

# Association between body mass index in the first half of pregnancy and gestational diabetes: A systematic review

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## Abstract

Gestational diabetes mellitus is a more common complication in pregnancy and rising worldwide and screening for treating gestational diabetes mellitus is an opportunity for preventing its complications. Abnormal body mass index is the cause of many complications in pregnancy that is one of the major and modifiable risk factors in pregnancy too. This systematic review aimed to define the association between body mass index in the first half of pregnancy (before 20 weeks of gestation) and gestational diabetes mellitus. Web of Science, PubMed/Medline, Embase, Scopus, ProQuest, Cochrane library, and Google Scholar databases were systematically explored for articles published until April 31, 2022. Participation, exposure, comparators, outcomes, study design criteria include pregnant women (P), body mass index (E), healthy pregnant women (C), gestational diabetes mellitus (O), and study design (cohort, case–control, and cross-sectional). Newcastle–Ottawa scale checklists were used to report the quality of the studies. Eighteen quality studies were analyzed. A total of 41,017 pregnant women were in the gestational diabetes mellitus group and 285,351 pregnant women in the normal glucose tolerance group. Studies have reported an association between increased body mass index and gestational diabetes mellitus. Women who had a higher body mass index in the first half of pregnancy were at higher risk for gestational diabetes mellitus. In the first half of pregnancy, body mass index can be used as a reliable and available risk factor to assess gestational diabetes mellitus, especially in some situations where the pre-pregnancy body mass index is not available.

## Keywords

Gestational diabetes mellitus, body mass index, pregnancy, BMI

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## Introduction

Gestational diabetes mellitus (GDM) is a more common complication in pregnancy and is defined as any degree of carbohydrate intolerance, which is first recognized during pregnancy<sup>1</sup> and considered to be a major public health concern.<sup>2</sup> The prevalence of GDM is rising worldwide, and varying ranges from 1% to 14%. According to the International Diabetes Federation (IDF), almost 21.3 million (16.2%) of births were affected by maternal hyperglycemia, with 84.6% of cases caused by GDM.<sup>3</sup> GDM was described using the International Association of the Diabetes and Pregnancy Study Group's criteria based on any of the following cut-off points: fasting plasma glucose (FPG)  $\geq 5.1$  mmol/L, 1 h plasma glucose  $\geq 10.0$  mmol/L, or 2 h plasma glucose  $\geq 8.5$  mmol/L.<sup>4</sup>

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Several factors that increase the risk of developing GDM include older age, previous GDM, body mass index (BMI)  $> 30 \text{ kg/m}^2$ , family history of diabetes, previous macrosomic baby weighing  $\geq 4.5 \text{ kg}$ , and ethnicity.<sup>5</sup> GDM increases the risk of neonatal birth trauma, hypoglycemia, respiratory distress syndrome, hyperbilirubinemia, hypocalcemia, polycythemia, and even mortality.<sup>6,7</sup> Screening for treating GDM is an opportunity for preventing its complications.<sup>8</sup> According to the World Health Organization (WHO), Maternal overweight and obesity are defined as BMI of 25–29.9 and  $\geq 30 \text{ kg/m}^2$ , respectively.<sup>9</sup> During pregnancy, high BMI has been correlated with noxious maternal and neonatal outcomes and is a known risk factor for GDM and insulin resistance.<sup>10</sup> A normal pregnancy is characterized by a 50%–60% physiological decrease in insulin sensitivity.<sup>11</sup> Studies reported that the probability of GDM increased as maternal weight gain increased, especially in early pregnancy.<sup>12</sup> The risk of GDM among obese pregnant women was higher than in those who were overweight which shows that BMI can be used as a predictive factor.<sup>13</sup>

Some studies have shown that weight gain in the first two trimesters is consist of more fat mass and the patients with higher BMI gain a higher fat mass,<sup>14,15</sup> which could affect subsequent maternal insulin resistance.<sup>15</sup> Furthermore, maternal height as a component of BMI could independently influence birth outcomes.<sup>16</sup> Height is associated inversely with the level of insulin resistance in adults without diabetes, regardless of BMI and age. Height is also shown to be an independent risk factor for the development of GDM, and this association is strongest among Asians.<sup>14</sup> Different studies demonstrated that short stature could be a risk factor for GDM.<sup>17</sup> In nonpregnant women, BMI and high body fat mass are associated with elevated levels of serum interleukin-6 (IL-6). IL-6 is also secreted by the placenta during pregnancy, which results in a chronic inflammatory process in adipose tissue and further aid in the development of pregnancy-induced insulin resistance.<sup>18</sup>

The latest systematic review and meta-analysis of 13 English or French publications aimed to show the effect of BMI on pregnancy outcomes, they reported that women with BMI  $> 40 \text{ kg/m}^2$  were at increased risk for GDM.<sup>19</sup> The main advantage of this study over other studies is that we assessed 18 studies, searching with no language filtering, to evaluate the association between BMI of the first half of pregnancy and GDM, although a previous cohort study conducted to examine the body composition of pregnant women at 17 weeks of gestation and the risk of GDM in large number of pregnant women were shown to increase BMI significantly increases the risk of GDM. We also reviewed this cohort study with a high sample size in this present study. According to the description provided and the relationship between gestational diabetes and BMI in pregnancy, this systematic review aimed to determine the association between BMI in the first half of pregnancy (before 20 weeks of gestation) and GDM.

