The prevention of gestational diabetes mellitus (The role of lifestyle): a meta-analysis

Abdullah H. Altemani1* and Riyadh A. Alzaheb2

Abstract
Gestational diabetes mellitus (GDM) is the most common complication of pregnancy. The disease is on the rise worldwide with deleterious consequences on the fetus, mother, and children. The study aimed to review the role of lifestyle in the prevention of GDM. We searched PubMed, SCOPUS, Web of Science, Cochrane Library, EBSCO, and Google Scholar from the first published article up to December 2021; articles were eligible if they were controlled trials, prospective cohorts, and case–control. Out of 5559 articles retrieved, 66 full texts were screened, and 19 studies were included in the meta-analysis. (6 studies assessed the effects of diet, and 13 were on exercise). The dietary intervention showed significant positive effect on GDM, odd ratio = 0.69, 95% CI, 0.56–84, P-value for overall effect = 0.002. The DASH diet was better than Mediterranean Diet (odd ratio, 0.71, 95% CI, 68–74, P-value < 0.001). Regarding exercise, no significant prevention was evident on GDM, odd ratio, 0.77, 95% CI, 0.55–1.06, P-value = 0.11. However, a significant prevention of gestational diabetes was found when the exercise was mild-moderate (odd ratio = 0.65, 95% CI, 0.53–80, P < 0.0001) and started in the first trimester (odd ratio, 0.57, 95% CI, 0.43–0.75, P < 0.0001). No significant effect was found when the exercise was vigorous (odd ratio = 1.09, 95% CI, 0.50–2.38, P = 0.83) and started during the second trimester of pregnancy (odd ratio, 1.08, 95% CI, 0.65–1.80, P = 0.77. Diet and early mild-moderate exercise were effective in GDM prevention. Exercise during the second trimester and moderate-vigorous were not. Further studies assessing the type, duration, and frequency of physical activity are needed.

Keywords: Diet, Exercise, Lifestyle, Gestational diabetes mellitus, Prevention

Background
Gestational diabetes mellitus (GDM) is the most common medical complication of pregnancy, it affects 5–6% of pregnant women in the USA according to the Carpenter-Coustan criteria, and the rate would increase to 15–20% when the International Association of Diabetes in Pregnancy Study Groups criteria is applied. GDM is on the rise due to increasing age and obesity [1]. The rate of obesity and overweight is rapidly increasing globally and in particular, for the Gulf countries including the Kingdom of Saudi Arabia, this is mirrored by the high prevalence of obesity-related disorders including diabetes [2]. Diabetes mellitus is more prevalent among Saudi females mainly due to an unfriendly diet. The rapid development in Saudi Arabia substantially shifted the diet from the healthy traditional diet to a more Westernized diet with deleterious consequences [3]. GDM increases both maternal and fetal complications including excess fetal growth, cardiovascular disease, impaired glucose metabolism, and pregnancy-related hypertensive disease. Physical activity and dietary modifications are the mainstay of management with insulin, Glyburide, and metformin used when normoglycemia is not achieved [4]. Lifestyle modifications need great effort from both the healthcare professionals and the patients and are usually faced with numerous barriers that may lead to poor glycemic control [5]. The role of lifestyle in the
prevention of GDM is a matter of controversy. The available evidence regarding the lifestyle modification effects on GDM is weak due to the different diets included; furthermore, no single diet fits all. Mediterranean diet is the only diet that is recommended to patients with diabetes mellitus [6]. Besides, both diet and exercise might be affected by the type, timing, and amount (exercise is also affected by the duration). In addition, non-adherence is a substantial factor compromising the quality of studies [7]. Individual food items were extensively studied, but nutrients are not consumed in isolation either they are consumed in different combinations (dietary patterns). In addition, dietary patterns mimic real-world scenarios and can be translated into simple and easy-to-follow recommendations. Dietary Approaches to Stop Hypertension (DASH), Alternate Healthy Eating Index diet (AHEI), and Mediterranean Diet (MedDiet) were shown to reduce diabetes, mortality, and cardiovascular disease. However, their effects on gestational diabetes prevention are scarce [8–11]. Tobias and colleagues in their retrospective cohort showed that aHEI lowered the risk of GDM by 46%, followed by the DASH diet (34%), and MedDiet (24%) [12]. The previous observation was supported by another study (57%, 46%, and 40% reduction in aHEI diet, DASH diet, and MedDiet respectively) [13]. Another study showed a higher reduction in GDM among patients adherent to MedDiet compared to the DASH diet (80% vs. 71%) [14] A randomized trial supported the above observations and showed the beneficial effects of the DASH diet on glycemic and lipid parameters [15]. Further randomized controlled trials showed the beneficial effects of the DASH diet on insulin resistance and glycemic parameters [16]. To the best of our knowledge, no review compared different dietary patterns in the prevention of gestational diabetes mellitus. Therefore, the current review assessed the effects of MedDiet, DASH diet, and aA He diet on the prevention of gestational diabetes and assessed if one diet is superior. In addition, this meta-analysis assessed the effectiveness of exercise (throughout, first and second trimester).

