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REVIEW ARTICLE

Maternal height and risk of gestational diabetes: a systematic review and meta-analysis

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Abstract

Aims Identifying women at high risk of developing gestational diabetes mellitus (GDM) is a public health interest. This study aims to investigate the association between maternal height and risk of GDM through meta-analysis.
Methods We retrieved the studies that assessed maternal height in relation to GDM. Pooled risk estimates of the included articles and their 95% confidence intervals (95% CIs) were calculated using a fixed- or random-effects model. Subgroup analyses were conducted according to study design and study location. Quality of studies was determined using the Newcastle–Ottawa Scale. Publication bias was detected using the Egger's and Begg's tests.
Results A total of 10 studies including 7 cohort and 3 cross-sectional studies with a total of 126,094 women were included for meta-analysis. Combined, each 5-cm increase in height was associated with about 20% reduction in risk of GDM [pooled odds ratio = 0.80, (95% CI 0.76, 0.85)]. The analysis revealed high heterogeneity between studies which dissolved after subgroup analysis by study design. This significant association did not differ between Asian and non-Asian populations. Egger's and Begg's tests showed little evidence of publication bias.
Conclusions The present meta-analysis supports the conception that short stature is associated with GDM. Further studies of high quality are needed to confirm the findings.

Keywords Height · Stature · Gestational diabetes · Meta-analysis

Introduction

The prevalence of gestational diabetes mellitus (GDM) has been increasing over time [1]. GDM carries a high risk of adverse pregnancy outcomes and long-term consequences for both mothers and their offspring [2]. For instance, mothers with a history of GDM were more likely to develop type 2 diabetes [3, 4] and cardiovascular disease [5], and their children were also at an increased risk of insulin resistance and obesity [6, 7]. Therefore, identifying women at risk of GDM with the aim of applying monitoring approaches and prevention strategies is considered a public health interest.

Advanced age at pregnancy, obesity, and family history of diabetes are well-known risk factors of GDM [8]. Emerging evidence has suggested a link between height and risk of GDM. Anastasiou et al. reported that short stature was inversely correlated with glucose tolerance among pregnant women [9]. Subsequent studies showed a higher risk of GDM among women with short stature, though the magnitude of the association differed between studies [10–19].

Previous studies examining height and GDM had several limitations, including limited sample size and lack of control for important risk factors. Furthermore, individual studies used different cutoffs to define short and tall participants. For example, in the study by Rudra et al., subjects ≤ 160 cm were defined as having short stature [13], while Li et al. [18] assigned subjects ≥ 158 cm to the tall stature category. Herein, we aimed to study whether women's height is associated with GMD by conducting a meta-analysis of available evidence.

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Methods

Searching strategy

The present meta-analysis was reported according to the checklist of MOOSE [20] and the checklist of PRISMA [21]. Two investigators independently searched MEDLINE (PubMed), Web of Science, and Cochrane Library for potential studies published in English before January 31, 2019, using the following search terms: (height OR stature) AND (gestational diabetes mellitus OR diabetes mellitus in pregnancy OR pregnancy diabetes mellitus). No time restrictions were imposed. We searched for additional studies by a manual review of the reference lists of retrieved articles. Only published full-text articles were searched, and no effort was made to identify unpublished studies.

Eligibility criteria

We first scanned the titles and abstracts identified by the electronic search before conducting a full-text search in case of uncertainty about relevance. Studies were included for meta-analysis if they met the following criteria: The study was conducted in humans, and risk estimates in the form of odds ratios (ORs) or relative risks (RRs) with their 95% confidence intervals (CIs) between maternal height and GDM were provided.

Study selection

The authors conducted the literature search independently by reviewing the full manuscript of all articles detected by the primary search. Then, the extracted articles were subjected to the above-mentioned eligibility criteria to reach a list of studies to be included in this meta-analysis. Relevant information was extracted from the selected studies: last name of the first author, publication year, country, sample size, study design, cutoffs of height, assessment methods of GDM, adjusted risk estimate with corresponding 95% CIs, and quality of study as determined using the Newcastle–Ottawa Scale. When a given study presented different models that adjusted for several potential confounders, we included the model that adjusted for the largest number of confounders. Two investigators individually extracted the data and assessed the study quality, with differences resolved bydiscussion.