## Methods

The guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) (2020) were followed while reporting the study protocol.<sup>20</sup> The protocol of this study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) at the National Institute for Health Research. The registration Number in PROSPERO is CRD42021241049.

### Search strategy

Web of Science (WoS), PubMed/Medline, Embase, Scopus, ProQuest, Cochrane library, and Google Scholar databases were systematically explored for relevant articles. In addition, we searched according to Mesh keywords:

1. “Gestational diabetes” [tiab], OR “GD” [tiab], OR “Gestational Diabetes Mellitus” [tiab], OR “GDM” [tiab], OR “pregnancy-induced diabetes” [tiab], OR “Diabetes Mellitus, Gestational” [tiab], OR “Diabetes, Pregnancy-Induced” [tiab], OR “Diabetes, Pregnancy Induced” [tiab]
2. “Body mass index” [tiab], OR “BMI” [tiab], OR “Index, Body Mass” [tiab], OR “Quetelet’s Index” [tiab], “Quetelet Index” [tiab], OR “Queteletes Index” [tiab]
3. “Pregnancy” [tiab], OR “Pregnancies” [tiab], OR “Gestation” [tiab]
4. “risk factor” [tiab], OR “risk score” [tiab], OR “health correlate” [tiab]
5. #1 AND #2
6. #1 AND #2 AND #3 AND #4

### Time of searching

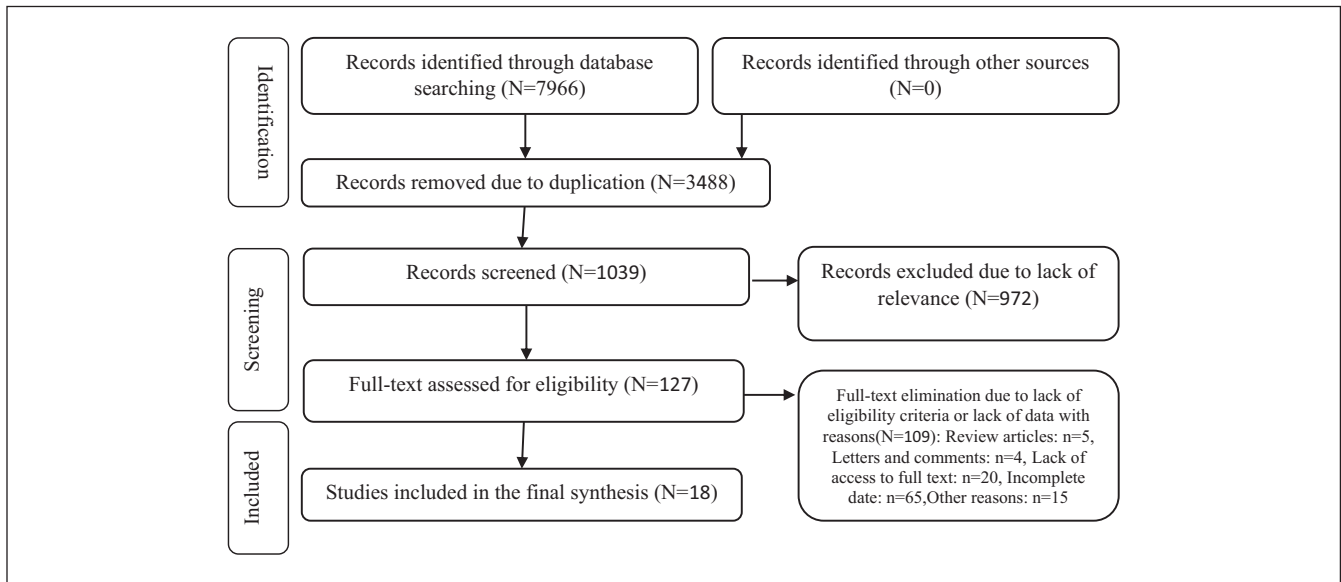
Listed databases were searched for relevant studies published until 31 April 2022 based on PRISMA guideline.

### Study selection

The two authors (F.A.R. and F.A.) independently reviewed qualified articles and any disagreements by consulting a third author. The title and abstract of all studies reviewed. Duplicated studies were identified and deleted using Endnote software version 8X. The full texts of relevant articles were examined based on the mentioned criteria (Figure 1).

### Eligible criteria

The study inclusion criteria were as follows: women with singleton pregnancy in the first half of pregnancy (lower than 20 gestational weeks) and with age 18 and more, cohort, case–control, and cross-sectional studies that assessed BMI in the first half of pregnancy (20 gestational weeks and lower), diagnosis of GDM according to the criteria of each



**Figure 1.** PRISMA flowchart of selected studies.

study, for example, WHO, American Diabetes Association (ADA), and so on. BMI measurement by measuring the pregnant women's weight and height in the first half of pregnancy by weight formula divided by height squared, and studies that divided BMI into four groups: lower than 18.5 (thin), 18.5–24.9 (normal), 25–29.9 (overweight), and more than 30 (obese).