Methods

Articles selection according to PICOS

We searched PubMed, SCOPUS, Web of Science, Cochrane Library, EBSCO, and the first 100 articles in Google Scholar from the first published article up to December 2021, articles were eligible if they were controlled trials, prospective cohorts, and case-control studies and published in English. Article in languages other than English, other methodologies (case series, and case reports were not included. The trials must fulfill the following outcomes to be included:

- The effect of the Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH), Alternate Healthy Eating Index diet (AHEI) on GDM prevention
- The effect of first and second-trimester exercise on GDM prevention.

We excluded diabetes mellitus prevention programs carried on patients with type 2 diabetes mellitus or women with established GDM.

Literature search and data extraction

The two authors (A.H, and R.A) searched the mentioned databases for relevant articles, out of 5559 articles retrieved, 66 full texts were screened, and 19 studies were included in the meta-analysis. Fig. 1. In the current review, 6 studies assessed the effects of diet, and 13 were on exercise. Of them, eight assessed exercises in the first trimester and five in the second trimester. We did not specify any criteria for GDM diagnosis due to the different methods that might be applied during the long period of the search engine. The retrieved data were exported to an excel sheet detailing the author's names, country of origin of the study, the number of patients and control subjects, and the total number of events in the interventional and exercise groups (Tables 1, 2). The details of exercise including the type, duration, and intensity, the diet type, and the compliance when reported were also recorded. In this review we concentrated on dietary habits and detailed exercise (timing and duration). Tables 3, 4 and Fig. 1.

Quality assessment of the cited trials

The quality of the included studies was assessed using a modified Cochrane risk of bias. Table 5.

Data analysis

We use RevMan (version 5, 4) for data analysis, the data were entered manually, and dichotomous variables were compared. The fixed effect was applied unless a significant heterogeneity (>50%) was observed. A P-value of 0.05 is significant except when a significant heterogeneity.

Ethical consideration

We did not include studies published by the authors.

Results

The dietary intervention included three studies [18, 19] with significant positive effect on GDM, odd ratio = 0.69, 95% CI, 0.56–84, P-value for overall effect = 0.002, with no significant heterogeneity, I^2 = 0.0%. Fig. 2. The DASH diet showed superiority to MedDiet Mediterranean Diet [13–15] (odd ratio, 0.71, 95% CI, 68–74,
P-value < 0.001). Furthermore, the Alternate Healthy Eating Index diet was better than the DASH diet (odd ratio, 0.69, 95% CI, 0.53–0.91, P-value, 0.008). Fig. 3 and 4.

Regarding exercise, there were thirteen studies [20–32] with no significant prevention on GDM (total patients 4202 and 418 events), odd ratio, 0.77, 95% CI, 0.55–1.06, P-value for overall effect = 0.11, with significant heterogeneity, $I^2 = 62\%$ and P-value for heterogeneity, 0.002. Fig. 5
However, when a sub-analysis was conducted, significant prevention of gestational diabetes was found when the exercise started in the first trimester (odd ratio, 0.57, 95% CI, 0.43–0.75, P-value for overall effect < 0.0001, with significant heterogeneity, $I^2 = 40\%$. Fig. 6.

