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Prevalence of gestational diabetes mellitus in mainland China: A systematic review and meta-analysis

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ABSTRACT

Aims/Introduction: Pregnant women with gestational diabetes mellitus (GDM) are at a higher risk of adverse pregnancy outcomes. The aim of the present study was to estimate the pooled prevalence of GDM in mainland China according to International Association of Diabetes and Pregnancy Study Groups criteria.

Materials and Methods: We carried out a systematic review by searching both English and Chinese literature databases. Random effects models were used to summarize the prevalence of GDM in mainland China. Subgroup and sensitivity analyses were carried out to address heterogeneity. Publication bias was evaluated using Egger's test.

Results: A total of 25 papers were included in the meta-analysis, involving 79,064 Chinese participants. The total incidence of GDM in mainland China was 14.8% (95% confidence interval 12.8–16.7%). Subgroup analysis showed that the age, bodyweight and family history of diabetes mellitus could significantly increase the incidence of GDM.

Conclusions: To the best of our knowledge, this systematic review is the first to estimate the pooled prevalence of GDM among women in mainland China according to International Association of Diabetes and Pregnancy Study Groups criteria. The results of our systematic review suggest a high prevalence of GDM in mainland China, indicating that this country might have the largest number of GDM patients worldwide.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance resulting in hyperglycemia with first onset or detection during pregnancy. GDM is seriously harmful to both the woman and the fetus. Pregnant women and puerperae are prone to complications of gestational hypertensive disease, polyhydramnios, premature rupture of fetal membranes, infection and premature birth; in severe cases, ketoacidosis can occur, and puerperae might have long-term postpartum diabetes[1,2]. In addition, the fetus is prone to spontaneous abortion, malformation and hypoxia; in severe cases, intrauterine death can occur. Hyperglycemia tends to cause fetal macrosomia; the chances of dystocia at parturition are increased, and the newborn is prone to neonatal respiratory distress syndrome, hypoglycemia and other complications after birth, including death in severe instances[3].

In 2008, the hyperglycemia and adverse pregnancy outcome (HAPO) study, which involved multiple countries, showed that at 24–32 weeks-of-gestation, a higher blood glucose level in the 75-g oral glucose tolerance test (OGTT) indicates a greater risk of adverse gestational outcomes. Indeed, even with a normal blood glucose level, the risk of having an adverse outcome for both mother and baby is greater with an increase in blood glucose level, whereas significant thresholds were not observed for most comorbidities. Based on that study, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed new GDM diagnostic criteria in 2010: boundary blood glucose levels for fasting, 1 and 2 h after oral glucose of 5.1, 10.0 and 8.5 mmol/L, respectively, by 75-g OGTT. If any one of these three values reaches or exceeds the boundary level, the patient should be diagnosed with GDM[4]. The publication of this diagnostic standard had a "milestone" significance. In 2011, the American Diabetes Association (ADA) recommended the IADPSG criteria be adopted as GDM diagnostic criteria, and in August 2013, the World Health Organization (WHO) used the HAPO study results as an important reference to develop new GDM diagnostic

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criteria[5]. In 2014, the ADA once again noted that although the new diagnostic criteria would increase healthcare costs, they might also reduce the incidence of adverse gestation events, especially for pregnant women with slightly high blood glucose levels. In October 2015, the International Federation of Gynecology and Obstetrics published a practical guide to GDM, which also utilizes the IADPSG criteria to diagnose GDM[6].

As a result of economic development and improvements in living standards, together with increased attention to GDM screening, an increase has been observed in the incidence of GDM. China has a high incidence of diabetes, and the increase in GDM incidence in China is also alarming. Furthermore, China encompasses a vast territory, and has a large population with considerable differences in regions, ethnicities, diets and living habits, and these factors lead to differences in the incidence of GDM reported in various regions. For example, studies have found that even if the IADPSG diagnostic criteria are applied, the incidence of GDM in mainland China fluctuates between 5.12% and 33.3%[7,8]. As there is currently no systematic analysis of the incidence of GDM in China, the present study aimed to explore the incidence of GDM among pregnant women in mainland China, and the impact of relevant factors on GDM incidence through a systematic meta-analysis.

METHODS

A completed Preferred Reporting Items for Systematic Review and Meta-Analyses checklist is presented in Data S1.