The study exclusion criteria include multiple pregnancies, in vitro fertilization (IVF)-conceived pregnancies, having a disease, such as pre-pregnancy diabetes, studies, such as comment, letter, and review, and studies with contradictory data, such as BMI measurement after the second half of pregnancy (20 gestational weeks and more).

Studies including observational design were included. Also, studies met the inclusion criteria if they were published until 31 April 2022. There was no language filtering. If the language used in studies is other than Persian or English, we asked a translator to translate the article.

The studies were selected if their participants: pregnant women with GDM and single pregnancy. Participation, exposure, comparators, outcomes, study design (PECOS) criteria include: pregnant women (P), BMI (E), healthy pregnant women (C), GDM (O), and study design (cohort, case-control, and cross-sectional) (S).

### Quality assessment

The quality of each study was determined according to the Newcastle–Ottawa scale (NOS)<sup>21</sup> (Table 1). A maximum of ten stars can be given to each study based on the NOS. The validity and reliability of this tool have been proven in various studies. NOS scoring for cross-sectional study included: very good: 8–10 stars, good: 6–7 stars, satisfactory: 4–5 stars, and

unsatisfactory: 3–0 stars. NOS scoring for cohort and case-control studies included: very good: 7–9 stars, good: 5–6 stars, satisfactory: 4, and unsatisfactory: 3–0 stars.<sup>22</sup>

### Data extraction

Three researchers extracted the data. Two researchers (F.A.R. and F.A.) independently searched for relevant scientific publications, carried out validity assessments, and resolved any disagreements by consulting a third researcher (E.K.).<sup>40</sup> Data were collected as follows:

1. Research information (author, reference, location, type of study, sample size, diagnostic criteria of GDM, and accompanying factors with BMI)
2. Characteristics of the participants (maternal age)
3. Details of GDM and comparison group (number of groups, BMI, and time of applying GDM test)
4. Outcome measures (GDM)

### Result

The initial search yielded 7966 results. The eligibility of these articles was independently evaluated by two authors (F.A.R. and F.A.) and any disagreements were resolved by consensus (E.K.). In the first stage, 3488 articles were excluded due to being irrelevant or duplicated. After reviewing the titles and abstracts of the remaining articles, 972 more articles were excluded. In the evaluation of the full texts, 109 out of the remaining 127 articles were excluded due to being ineligible (review articles:  $n=5$ , letters and comments:  $n=4$ , lack of access to full text:  $n=20$ , incomplete date:  $n=65$ , and other reasons:  $n=15$ ). Finally, a total of 18 eligible articles were reviewed.

Table 1. Quality assessment of the studies by the “Ottawa Newcastle” scale.

Study, Ref	Zhang et al. <sup>23</sup>	Zhang et al. <sup>24</sup>	Zhang et al. <sup>25</sup>	Yong et al. <sup>26</sup>	Deniz <sup>26</sup>	Gao et al. <sup>27</sup>	Li et al. <sup>2</sup>	Rezaei et al. <sup>28</sup>	Pratt et al. <sup>29</sup>	Nassr et al. <sup>30</sup>	Hashemi-Nazari et al. <sup>31</sup>	Han et al. <sup>32</sup>	Hao and Lin <sup>33</sup>	Basraon et al. <sup>34</sup>	McDonald et al. <sup>35</sup>	Makgoba et al. <sup>36</sup>	Sweeting et al. <sup>37</sup>	Sawidou et al. <sup>38</sup>	Agüero-Domenech et al. <sup>39</sup>
Selection	***	**	***	***	***	**	***	***	***	***	***	***	***	***	***	**	**	***	**
Comparability	**	***	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
Outcome	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**

Out of a total of 18 related studies, 15 were cohort studies,<sup>2,23–36</sup> two were case–control studies,<sup>37,38</sup> and one was cross-sectional.<sup>39</sup> The frequency of countries in which the articles were conducted is as follows: China,<sup>6</sup> Australia,<sup>3</sup> Iran,<sup>2</sup> the United States,<sup>2</sup> the United Kingdom,<sup>2</sup> Malaysia,<sup>1</sup> Turkey,<sup>1</sup> and Spain.<sup>1</sup> A total of 41,017 pregnant women were in the GDM group and 285,351 pregnant women in the normal glucose tolerance (NGT) group. Women were 18 years old and older. Screening for GDM was performed in the second and third trimesters of pregnancy. And BMI was measured during the first half of pregnancy. The data obtained from studies are given in Table 2.