No significant effect was found when the exercise started during the second trimester of pregnancy [22, 25, 26, 27, 28, 29, 30, 31].

| Author                  | Outcomes interventional | Outcomes control | Intervention type | Results                           |
|-------------------------|-------------------------|------------------|------------------|-----------------------------------|
| Assaf-Balut et al. 2017 [17] | 74/434                  | 103/440          | Med Diet         | Significant reduction, P = 0.05   |
| HA I Wattar B et al. 2019 [18] | 84/477                  | 124/497          | Med Diet         | Significant reduction, P = 0.01   |
| Sahriah A et al. 2016 [19] | 44/492                  | 57/516           | Local diet       | Non-significant, P = 0.27         |
| Baraakat R et al. 2019 [20] | 6/234                   | 15/222           | Exercise         | Significant reduction, P = 0.033  |
| Cordero Y et al. 2015 [21] | 1/101                   | 13/156           | Exercise         | Significant reduction, P = 0.009  |
| da Silva G et al. 2017 [22] | 16/205                  | 31/470           | Exercise         | Non-significant                  |
| Daly et al. 2017 [23]    | 25/44                   | 21/44            | Exercise         | Non-significant, P = 0.51         |
| Gallaway et al. 2010 [24] | 5/22                    | 3/19             | Exercise         | Non-significant, P = 0.29         |
| Nobles C et al. 2015 [25] | 12/124                  | 19/127           | Exercise         | Non-significant, P = 0.20         |
| Oostdam et al. 2012 [26] | 7/62                    | 11/59            | Exercise         | Non-significant                  |
| Ruiz et al. 2013 [27]    | 7/335                   | 18/352           | Exercise         | Non-significant                  |
| Seneviratne et al. 2016 [28] | 4/38                    | 2/37             | Exercise         | Non-significant                  |
| Simmons et al. 2016 [29] | 30/110                  | 35/105           | Exercise         | Non-significant                  |
| Stafine et al. 2012 [30] | 25/325                  | 18/327           | Exercise         | Non-significant, P = 0.52         |
| Tomic et al. 2013 [31]   | 3/168                   | 14/168           | Exercise         | Non-significant                  |
| Wang C et al. 2017 [32]  | 33/150                  | 61/150           | Exercise         | Significant reduction, P = < 0.001 |

| Author                  | Exercise type | Duration | Intensity | Results                  |
|-------------------------|--------------|----------|-----------|--------------------------|
| Stafine et al [22]      | Aerobic, three or more times, | From week 18, poor compliance, 55% | Moderate-high strong | Not sig Improved glucose intolerance |
| Cordero et al. [21]     | Aerobic, three times | 50–60 min throughout pregnancy | strong | Not sig Improved glucose intolerance |
| Daly et al. [23]        | Aerobic and resistance | 50–60 min throughout pregnancy | strong | Not sig |
| Callaway et al. [24]    | Energy expenditure goal of 900 kcal/week | Energy expenditure goal of 900 kcal/week | Moderate-vigorous | Not sig |

| Author                  | Exercise type | Duration | Intensity | Results                  |
|-------------------------|--------------|----------|-----------|--------------------------|
| da Silva et al. [22]    | Aerobic and resistance, three times | 60 min, from week 16, overweight | Moderate | Not sign |
| Nobles et al. [25]      | Aerobic, most days | 30 min, from 12 weeks, overweight | Moderate | Not sig |
| Oostdam et al. [26]     | Aerobic and resistance, three times | Duration not stated, from 12 weeks, overweight | Moderate | Not sig |
| Seneviratne et al. [28] | Aerobic, cycling | Compliance was poor, 33%, from 20 weeks, overweight | Moderate | Not sig |
| Baraakat et al. [20]    | Aerobic, three times | 50–55 min throughout pregnancy | Moderate | Improved glucose intolerance |
| Ruiz et al. [27]        | Aerobic and resistance, three times | 50–55 min throughout pregnancy | Mild-moderate | Improved glucose intolerance |
| Simmons et al. [29]     | Aerobic and resistance daily | Throughout pregnancy, no specific duration | Mild-moderate | Not sig |
| Tomic et al. [31]       | Aerobic, three times | 50 min throughout pregnancy | Moderate | Improved glucose intolerance |
| Wang et al. [32]        | Aerobic, three times | 30 min of cycling throughout pregnancy | Moderate | Improved glucose intolerance |
26, 28, 30] (odd ratio, 1.08, 95% CI, 0.65–1.80, P-value for overall effect = 0.77, with significant heterogeneity, $I^2 = 51\%$. Fig. 7.