Search strategy

We searched for epidemiological studies on GDM in several electronic databases, including Medline, PubMed, China National Knowledge Infrastructure, Wanfang and Chongqing VIP. Each search strategy is listed as follows. Medline: (TS = gestational diabetes mellitus OR TS = GDM) AND ([TS = prevalence] OR TS = epidemi*) AND ([(TS = Chinese) OR TS = China] OR TS = mainland); Pubmed: ([gestational diabetes mellitus(Title/Abstract)] OR GDM(Title/Abstract)] AND [(prevalence(Title/Abstract)] OR epidemi*[Title/Abstract]) AND ([(Chinese[Title/Abstract]) OR China[Title/Abstract]) OR mainland[Title/Abstract]); China National Knowledge Infrastructure: AB = gestational diabetes mellitus AND (AB = prevalence OR AB = epidemiology); Wangfang: Abstract: (gestational diabetes mellitus)*(prevalence + epidemiology). Chongqing VIP: R = gestational diabetes mellitus*(R = prevalence + R = epidemiology). All studies published from 1 January 2010 to 30 April 2017, were searched. In addition, the reference lists of the retrieved articles were examined to identify additional eligible studies. Unpublished studies were not retrieved. The search languages were limited to English and Chinese.

Inclusion and exclusion criteria

To satisfy the analysis requirements and to reduce selection deviation, studies needed to meet the following criteria for inclusion: (i) a cross-sectional study or retrospective study collected in mainland China; (ii) sufficient information on the sample size and crude prevalence of GDM; (iii) GDM diagnostic criteria proposed by IADPSG in 2010[4]; (iv) containing information for at least family history of diabetes mellitus, body mass index (BMI), age, pregnancy history and delivery history. Studies were excluded if they recruited patients with serious and chronic diseases, including thyroid disease, heart disease and overt diabetes mellitus. In the case of multiple articles based on the same population, only the study reporting the most detailed data was included.

Data extraction and quality assessment

All searched articles from different electronic databases were combined in Endnote, and duplicates were removed. Two researchers independently screened the title and abstract, and reviewed the full text of eligible citations. In the case of disagreement, a third reviewer made the final decision. For each included study, the two researchers independently extracted the following information: general information (e.g., first author and publication year), study characteristics (including study period, study area and sample size) and all possible participant information (e.g., age, family history of diabetes mellitus, BMI, region etc.). The two researchers independently assessed the quality of each included study using the Newcastle–Ottawa Scale recommended by the Cochrane Handbook for Systematic Reviews of Interventions.

Statistical analysis

We used a systematic analysis approach to calculate the pooled prevalence of GDM for all eligible studies. A random effects model was selected to summarize the prevalence of GDM; heterogeneity among studies was assessed using Cochran's *Q*-test and the I^2 statistic, which shows the percentage of variation across studies. Subgroup analyses by age, family history of diabetes mellitus, BMI, region and so on were carried out to address heterogeneity. Additionally, sensitivity analysis was carried out to examine the influence of any particular study on the pooled estimate. Publication bias was evaluated using Egger's test, and independent *t*-tests were carried out as appropriate. The significance level was set at a P-value of <0.05. All statistical analyses were carried out using Stata version 12.0 (StataCorp, College Station, TX, USA) and SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The initial search retrieved 2,576 records from Medline, PubMed, China National Knowledge Infrastructure, Wanfang and Chongqing VIP databases, and 508 articles remained after excluding duplicates, reviews and letters. After screening for eligibility based on the title and abstract, 107 articles were selected; of these, 25 articles were included after screening the full text. The main reasons for inclusion in the full-text selection are shown in Figure 1[7–31]. The 25 articles that met the requirements and were eventually included in the study covered

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the prevalence of GDM in pregnant women in 21 regions of mainland China between 2010 and 2017, including 79,064 participants. The characteristics of the selected studies are summarized in Table 1. Among the included articles, 24 focused on women of Han nationality, one involved other ethnic groups and two included a multiple pregnancy. The economic levels of the regions in the included papers had per capita annual incomes ranging from less than $US1,000 to $US30,000, and the papers included age, family history of diabetes mellitus, history of pregnancy and delivery, BMI, per capita income, and many other factors that affect GDM. In accordance with the recommended criteria of the Newcastle–Ottawa Scale, the studies included in the present meta-analysis were of acceptable quality; therefore, we did not exclude any article from the meta-analysis for quality reasons.