Studies have shown that women with diabetes were more likely to be overweight, and a BMI greater than 25 in the first half of pregnancy significantly increased the risk of abnormal glucose tolerance in screening for more than 24 weeks and GDM. The results of studies show that higher BMI in pregnancy is associated with GDM and can be considered a risk factor for it. Being overweight and especially obese (BMI  $\geq 25$ ) and morbid obesity (BMI  $\geq 50$ ) increases the risk of developing GDM in the T1 of pregnancy. Obviously, T1 BMI can be considered as a risk factor for GDM in the later stages of pregnancy because the weight gain in the first trimester of pregnancy is not enough to affect the BMI, so that, it is a useful indicator that the pregnant mother does not have weight before pregnancy or does not remember it.

### Accompanying factors

Demographic factors, such as maternal age, parity, smoking and alcohol use, family history of diabetes, education, social and economic status, previous history of gestational diabetes, ethnicity, history of miscarriage, and type of delivery are associated with gestational diabetes. Underlying diseases, such as hypertension, a history of preeclampsia, anemia, thyroid disease, polycystic ovary syndrome (PCOS), and a history of macrosomic birth can affect gestational diabetes. Other anthropometric indicators, such as body fat mass, waist circumference (WC), weight gain per week of pregnancy, and waist to hip ratio are also associated with gestational diabetes.

The most common factors that have been evaluated as risk factors for GDM along with BMI are maternal age, parity, history of GDM, and family history of diabetes.

### Other results

#### Other anthropometric indices

Zhang et al.<sup>24</sup> estimated that fat mass of about  $17.95 \pm 5.65$  kg in the GDM group and  $15.51 \pm 5.18$  kg in the NGT group was significant. It means higher fat mass can predict GDM.

Yong et al.<sup>25</sup> showed that excessive gestational weight gain (GWG) in the first trimester of 23 (9%) of people with GDM and 177 (10.4%) statistically cannot predict GDM ( $p=0.49$ ).



Gao et al.<sup>27</sup> investigated that WC in the GDM is  $82.9 \pm 9.7$  cm and in the NGT is  $78.7 \pm 8.6$  cm, which was statistically significant. It means higher WC in pregnant women can predict GDM.

Body fat index (BFI)  $> 0.5$  mm<sup>2</sup>, subcutaneous fat  $\geq 13$  mm, and pre-peritoneal fat  $\geq 9$  mm expected probability of 3%, 4%, and 8.3% for GDM, respectively.<sup>30</sup>

There was a synergistic interaction between WC  $\geq 78.5$  cm and BMI  $\geq 22.5$  kg/m<sup>2</sup> in conferring an increased risk of GDM in both uni- and multivariable analyses.<sup>32</sup>

### Micronutrients

In one study,<sup>39</sup> it was shown that insufficient levels of vitamin D in pregnancy could be associated with the occurrence of gestational diabetes, regardless of BMI.

### Discussion

In this present study, there is an association between BMI in the first half of pregnancy and GDM, which defined that overweight and BMI more than normal in the first half of pregnancy is considered a risk factor for GDM.

The body undergoes dynamic changes during pregnancy to meet the needs of a growing fetus. The pattern of weight gain in pregnancy is different. For example, total weight gain in the first trimester of pregnancy in non-Hispanic white women in the United States is  $-0.4$ ,  $2.7$ , and  $6.9$  kg in the 10th, 50th, and 90th percentiles, respectively.<sup>41</sup> In addition, the medical institute's guidelines state that the average in the first trimester is  $0.5$ – $2$  kg based on pre-pregnancy BMI.<sup>42</sup> These changes in body composition reflect changes in body composition during pregnancy, thus measuring body weight at the right time when it is possible to accurately estimate the desired weight for each person in pregnancy seems very important and necessary in settings with the ultimate goal of improving maternal and offspring health in pregnancy and thereafter. The National Heart, Lung, and Blood Institute, in collaboration with the National Institute of Diabetes and Gastrointestinal and Kidney Diseases, has proposed using BMI to measure adult weight instead of absolute weight or compare it with life insurance tables.<sup>43</sup> Also, BMI reference curves may be an additional helpful tool to control maternal weight gain according to height, as it is known that taller women gain more weight in pregnancy.<sup>44</sup> Special attention to BMI should be considered a health problem to reduce maternal and fetal complications due to excessive weight gain in pregnancy. Although two large studies from the Swedish Medical Birth Registry have shown that a pre-pregnancy diagnosis of obesity and morbid obesity are related to late fetal death and adverse pregnancy outcomes.<sup>45,46</sup> However, due to circumstances, the pregnant mother may not have taken pre-pregnancy care and may not have access to pre-pregnancy weight, and the mother may not be able to remember her pre-pregnancy weight. In a study on 1000 pregnant

women (2010), mean maternal weight and thus, mean BMI did not change in the first trimester. Bioelectrical impedance analysis also showed no change in maternal body composition means. In particular, body fat measurements mean remained unchanged. These findings indicate that changes in maternal weight or body composition in pregnancy usually occur after the first trimester, so that, they suggested that accurate measurement of weight or body composition at any time in the first trimester may be used as a baseline for subsequent comparison.<sup>47</sup> Although factors, such as nausea and vomiting in the first trimester can affect maternal weight in the first trimester of pregnancy, it does not seem to affect maternal weight much except in cases of severe hyperemesis<sup>48</sup> which ultimately leads to a 5% reduction in body weight and affects 0.3%–2% of pregnancies, and many factors are involved in its occurrence.<sup>49</sup> Although excessive GWG in the T1 and T2 was not a significant risk factor for GDM, the combination of three risk factors, such as aged 35 years and above, overweight/obese, and having an excessive GWG in the T2 significantly increased the risk of GDM. This finding shows that maternal age and BMI are more important risk factors than GWG, although a recent meta-analysis demonstrated the association between maternal pre-pregnancy BMI with the risk for any adverse outcome in pregnancy, including GDM which can more strongly predict GDM better than GWG.<sup>32,50</sup>