Statistical analysis

ORs and their CIs were used as measures of the association. RR was considered as OR directly. We converted the ORs of GDM for each 5-cm increment in height if they were reported for each 1-cm increment. I^2 was calculated to test statistical heterogeneity across studies [22], and a fixed-effects model or in the presence of heterogeneity a random-effects model was used to compute the pooled ORs [23]. Subgroup analyses were conducted according to study design (cross-sectional, retrospective cohort, and prospective cohort studies) and study location (Asia, Europe or the United States). We conducted a sensitivity analysis to identify the influence of a single study on the pooled ORs by removing studies one by one and combining the remainders in separate analyses. Publication bias was assessed using Begg's test [24] and Egger's test [25]. All analyses were conducted using STATA 12.

Results

The primary literature search retrieved 1273 studies, and most of them were excluded because they were duplication reports ($n = 631$), reviews ($n = 10$), or not relevant ($n = 590$). Among 42 studies for full-text review, 32 studies were excluded because they did not report the risk estimates and corresponding CIs for the association. Finally, 10 studies were included for this meta-analysis (Fig. 1).

Characteristics of the studies are shown in Table 1. Of them, 5 were prospective cohort studies, 2 were retrospective cohort studies, and 3 were cross-sectional studies. They were published between 1998 and 2018, with a total population of 126,094 women. Among them, 4 studies were conducted in Asia, 3 in Europe, 2 in the USA, and 1 in Brazil. The cutoffs used to differentiate between shortest and tallest

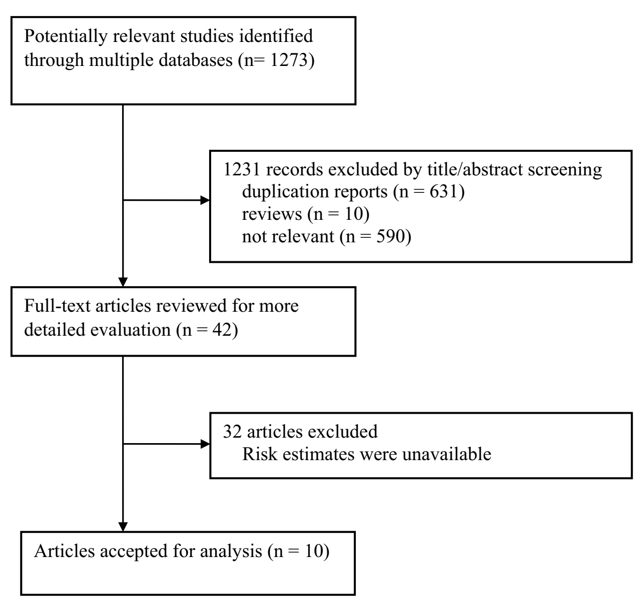

Fig. 1 Flowchart of the study selection process

Table 1 Characteristics of the included studies

References	Country	Sample	Design	Diabetes Diagnosis	Shortest versus tallest category of height	Covariates	Quality
Jang et al. [10]	Korea	9005	CS	OGTT	≤ 157 versus ≥ 163	1, 2	Poor
Branchtein et al. [11]	Brazil	5564	PC	OGTT	≤ 151 versus ≥ 160	1, 2, 3, 4, 5, 6, 7	Good
Yang et al. [12]	China	9741	CS	OGTT	NA	1, 2, 4, 5, 6, 7	Fair
Rudra et al. [13]	USA	1644	PC	OGTT	≤ 160 versus > 170	1, 2, 3, 4	Good
Ogonowski et al. [14]	Poland	2841	RC	OGTT	NA	1, 2, 6, 7	Fair
Brite et al. [15]	USA	135,861	RC	Medical record	< 157.5 versus > 167.7	1, 2, 3, 4	Good
Syngelaki et al. [16]	UK	75,161	CS	OGTT	NA	1, 2, 3, 6, 7	Fair
Mendoza et al. [19]	Europe	971	PC	OGTT	≤ 169 versus > 169	1, 2, 3, 4, 5, 6, 7	Good
Li et al. [18]	China	19,962	PC	OGTT	< 158 versus ≥ 158	1, 3, 4, 5, 6	Good
Li et al. [17]	China	6941	PC	OGTT	≤ 158 versus > 164	1, 2, 4, 5	Good