The total incidence of GDM in mainland China was 14.8% (95% confidence interval [CI] 12.8–16.7%; Figure 2). Table 2 shows the results of subgroup analysis in different groups. Subgroup analysis showed an incidence of GDM in older pregnant women of 26.7% (95% CI 23.2–30.3%), whereas that in younger pregnant women was just 13.4% (95% CI 11.0–15.7%), with a significant difference between the two subgroups ($P < 0.01$). The incidence of GDM in overweight or obese women was 30.3% (95% CI 25.9–34.7%), which was significantly higher than that of women who had a normal bodyweight (14.9%, 95% CI 11.7–18.1%; $P < 0.01$). The incidence of GDM in women with a family history of diabetes mellitus was 32.9% (95% CI 27.5–38.4%), approximately threefold that in women without a family history ($P < 0.01$). Using the per capita income of $US10,000 as a boundary, the regional economic level did not have a significant impact on the incidence of GDM (14.8% and 15.4%, $P = 0.53$). We carefully and comprehensively searched the articles in the database. Sensitivity analysis was carried out to examine the influence of any particular

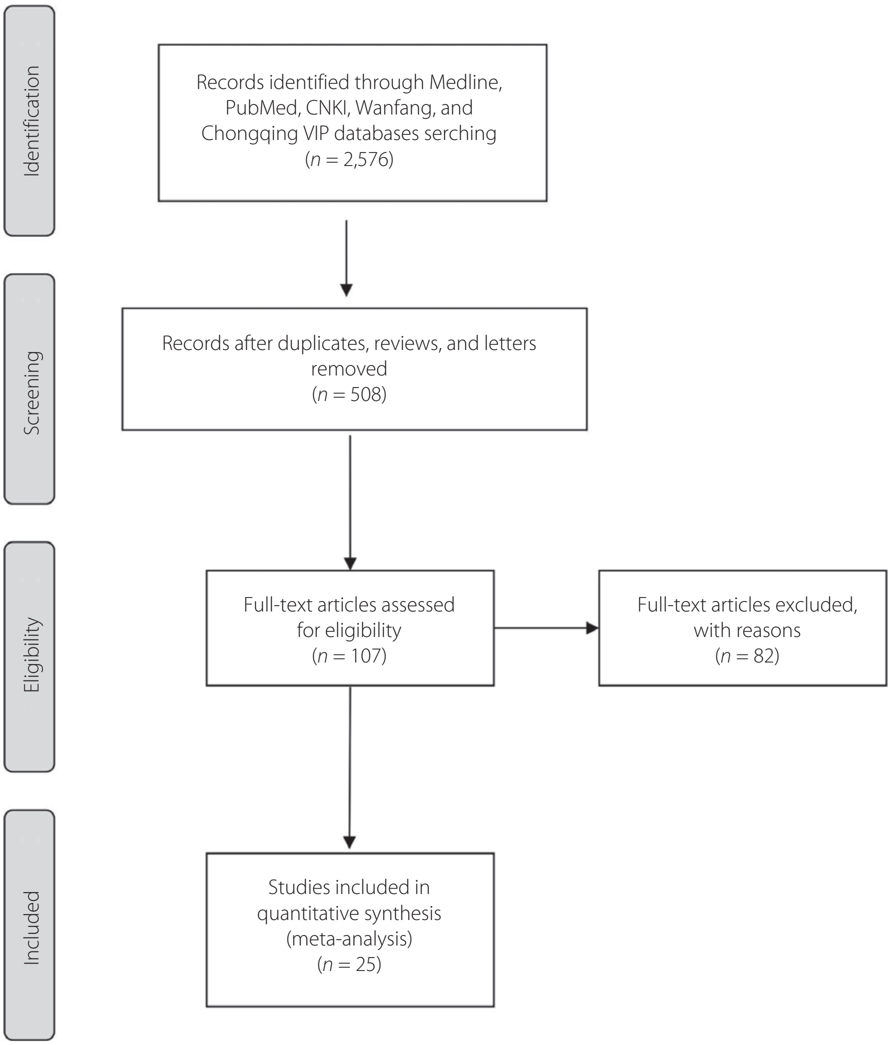

Figure 1 | Flow chart showing the detailed procedure for the inclusion or exclusion of studies.