Overweight and obesity are described as an excess accumulation of adipose tissue to an extent that impairs both physical and psychosocial well-being and lower levels of health-related quality of life.<sup>51</sup> Obesity is associated with insulin resistance.<sup>52</sup> Insulin resistance is also involved in the pathophysiology of GDM, and in normal pregnancy, there is a decrease in glucose uptake and a rising in insulin secretion based on the changes made, leading to insulin resistance.<sup>53</sup> Excessive nutrition, obesity, and GDM affect embryos during early development and their health status in their lifetime.<sup>50</sup>

Today changes in lifestyle, such as reduced levels of physical activity,<sup>54</sup> changes in diet habits,<sup>55</sup> and obesity<sup>56</sup> can lead to GDM. Healthy dietary patterns of pregnant women were inversely associated with obesity and GDM.<sup>57</sup> In contrast to the prevention of obesity and GDM, preventing excess GWG may be more feasible as it is monitored during pregnancy.<sup>12</sup> The American College of Obstetricians and Gynecologists (ACOG) suggested that health care providers determine a woman's BMI at her first prenatal visit and discuss appropriate weight gain, diet, and exercise at both the initial visit and periodically throughout the pregnancy.<sup>58</sup> according to previous studies, the most successful interventions for the prevention of excessive GWG closely reflect effective lifestyle programs which are used in nonpregnant women.<sup>59</sup>

FPG with a cut-off point of 80–85 mg/dL (with a sensitivity of 55–75% and a specificity of 52–75%) and 90 mg/dL (with a sensitivity of 55.1% and a specificity of 71%) has been used to determine diabetes.<sup>58</sup> GDM occurs in about 14% of all pregnancies worldwide.<sup>60</sup>

**Table 2.** Overview of all included studies in the systematic review.

ID	Author/ year (ref.)	location	Study design	Sample size (N)		Age (year)	BMI (kg/m <sup>2</sup> )		Applying test time (trimester)	Accompanying factors	Diagnostic criteria of GDM	Results	Quality score
				GDM	NGT		GDM	NGT					
1	Zhang et al. <sup>23</sup>	China	Cohort	4257	37,588	18–45	24.49 ± 4.21	22.49 ± 3.64	T1	Age Parity PCOs History of macrosomia History of adverse fertility Family history of diabetes Habitual smoking	WHO	Early pregnancy BMI was a risk factor for GDM (OR = 1.131, 95% CI = 1.122–1.139)	7
2	Zhang et al. <sup>24</sup>	China	Cohort	6029	16,194	28.09 ± 4.48	23.18 ± 3.48	21.30 ± 2.98	T2	Age Total body water Fat mass Fat-free mass Percent body fat Muscle mass visceral fat levels Proteins Bone minerals Basal metabolic rate Lean trunk mass -Lean right arm mass -Lean left arm mass Lean right leg mass Lean left leg mass	IADPSG	BMI more than 23 was significantly associated with an increased risk of GDM	7
3	Yong et al. <sup>25</sup>	Malaysia	Cohort	255	2696	29.08 ± 4.44	Overweight/obese (≥ 25.00 kg/m <sup>2</sup> ): 131 (51.4%)	Overweight/ obese (≥ 25.00 kg/m <sup>2</sup> ): 717 (42.3%)	T3	Age Ethnicity Education Occupation Parity GWG in the first trimester GWG in the second trimester Maternal glucose level Family history of DM History of GDM History of macrosomic birth History of recurrent pregnancy loss History of unexplained intrauterine fetal demise Having risk factors Smoking habit Sleeping time during pregnancy Waist circumference Systolic and diastolic pressure Han ethnicity ALT Education Parity Family history of diabetes Non-AB blood type Waist: circumference Physical activity during pregnancy Sitting time at home during pregnancy	ADA	Early pregnancy BMI was a stronger contributor to the risk of GDM than GWG	8
4	Deniz <sup>26</sup>	Turkey	Cohort	323	NR	29.35 ± 5.29	27.23 ± 6.07	NR	T2	Family history of DM History of GDM	IADPSG	There was no statistically significant difference in the rate of GDM diagnosis among the BMI groups	7
5	Gao et al. <sup>27</sup>	China	Cohort	1485	178,46	29 ± 3.05	24.2 ± 3.9	22.1 ± 3.3	T2	Having risk factors Smoking habit Sleeping time during pregnancy Waist circumference Systolic and diastolic pressure Han ethnicity ALT Education Parity Family history of diabetes Non-AB blood type Waist: circumference Physical activity during pregnancy Sitting time at home during pregnancy	IADPSG	BMI is associated with an increased risk of GDM	7