Covariates: 1: age, 2: weight, 3: race/ethnicity, 4: education, 5: parity, 6: family history of diabetes, 7: previous gestational diabetes

CS cross-sectional, *NA* not available, *OGTT* oral glucose tolerance test, *PC* prospective cohort, *RC* retrospective cohort

categories varied among the studies. All included studies but one used the oral glucose tolerance test to diagnose GDM. Most adjusted covariates included age, weight, race/ethnicity, education level, parity, family history of diabetes, and previous history of GDM.

Eight studies provided ORs of GDM for each 1-cm or 5-cm increment in height, and all of them reported a significant inverse association between height and GDM. All combined, each 5-cm increment in height was associated with about 20% reduction in risk of GDM (pooled OR = 0.80, 95% CI 0.76, 0.85) (Fig. 2). There was a high degree of heterogeneity among studies ($I^2 = 72.7\%$, p value for heterogeneity = 0.001). Stratified analysis by study design obtained ORs (95% CI) of 0.74 (0.71, 0.78), 0.80 (0.78, 0.82), and 0.89 (0.83, 0.95) for the cross-sectional, retrospective cohort, and prospective cohort studies, respectively. We observed no evidence of heterogeneity within each study design (all $I^2 < 10\%$, all p value for heterogeneity > 0.35).

We further conducted a stratified analysis by study area. The results were following: pooled ORs were 0.82 (95% CI 0.72, 0.94) in Asia ($n = 3$) and 0.75 (95% CI 0.72, 0.79) in Europe or the USA ($n = 4$), respectively. There was a

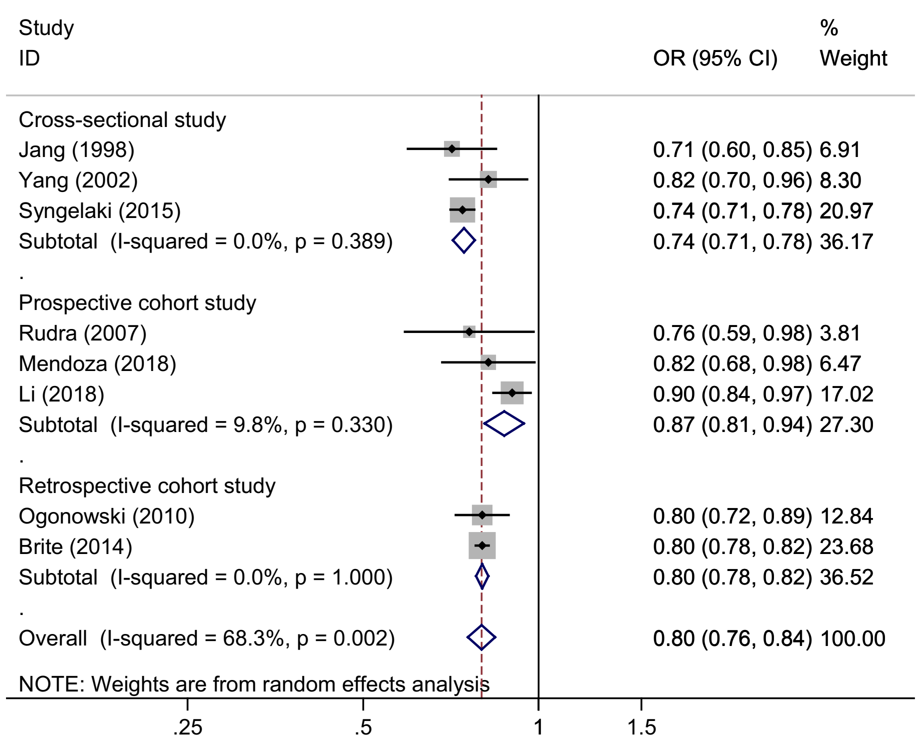

Fig. 2 Meta-analysis of the studies examining the association between height and risk of gestational diabetes [odds ratio (OR) for each 5-cm increment in height]