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Table 1 | Study characteristics of the published studies included in the meta-analysis

Study	Period	Sample (*n*)	Region (province)	Economic level[†]	Native	Maternal age (year)	Gestational age (weeks)	Case	Subgroup of risk factor[‡]	Prevalence	Other confounders
Chen Y, 2013	Sep 2012 to Mar 2013	410	Xinjiang	Low	Yes	27.07 ± 0.42	25.1 ± 0.22	21	Age, BMI	5.12%	Multiple race included, maternity hospital
Li GP, 2015	Dec 2012 to Feb 2014	690	Henan	Low	Yes	28.9 ± 4.17	14.4 ± 2.8	230	Age, BMI	33.3%	Comprehensive hospital
Chen JY, 2014	Jan 2012 Jun 2013	850	Shenzhen	High	No	25.5 ± 1.75	24–28	82	Age, pregnancy history, BMI	9.65%	Comprehensive hospital
Gu Q, 2016	Jan 2013 Dec 2014	845	Jiangsu	High	Yes	–	24–28	140	Age	16.57%	Primary hospital
Chen XW, 2016	Jan 2014 Oct 2015	3098	Jiangsu	High	Yes	18–45	24–28	384	Age	12.4%	Primary hospital
Liu J, 2016	Jan–Jun 2014	1861	Shandong	Low	Yes	–	24–28	406	Age, BMI, family history of DM, pregnancy history, delivery history	21.82%	Maternity hospital
Li XJ, 2014	Jun 2013.6 to Mar 2014	1288	Tianjin	High	Yes	–	24–28	294	Age, BMI, family history of DM	22.8%	Maternity hospital
Hao BJ, 2014	Oct 2012 to Dec 2013	1250	Guangzhou	High	Yes	30.4 ± 4.32	24–28	165	Age	13.2%	Comprehensive hospital
Wu JH, 2016	Jan 2015 to Jun 2016	1723	Jiangsu	High	Yes	28.5 ± 4.3	25.3 ± 2.4	102	Age	5.92%	Primary hospital
Wang XR, 2014	Nov 2012 to Jun 2013	1132	Liaoning	High	Yes	–	24–28	136	Age, BMI, family history of DM, pregnancy history, delivery history	12.07%	Maternity hospital
Xu X, 2015	Jan 2012 to Dec 2013	2748	Jiangsu	High	Yes	–	24–28	540	Age, BMI, family history of DM	19.65%	Comprehensive hospital
Zeng SY, 2015	Jan 2013 Dec 2014	2032	Jiangxi	Low	Yes	–	24–28	225	Age, BMI, family history of DM, pregnancy history, delivery history	11.07%	Comprehensive hospital
Zhang CJ, 2016	Jan–Oct 2014	3134	Jiangsu	High	Yes	29.8 ± 2.9	22–40	596	Age, BMI, delivery history	19%	Maternity hospital
Guo HJ, 2016	Jan–Dec 2014	2588	Shanghai	High	No	–	24–28	241	Age, pregnancy history, delivery history	9.31%	Multiple pregnancy included, comprehensive hospital
Wang JJ, 2016	Jun–Nov 2013	965	Beijing	High	Yes	–	24–28	125	BMI, family history of DM	12.95%	Comprehensive hospital
Liu ZG, 2014	Apr 2013 to Jun 2014	951	Jiangxi	Low	Yes	1,742	24–28	182	Age	19.45%	Primary hospital

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Table 1 (*Continued*)

Study	Period	Sample (*n*)	Region (province)	Economic level†	Native	Maternal age (year)	Gestational age (weeks)	Case	Subgroup of risk factor‡	Prevalence	Other confounders
Liu HW, 2016	Jul 2011 to Apr 2014	1529	Hebei	Low	Yes	26.6 ± 5.29	24–28	275	Age	17.98%	Maternity hospital
Li QY, 2016	2012–2014	1035	Hebei	Low	Yes	29.5 ± 3.4	24–28	82	Age, family history of DM	7.92%	Comprehensive hospital, rural and urban population included
Feng L, 2016	2007–2015	21371	Beijing	High	Yes	–	24–32	2,577	Age	12.1%	Comprehensive hospital
Diao YF, 2016	Jun–Sep 2015	4431	Hebei	Low	Yes	–	24–28	372	Age, BMI	8.4%	Comprehensive hospital, rural and urban population included
Zhang J, 2016	Mar 2013 to Apr 2014	719	Sichuan	High	Yes	29.2 ± 4.4	24–28	124	Age, BMI	17.2%	Multicenter clinical study include primary and comprehensive hospital
Su RN, 2016	Jun–Nov 2013	15194	Beijing	High	Yes	28.3 ± 4.3	24–28	2,987	Age, BMI, family history of DM, delivery history	19.7%	Multiply pregnancy included, rural and urban population included, multicenter clinical study include primary and comprehensive hospital
Chen HT, 2017	Jun–Dec 2013	6224	Guangzhou	High	Yes	–	24–28	1,147	Age, BMI, family history of DM, delivery history	18.4%	Rural and urban population included, multicenter clinical study include primary and comprehensive hospital
Li GP, 2017	Jul 2014 to Jan 2015	1401	Zhejiang	High	Yes	–	24–28	156	Age, BMI	11.1%	Primary hospital
Mao LJ, 2015	May 2013 to Sep 2014	1595	Anhui	Low	Yes	26.69 ± 3.64	24–28	235	Age, BMI, pregnancy history, delivery history	14.7%	Comprehensive hospital, rural and urban population included

