the majority of pregnant women included in this study were nulliparous. In addition, none of pregnant women smoke as a result of the Chinese traditional culture. Our unpublished survey data showed that women undertake less physical activity during pregnancy to avoid unexpected miscarriage which again is in line with traditional Chinese culture. Although data on physical activity was not available in this study, we speculate that physical inactivity may be one of the reasons for higher incidence of GDM in our study population. Future studies are required to confirm this hypothesis.

There are some limitations in this study. Firstly, we only investigated the trends in the incidence of GDM in Shanghai, the largest city in China, which may not be representative of China as a whole but our data do provide information regarding the trends of GDM in a relative long study period using new diagnostic criteria for GDM. Secondly, data on family history, history of diabetes or hypertension and preeclampsia which are all risk factors for GDM were not available.

In conclusion, in this relative large sample size study, we found an increased trend of GDM in a Chinese population that corresponds with increased maternal age. Maternal BMI did not contribute to this increase. Future studies are required to identify other associated factors which contribute to the increase in GDM increase.

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REFERENCES


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