(Continued)

Table 2. (Continued)

ID	Author/ year (ref.)	location	Study design	Sample size (N)		Age (year)	BMI (kg/m <sup>2</sup> )		Applying test time (trimester)	Accompanying factors	Diagnostic criteria of GDM	Results	Quality score
				GDM	NGT		GDM	NGT					
6	Li et al. <sup>2</sup>	China	Cohort	2986	14,159	30.20 ± 4.62	< 25: 1730 (59.19%) 25–30: 938 (32.09%) ≥ 30: 255 (8.72%)**	< 25: 10,117 (73.93%) 25–30: 2,930 (21.41%) ≥ 30: 638 (4.66%)**	T2	Anemia Thyroid disease Dietary pattern Cigarette smoker Alcohol smoker Assisted reproduction History of previous GDM Parity Folic acid supplements	IADPSG	Gestational BMI gain from conception to 15–20 weeks of gestation was correlated with an increased risk of GDM	8
7	Rezaei et al. <sup>28</sup>	Iran	Cohort	202	457	27.81 ± 5.85	Total BMI: 24.40 ± 4.02 < 18.9: 10 (21.8%) 19–24/9: 64 (18.5%) 25–29.9: 81 (40.3%) > 30: 46 (79.3%)**	< 18.9: 37 (78.7%) 19–24/9: 282 (81.5%) 25–29.9: 120 (59.7%) > 30: 12 (20.7%)**	T2, T3	Education Husband education Economic status Parity	IADPSG	There is a significant association between BMI and GDM in the overweight and obese group	7
8	Pratt et al. <sup>29</sup>	Australia	Cohort	18402	NR	29 (7)*	Total: 2713 (14.74%) < 18/9: 10 (21.8%) 19–24/9: 64 (18.5%) 25–29.9: 81 (40.3%) > 30: 46 (79.3%) ≤ 18: 23 (5.01%) 19–24: 659 (9.51%) 25–29: 888 (15.29%) 30–49: 1116 (21.80%) > 50: 27 (29.35%)**	NR	T2, T3	Age Parity Gestational age at first antenatal visit Indigenous status Country of birth outside Australia Preferred language is spoken other than English Primiparous Smoking during pregnancy Aboriginal or Torres Strait Islander	NR	Women with BMI ≥ 50 kg/m <sup>2</sup> are an important subgroup who experience high rates of complications, such as GDM	8

(Continued)

Table 2. (Continued)

ID	Author/ year (ref.)	location	Study design	Sample size (N)		Age (year)	BMI (kg/m <sup>2</sup> )		Applying test time (trimester)	Accompanying factors	Diagnostic criteria of GDM	Results	Quality score
				GDM	NGT		GDM	NGT					
9	Nassar et al. <sup>30</sup>	USA	Cohort	389	NR	29.7 ± 4.67	25.1 (21.9–30.3)* ≥ 25: 196 (50.4%) ≥ 30: 107 (26.0%)	NR	T2	Maternal age in years Parity Baseline BMI in kg/m <sup>2</sup> History of GDM Positive family history of diabetes History of gestational hypertension or preeclampsia History of bariatric surgery Gestation diabetes mellitus Hypertension with pregnancy Gestational age at ultrasound assessment in weeks Centile of expected fetal weight in the second trimester Pre-peritoneal fat measurement in mm Subcutaneous fat measurement in mm BFI in mm <sup>2</sup> /cm Mode of delivery Birth weight in grams Family history of diabetes History of GDM Abortion	ACOG	BFI was a better predictor than BMI for the development of GDM (BFI > 0.5 was statistically superior to a BMI > 25 or 30 as a predictor of gestational diabetes (adjusted OR = 6.24, 95% CI = 1.86–20.96).	8
10	Hashemi- Nazari et al. <sup>31</sup>	Iran	Cohort	80	929	28 (24–32)*	27.5 (24.6–30.5)*	25.1 (22.3–27.8)*	T2	Pre-pregnancy weight Waist circumference Systolic and diastolic blood pressure Weight gain per week from registration to GCT Han-nationality Family history of diabetes in first-degree relatives Education > 12 years Parity ≥ 1 Smoking habit Alcohol drinking habit	IADPSG	There was a significant association between the GDM and higher levels of BMI at the beginning of pregnancy	7
11	Han et al. <sup>32</sup>	China	Cohort	1383	16,420	28.95 ± 3.0	24.1 ± 3.9	22.1 ± 3.3	T2	Weight gain per week from registration to GCT Han-nationality Family history of diabetes in first-degree relatives Education > 12 years Parity ≥ 1 Smoking habit Alcohol drinking habit Systolic and diastolic pressure Parity Family history of GDM Weight gain Insulin resistance Waist-to-hip ratio smoking Education Country of birth Age Parity	IADPSG	BMI ≥ 22.5 to < 24.0 kg/m <sup>2</sup> within 12 weeks of gestation were associated with increased risks of GDM	7
12	Hao and Lin <sup>33</sup>	China	Cohort	167	653	29.5	23.2 (21.2, 25.8)*	21.7 (20.1, 23.7)*	T2	Family history of GDM Weight gain Insulin resistance Waist-to-hip ratio smoking Education Country of birth Age Parity	IADPSG	BMI (OR = 1.144; 95% CI = 1.083–1.208) were independent risk factors for later development of GDM.	8
13	Basraon et al. <sup>34</sup>	USA	Cohort	2300	NR	23.35 ± 4.75	< 25: 19 (1.6%) 25–29.9: 26 (4.3%) ≥ 30: 35 (7.0%)*	NR	T2	Family history of GDM Weight gain Insulin resistance Waist-to-hip ratio smoking Education Country of birth Age Parity	Per the guidelines of each clinical center	BMI and WHR are as significant risk factors for the development of gestational diabetes	7
14	McDonald et al. <sup>35</sup>	Australia	Cohort	606	4004	29.2 ± 6.1	< 18.5: 22 ≥ 18.5–< 25: 221 ≥ 25–< 30: 184 ≥ 30–< 35: 84 ≥ 35: 95	< 18.5: 176 ≥ 18.5–< 25: 1845 ≥ 25–< 30: 1047 ≥ 30–< 35: 472 ≥ 35: 464	T2	Country of birth Age Parity	ADIPS	BMI is associated with an increased prevalence of GDM	8