†The economic levels of the regions in the included papers had per capita annual incomes ranging from less than $US1,000 to $US30,000, and we used the per capita income of $US10,000 as a boundary between low and high. ‡Subgroup of risk factor referred to the article included in the meta-analysis provided enough case information in different subgroups (the number of gestational diabetes mellitus patients in maternal age, body mass index [BMI], family history of diabetes mellitus (DM), pregnancy history, delivery history).

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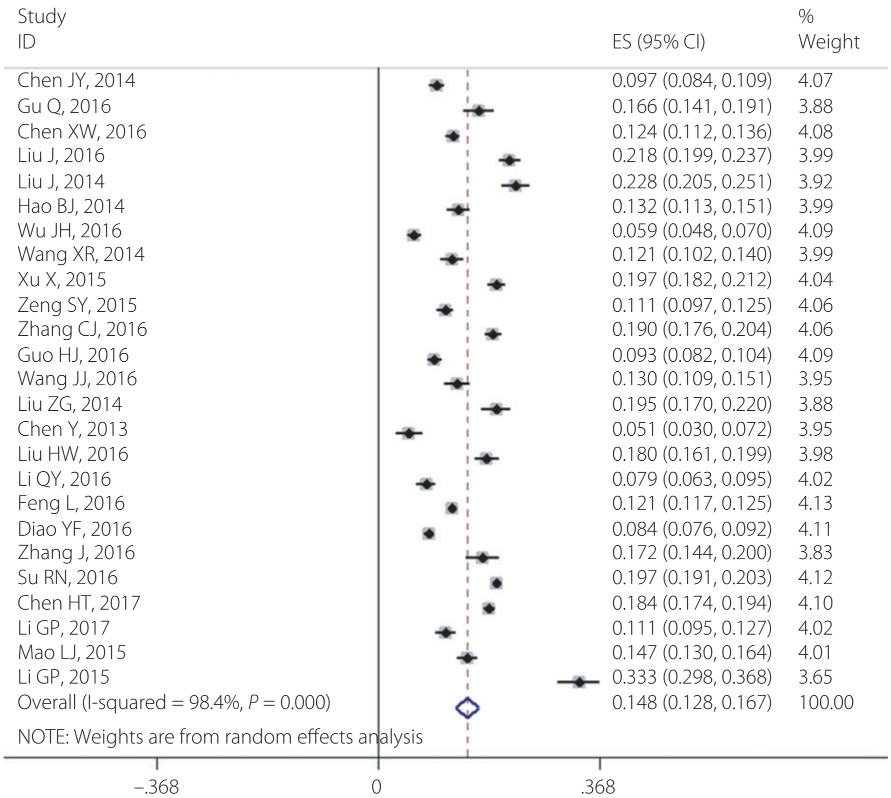

Figure 2 | Forest plots for total incidence of gestational diabetes mellitus (GDM) in mainland China. The diamond represents the pooled odds ratio and 95% confidence interval.

study in Figure 3. To determine whether potential publication bias existed in the reviewed literature, Egger's test was also carried out. The results of Egger's test (P = 0.437) did not suggest the existence of publication bias.