significant heterogeneity among studies conducted in Asia (I^2 = 69.2%, *p* value for heterogeneity = 0.04) but not in studies conducted in Europe or the USA (I^2 = 0, *p* value for heterogeneity = 0.45). Although the association appeared to be weaker in Asian studies, the difference did not reach statistical significance (*p* value for interaction = 0.31). Also, results of sensitivity analysis indicated that no single study had a substantial impact on the overall risk, with pooled ORs ranging from 0.78 (95% CI 0.74, 0.82) to 0.82 (95% CI 0.77, 0.87). Egger's and Begg's tests showed little evidence of publication bias (both *p* values for publication bias > 0.65).

In addition, we conducted a meta-analysis by combining ORs for the highest versus the lowest category of height. As shown in Fig. 3, women in the tallest category, compared with those in the shortest category had a lower risk of GDM (pooled OR = 0.53, 95% CI 0.38, 0.73), with strong evidence of heterogeneity observed (I^2 = 88.6%, *p* value for heterogeneity < 0.001). Heterogeneity disappeared among studies with a prospective cohort design (I^2 = 20%, *p* value for heterogeneity = 0.29).

Discussion

In this meta-analysis, we found that each 5-cm increment in height was associated with about 20% reduction in risk of GDM. The results were stable as shown by the stratified and sensitivity analyses and were independent of the study design and study area.

We observed a high degree of heterogeneity between studies, which was not unexpected given the different study design of individual studies, the wide variations in the racial and socio-demographic characteristics of the subjects included. By a stratified analysis, we were able to identify study design as a possible contributor to the heterogeneity observed. In addition, a relatively weaker association among prospective cohort studies indicated that the results from cross-sectional and retrospective cohort studies might have been affected by the limitations of such study design, including the lack of control for important confounders, as shown in Table 1, and possibly the selection and misclassification biases.

In the subgroup analysis by study area, the association between height and GDM remained significant and did not significantly differ between Asian and non-Asian populations, suggesting that the height–GDM association may be independent of ethnicities. In agreement with our finding, Brite et al. detected an inverse association between height and GDM among white, black, Hispanic, and Asian USA women. However, in their study, the magnitude of the association varied significantly across ethnicities, with a significantly stronger association observed in Asian populations than that in other populations [15].

Short stature has been shown to be associated with increased risk of many non-communicable diseases. For example, previous meta-analyses showed that the shortest women had a 14% higher likelihood of type 2 diabetes compared to the tallest women [26] and that increased height led to a reduction in the risk of coronary heart