(Continued)



Table 2. (Continued)

ID	Author/ year (ref.)	location	Study design	Sample size (N)		Age (year)	BMI (kg/m <sup>2</sup> )		Applying test time (trimester)		Accompanying factors	Diagnostic criteria of GDM	Results	Quality score
				GDM	NGT		GDM	NGT	T1	T2				
15	Makgoba et al. <sup>36</sup>	UK	Cohort	1688	172 632	20–24	13.0 (12.0–16.0)	13.0 (12.0–16.0)	T1	Age Race Mode of delivery	NR	There was a strong positive association between advancing maternal age and increasing BMI, in women who developed GDM	7	
16	Sweeting et al. <sup>37</sup>	Australia	Case– control	248	732	32.5	24.5 (22.5–28.3)*	23.3 (21.6–26.1)*	T2	Maternal age Ethnicity Smoker Conception Family history of diabetes Parity Previous GDM Polycystic ovarian syndrome Previous macrosomia Gestation at delivery Birth weight Mode of delivery	ADIPS	BMI was significant predictor of GDM	7	
17	Savidou et al. <sup>38</sup>	UK	Case– control	124	248	33.45 ± 5.1	29.2 ± 7.9	25.4 ± 5.2	T2	Maternal age (years) Maternal BMI at booking Parity Ethnicity Previous GDM Family history of diabetes Smoker Gestational age at booking Systolic blood pressure Diastolic blood pressure Mode of delivery Sex	WHO	Women with higher BMIs were more susceptible to developed GDM	8	
18	Agüero- Domenech et al. <sup>39</sup>	Spain	Cross- sectional	93	793	34.2 ± 5.7	27.5 ± 5.9	24.5 ± 4.5	T1	Birth weight Age Parity Habitual smoking Physical activity Nutritional status Lifestyle Ethnicity Maternal hypothyroidism	ADA	Higher BMI and vitamin D deficiency are associated with GDM	7	

\*Median (IQR), \*\*N (%), GWG: gestational weight gain, BMI: body mass index, NGT: normal glucose tolerance, WHR: waist-hip ratio, ADIPS: Australian Diabetes in Pregnancy Society, WHO: World Health Organization, ADA: American Diabetes Association, ACOG: American College of Obstetricians and Gynecologists, GCT: glucose challenge test, IADPSG: International Association of Diabetes and Pregnancy Study Groups, NR: not reported.

Thus far, various other markers have been examined for screening for GDM, including hemoglobin A1c (HbA1c), lipid profile, adiponectin, liver enzymes, C-reactive protein (CRP) or high-sensitivity CRP (hs-CRP), sex hormone-binding globulin (SHBG), pregnancy-associated plasma protein-A (PAPP-A).<sup>3,61–65</sup> However, all of the mentioned factors have limitations and are not economically viable. Therefore, efforts are being done to find available and affordable factors to predict GDM. BMI is a cost-effective and available GDM risk evaluation tool in early pregnancy. BMI depends on the measurement of the individual's weight and height and is currently used as a surrogate for the measurement of body fat. Studies on the associations between pre-pregnancy BMI and GWG with the risk of GDM indicated that pre-pregnancy obesity and excessive GWG are independent risk factors for the development of GDM.

While compared to lean or normal-weight women, overweight or obese women had an increased risk of GDM.<sup>66</sup> Controlling BMI before pregnancy in young women should be a priority in public health for controlling the growing trend of GDM.<sup>67</sup> Also, there was a significant association between GDM and weight gain during pregnancy.<sup>68</sup> Basraon et al.<sup>34</sup> demonstrated that BMI and waist-to-hip ratio are risk factors for the development of insulin resistance and GDM. This association varies among different ethnicities.