DISCUSSION

As early as 1964, O'Sullivan and Mahan[32] suggested screening for high-risk pregnant women and, for the first time, proposed diagnostic criteria for GDM, whereby patients should be diagnosed with GDM when blood glucose levels are equal to or greater than boundary values for fasting, 1, 2 and 3 h after oral glucose of 5.0, 9.2, 8.1 and 7.0 mmol/L, respectively, according to the 100-g OGTT. In 1973, O'Sullivan *et al*[33] proposed a 50-g OGTT; if the blood glucose level was ≥7.2 mmol/L 1 h after glucose load, then the 100-g OGTT was carried out. The results of a number of subsequent studies showed that for GDM screening, it is most suitable to use 7.8 mmol/L as the boundary value for a blood glucose level at 1 h after glucose load, a value that is still used today. In 1979, the National Diabetes Data Group modified the diagnostic criteria of GDM based on O'Sullivan's standard[34]. In this case, the patient should be diagnosed with GDM when plasma glucose levels are ≥2 boundary points of the values for fasting, 1, 2 and 3 h after glucose load of 5.8, 10.6, 9.2 and 8.1 mmol/L, respectively. In 1982, Carpenter[35] recommended that the plasma glucose boundary values for fasting, 1, 2 and 3 h after taking glucose be 5.3, 10.0, 8.6 and 7.8 mmol/L, respectively, with GDM diagnosis at levels ≥2 boundary points. In 1998, this standard was recommended for application by the ADA, but the glucose load was changed from 100 to 75 g, and the 3-h blood glucose value was removed. As guidelines for the diagnosis and classification of diabetes were issued by the WHO in 1965, in 1999, it recommended after three discussions that patients should be diagnosed with GDM when fasting plasma glucose is ≥7.0 mmol/L or 2-h blood glucose is 11.1 mmol/L. Although the NDGG, ADA and WHO standards have been used for many years, for the past 50 years, the diagnostic methods and standards for GDM have been the subject of controversy. Both the standard proposed by O'Sullivan and the later National Diabetes Data Group or ADA standard are all based on the risk of a pregnant woman developing type 2 diabetes, but these standards lacked any consideration of gestational outcome. The WHO standard, which directly evolved from the non-pregnant standard, also had shortcomings when it was directly applied to pregnancy. In 2010, the IADPSG proposed a new standard for GDM diagnosis based on the HAPO study, and in this same year, the ADA

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Table 2 | Random effects analysis of multivariate risks of prevalence of gestational diabetes mellitus (GDM) in mainland China

Category	Subgroup	No. study	Prevalence % (95% CI)	Sample (*n*)	I^2	*P*
Total		25	14.8 (12.8–16.7)	79,064	0.984	
Age (years)	>35	20	26.7 (23.2–30.3)	4,493	0.838	<0.01
	<35	20	13.4 (11–15.7)	61,689	0.988	
BMI	Normal	13	14.9 (11.7–18.1)	32,057	0.984	<0.01
	Obese	13	30.3 (25.9–34.7)	7,623	0.931	
Family history of DM	Yes	9	32.9 (27.5–38.4)	3,012	0.807	<0.01
	No	9	13.7 (9.9–17.6)	23,869	0.984	
Pregnancy history	Yes	5	12.1 (9.1–15.0)	4,599	0.898	0.33
	No	5	15.2 (10.8–19.6)	4,609	0.959	
Delivery history	Yes	4	20.2 (18.3–22.2)	11,477	0.788	0.03
	No	4	16.5 (13.7–19.3)	14,429	0.918	
Economic level	High	16	14.8 (12.1–16.8)	64,530	0.984	0.53
	Low	9	15.4 (11.2–19.6)	14,534	0.983	
Area	Southern	14	20.3 (6.9–33.8)	29,158	0.999	0.62
	Northern	11	15.7 (12.4–19.0)	49,906	0.989	

BMI, body mass index; CI, confidence interval; DM, diabetes mellitus.