It is interesting to note that mild-moderate intensity exercise was effective in gestational diabetes prevention (odd ratio = 0.65, 95% CI, 0.53–80, P-value for overall effect < 0.0001, with significant heterogeneity, $I^2 = 36.0\%$. Fig. 8), while vigorous activity was not (odd ratio = 1.09, 95% CI, 0.50–2.38, P-value for overall effect = 0.83, with no significant heterogeneity, $I^2 = 51.0\%$. Fig. 9).

Table 5  Risk of bias of the included randomized controlled trials

| Study                          | Year | Selection | Performance | Attrition | Reporting | Other |
|-------------------------------|------|-----------|-------------|-----------|-----------|-------|
| Assaf-Balut et al. [17]       | 2017 | Low       | High        | Low       | Low       | Low   |
| H Al Wattar et al. [18]       | 2019 | Low       | High        | Low       | Low       | Low   |
| Sahariah et al. [19]          | 2016 | Unclear   | High        | Low       | Low       | Low   |
| Barakat et al. [20]           | 2019 | Low       | Low         | High      | Low       | Unclear |
| Cordero et al. [21]           | 2015 | High      | Unclear     | High      | Low       | Unclear |
| da Silve et al. [22]          | 2017 | Low       | Unclear     | Low       | Low       | Low   |
| Daly et al. [23]              | 2017 | Low       | Unclear     | High      | Low       | Low   |
| Callaway et al. [24]          | 2010 | Low       | Unclear     | High      | Low       | Low   |
| Nobles et al. [25]            | 2015 | High      | Low         | Unclear   | Low       | Low   |
| Oostdam et al. [26]           | 2012 | High      | Low         | High      | Low       | Low   |
| Ruiz et al. [27]              | 2013 | Low       | Unclear     | Nuclear   | High      | Unclear |
| Seneviratne et al. [28]       | 2016 | Unclear   | Low         | Low       | Low       | Low   |
| Simmons et al. [29]           | 2017 | Low       | High        | Low       | Low       | Low   |
| Sterm et al. [30]             | 2012 | Low       | Low         | Low       | High      | Unclear |
| Tomić et al. [31]             | 2013 | High      | Unclear     | High      | Unclear   | Unclear |
| Wang et al. [32]              | 2017 | Unclear   | High        | Low       | High      | Low   |

Fig. 2  The effects of diet on gestational diabetes prevention

Fig. 3  A comparison between Dietary Approach to Stop Hypertension (DASH) and Alternate Healthy Eating Index diet (AHEI) effects on gestational diabetes
Discussion

The present meta-analysis showed that diet was effective in gestational diabetes prevention, while exercise was not. However, a sub-analysis showed that exercise was effective only when introduced in the first trimester; physical activity started in the second trimester was not effective. In addition, mild-moderate exercise was effective in contrast to vigorous physical activity. Previous studies with a low quality of evidence showed the efficacy of combined diet and exercise [33,
The meta-analyses lack a face-to-face comparison between different forms of diets. In addition, they did not report the timing and intensity of exercise. Another study showed similar results but only among obese women [35]. Dietary supplementation with myo-inositol reduced GDM in a study that included four trials and lacked generalization [36].