Hashemi-Nazari et al.<sup>31</sup> investigated an increased risk of GDM associated with increasing BMI at the beginning of pregnancy. Rezaei et al.<sup>28</sup> A cohort study also showed that the BMI of pregnant women is associated with GDM and its increase with increasing incidence of diabetes.

Deniz<sup>26</sup> reported that women with BMI of more than 35 kg/m<sup>2</sup> are positive for insulin resistance with 50 g oral glucose tolerance test (OGTT). Also, Ali et al.<sup>1</sup> showed that BMI  $\geq$  30 kg/m<sup>2</sup> and previous macrosomic infant are dependent risks for GDM. Other study concluded that women with BMI  $\geq$  50 kg/m<sup>2</sup> as an important subgroup of the obese patients, experience more complications (such as GDM (29%), hypertensive disorders of pregnancy (20%), and cesarean section (48%)). Infants born to women with BMI  $\geq$  50 kg/m<sup>2</sup>, 12% were late-pre-term, 23% required special or intensive care, and 20% had birth weight  $\geq$  4.0 kg, and more interventions during pregnancy were needed.<sup>29</sup> Han et al.<sup>32</sup> were shown that BMI  $\geq$  22.5 kg/m<sup>2</sup> and WC  $\geq$  78.5 cm measured at 12 weeks of gestation were independently and synergistically associated with developed GDM in Chinese pregnant women.

Padmanabhan et al.<sup>17</sup> GWG and change in BMI at 28 weeks of gestation in women with GDM, and women with NGT. GDM was associated with a greater increment in BMI, but not with increased GWG in kilograms.

Gao et al.<sup>27</sup> found that six predictors collected at the first antenatal care visit (maternal age, BMI, systolic blood pressure (BP), alanine transaminase (ALT), and family history of diabetes in first-degree relatives) and four during pregnancy

modifiable risk factors, such as physical activity, sitting time at home, passive smoking, and weight gain from registration to glucose challenge test (GCT) were accompanied with a rising risk of GDM. Li et al.<sup>2</sup> reported that BMI gain from conception to 15–20 weeks of gestation and older age were correlated with an increased risk of GDM. Yong et al. demonstrated that older maternal age, and being overweight and obese were significantly associated with the risk of GDM. Overweight/obese women with age  $\geq$  35 years had a 2.45-fold higher risk of GDM and having excessive GWG in the dependent risk factors for GDM but not GWG in the first and second trimesters.<sup>25</sup>

There is a strong relationship between maternal age and increased BMI, and consequently the increased risk of GDM.<sup>36</sup> Furthermore, race/ethnicity can affect BMI and the risk of GDM.<sup>59</sup> The effect of race on GDM has been reported in another study. Women from other Asian countries compared to women from Australia or New Zealand had a three-fold increased risk of GDM. There was not any evidence of interaction by BMI.<sup>35</sup> There is a significant relationship between the prevalence of GDM and variables, such as household size, BMI, BP, parity, and number of abortion.<sup>69</sup> Risk factors for GDM contained age  $>$  35 years, obesity, poor neonatal outcomes, and prior cesarean delivery. Adolescent mothers and women who drank alcohol were less likely to have GDM. Mothers with GDM were at high risk for presenting with pre-eclampsia, premature rupture of membranes (PROMs), cesarean delivery, and preterm birth. Infants born to mothers with GDM were at higher risk of being large-for-gestational-age, also increasing age and BMI and previous GDM were the most significant risk factors for GDM.<sup>70</sup> Some underlying diseases can affect the development of GDM, a study showed that pregnant Iranian women with a history of PCOS and infertility are at increased risk for developing GDM.<sup>71</sup> Low socioeconomic levels, smoking during pregnancy, high parity, belonging to minority groups, and excessive weight gain during pregnancy have been found positive associations with GDM.<sup>72</sup>

The strengths of our study examine BMI as a useful and available anthropometry-based obesity classification for assessing GDM risk in a large group of pregnant women, and the limitation of our study gives no information about the extent of obesity-associated morbidity or functional limitations in individuals. For example, individuals may have no metabolic abnormalities even if they have a very high BMI. Future studies are recommended for meta-analysis and comparison with pre-pregnancy BMI.

## Conclusion

This study showed abnormal BMI is associated with GDM. Assessing and monitoring the BMI of pregnant women in the first half of pregnancy should be done carefully. Pregnant women's BMI assessment can be easily and inexpensively used at the first prenatal visit to assess the risk of GDM and

is better than the pre-pregnancy BMI because pregnant women do not have a pre-pregnancy evaluation and reminding of pre-pregnancy weight may be accompanied by bias.

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### Author contributions

FAR and FA conceived the study, interpreted the data, drafted the article, and approved the final version of the paper. Other authors interpreted the data.

### Availability of data and materials

All the data are included in this article.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Ethical approval and consent to participate

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