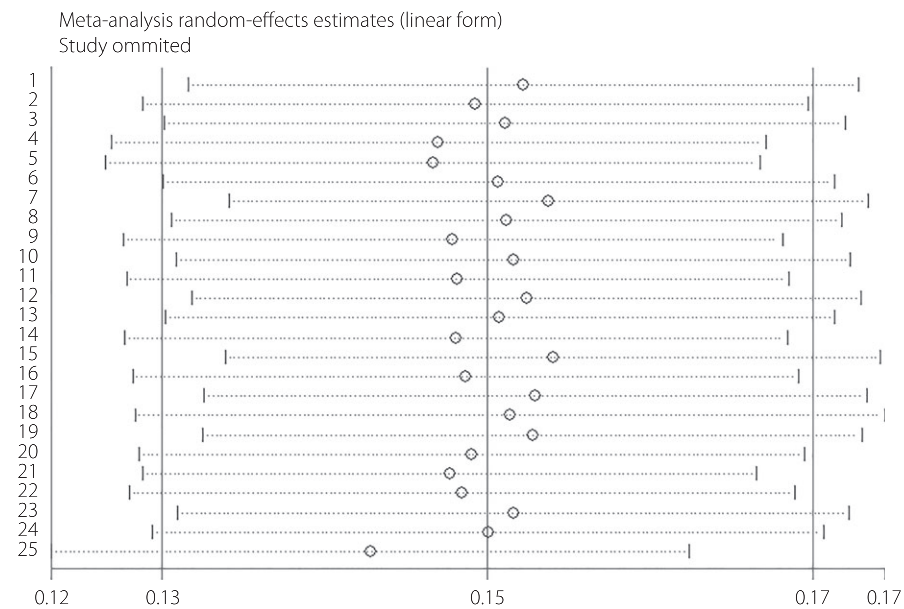

Figure 3 | The results of sensitivity analysis of the meta-analysis.

recommended adoption of the IADPSG standard as the new diagnostic standard for GDM. The 2011 edition of the GDM health industry standards by the Ministry of Health of China, the 2013 edition of the Chinese Guidelines for the Diagnosis and Treatment of Diabetes Mellitus, and the 2014 edition of the Guidelines for the Diagnosis and Treatment of Gestational Diabetes Mellitus all adopted the IADPSG standard.

The present study is the first meta-analysis of the incidence of GDM according to the IADPSG standard in mainland China. This study found an incidence of GDM in mainland China of 14.8%, which is similar to the reported incidence of GDM in Hong Kong – 14.4% by the HAPO multicenter study[36]. Although the incidence of GDM in mainland China is lower than that in the USA, Singapore and other developed nations, considering China's huge population, it is speculated that China might have the largest number of GDM patients. In addition, the incidence of GDM in China shows a clear upward trend. For example, the incidence of GDM in Tianjin, China, increased almost threefold from 1999 to 2008. Therefore, closer attention should be paid to GDM in China[37].

The results of subgroup analysis showed that the incidence of GDM in older women in China was 26.7%, though the

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incidence of GDM in younger women was just 13.4%; thus, the incidence of GDM among older women was approximately twice that among younger women. As China's fertility policy changes, divorce and remarriage rates increase, and multiparous women might have more children due to the death of offspring as a result of disease or accidents; thus, the incidence of advanced maternal age among pregnant women will continue to increase in China. Apart from the factor of age, the incidence of GDM in women with a family history of diabetes was threefold as high as that of women without a family history, suggesting that a family history of diabetes significantly increases the incidence of GDM. In addition, overweight or obesity also showed significant impacts on the incidence of GDM. Conversely, we found that the per capita economic levels of the 21 cities included did not influence the incidence of GDM. We suggest that this apparent lack of influence might be related to the mixed effects of diet, lifestyle, region and many other factors.

China is a multi-ethnic country, with the Han nationality as the main group. In the present study, the incidence of GDM among women of the Kirgiz nationality of Xinjiang was lower than that of the Han nationality, but only one study was included. In addition, some studies have found the incidence of GDM in multiparous women to be higher than that of women with a single pregnancy; again, the sample size was small, and thus, further study is required.

The limitation of the present study was that the main data from the studies included were from large-scale comprehensive hospitals and specialist hospitals; as only a few studies were multicenter, multilevel studies, the data lacked results from grass-roots hospitals. Furthermore, the study participants were mainly from urban populations; studies on the prevalence of GDM in pregnant women in China's rural areas are rare, which will impact the calculation of the total prevalence of GDM in mainland China. We hope that there will be more epidemiological studies on GDM in grass-roots hospitals and in rural populations in the future.

To the best of our knowledge, the present systematic review is the first to estimate the pooled prevalence of GDM among women in mainland China according to IADPSG criteria. The results of the present systematic review suggest that the total incidence of GDM in mainland China is 14.8%, indicating that China might have the largest number of GDM patients. Therefore, more attention should be paid to the prevention and control of GDM.

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DISCLOSURE

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Data S1. Preferred reporting items for systematic review and meta-analyses checklist.

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