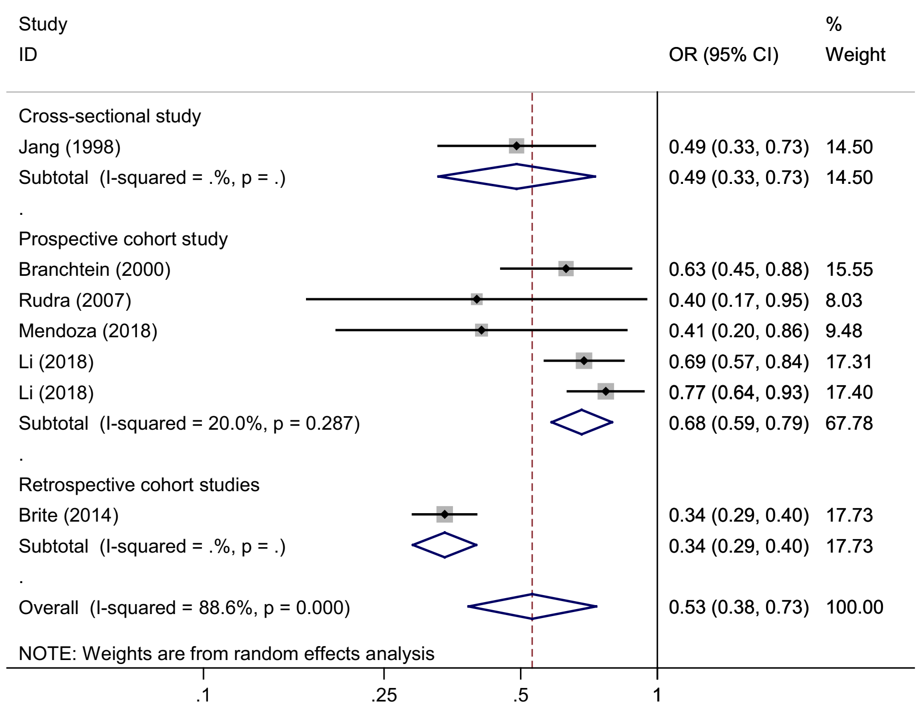

Fig. 3 Meta-analysis of the studies examining the association between height and risk of gestational diabetes [odds ratio (OR) for highest versus lowest category of height]

diseases [27]. In addition, a recent meta-analysis of 20 prospective studies reported that each 5-cm increment in height was associated with a 7% and 12% reduction in the risk of stroke among men and women, respectively [28].

Although the mechanisms underlying the association between short stature and risk of GDM are uncertain, the theory of shared risk factors can partially explain the findings. Nutritional, socioeconomic, and genetic factors have significant impacts on women's height and may affect their susceptibility to GDM as well [11]. It has been reported that inadequate childhood nutrition increases the risk of both short stature and diabetes during adulthood [29] and that the insufficient release of growth hormones, attributed to childhood malnutrition, is associated with short stature and impaired glucose tolerance in adulthood [30]. The role of socioeconomic status is supported by earlier studies which have shown that low socioeconomic position during childhood was a risk factor for short stature and diabetes [31, 32]. In contrast, Li et al. [17] conducted subgroup analysis by educational level and detected an inverse association between height and GDM across all subgroups suggesting a relationship between short stature and GDM regardless of the educational level.

Previous cross-sectional studies showed that adult short stature was associated with obesity [33, 34], which is also an established risk factor of GDM. On the other hand, there is little evidence from prospective studies examining whether adult height is independently associated with weight gain or risk of obesity. Such evidence, if any, could support the notion that short stature increases the risk of GDM mediated by weight gain and obesity. Besides, short stature and impaired glucose tolerance may share some genetic risk factors. For example, one study showed that participants who carried the risk alleles in the gene for the insulin-like growth factor I associated with a shorter height and increased risk of type 2 diabetes [35].

It should be noted that this meta-analysis had some limitations. Firstly, each study had its unique definition for short stature which may have resulted in a high degree of heterogeneity. We, therefore, conducted the main analysis by combining the risk estimates for every 5-cm increment in height, which to some extent reduced the heterogeneity. Secondly, several studies used self-reported height, which most likely causes measurement error. Thirdly, several studies did not adjust their results for potential confounders such as educational level, family history of diabetes, and previous history of GDM. Thus, residual confounding remained an alternative explanation for the observed association. Fourthly, in addition to the limited number of studies included, half of them were of cross-sectional or retrospective cohort design which may be more prone to biases than prospective studies. Finally, publication bias is always a threat to the validity of meta-analysis although we observed little evidence of such bias by the formal tests.

In conclusion, the results of the present meta-analysis support the conception that short stature is associated with GDM. Further studies of high quality are needed to confirm the findings of this study.

Author contributions AA collected the data, analyzed the data, and wrote the manuscript. JYD designed the study, collected the data, analyzed the data, conducted the technique review, and reviewed and edited the manuscript. JYD is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed consent For this type of study informed consent is not required.

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