**Special types of diets**

**Alternate healthy eating index-2010**

The AHEI-2010 is a measure of diet quality based on food items predictive of major chronic disease risk, particularly cardiometabolic disease including stroke and diabetes, and malignancies. It emphasizes a high intake of legumes and nuts, cereals, vegetables and fruits, omega-3...
fats, and polyunsaturated fatty acids while limiting the intake of red and processed meats, sodium, sugary beverages, and alcohol [37].

The effect of the Alternate Healthy Eating Index-2010 in reducing GDM ranged from 19–46%, interestingly, when the diet is combined with other risk factors reduction (physical activity, smoking, and normal body weight) the risk reduction may be as high as 83% [38]. A 41% lower risk of gestational diabetes was observed among patients adherent to aHEI [39]. A genetic interaction increases the like hood of developing GDM among patients on aHEI diet [40]. In addition, health education and self-efficacy substantially improved the quality of aHEI [41], the included studies showed that Alternate Healthy Eating Index is superior compared to the DASH diet and MedDiet [13–15].

**Mediterranean diet (MedDiet)**

The Mediterranean diet is a diet with high fruits and vegetables, bread, legumes, olive oil, cereals, fish, and limited animal products [42].

The Mediterranean diet is promising for the prevention of GDM, however, the results are contradictory. A recent meta-analysis of the randomized controlled trial showed the efficacy of MedDiet in preventing GDM [43]. A recent review examined the role of MedDiet in modulating immune response and inflammation during COVID-19 and showed that MedDiet reduced interleukin-6 and inflammatory markers [44]. A recent case–control study showed that MedDiet reduced GDM incidence [45], interestingly, women who have rs7903146 T-allele showed a high reduction of GDM compared to their counterparts who are not indicating a gene-diet interaction [46]. The protective effect of MedDiet ranged from 15 to 38% depending on compliance, genetic factors, and the diagnostic method used (8% when the American Diabetes Association was used and 24% if The International Association of the Diabetes and Pregnancy Study Groups was used [38]. Although MedDiet was effective in preventing gestational diabetes mellitus, DASH diet and aAEI showed superiority [13–15].

**Western and prudent diet**

Zhang and colleagues found a positive association between Western and a negative association of prudent diet with GDM risk, while Radesky et al. found no associations. [48, 49].

**Physical activity**

In the present study, exercise was effective in the first trimester and not during the second trimester; previous studies showed lifestyle before gestation was effective in reducing diabetes. However, exercise during pregnancy was not [50]. Other studies showed early pregnancy (before the 15th week) lifestyles were effective [51] in line with our findings. The effect of physical activity on GDM prevention depends on the time and duration of physical activity. Exercise before or in early pregnancy was effective in reducing GDM in the majority of studies [52–55], while few studies showed no significant reduction. [56, 57]. A leisure time of physical activity of 150 h/week before pregnancy was associated with 68% risk reduction, and the benefits increased with longer duration [57].

Davenport and colleagues found that exercise of moderate intensity is effective in the prevention of GDM when adopted prenatally in line with our findings [58], the same conclusion was shown by other studies [59]. Davenport et al. study was limited by including all types of articles except case studies. A meta-analysis from China showed that diet and exercise were effective in reducing GDM when introduced earlier (before the 15th week), an effect that was not robot after that [51]. Other studies published in Spain and Australia [9, 60] and concluded the effectiveness of dietary advice and moderate exercise combination in GDM prevention in contradiction to the present result, a plausible explanation might be the different methods of exercise and the type of diet adopted. The earlier adoption of 50–60 min of moderate physical activity and targeting at-risk women with a high body mass index was found to be more effective [61]. However, an update of the same study showed a limited ability to inform practice due to the risk of bias observed in the included studies [62]. Further studies limited by including retrospective, cross-sectional, and case–control studies support the above findings regarding exercise [63]. We found only one meta-analysis assessing the effect of early and late exercise on GDM. However, the small number of included studies and the high heterogeneity limited the studies [64]. The study found no effect throughout pregnancy. A non-linear negative association between exercise before and during early pregnancy was observed by the previous literature. The association was steeper at lower levels; however, the benefits plateaued at 8–10 h a week, a finding that may explain...
the contradiction between various studies assessing the effects of exercise on GDM [24]. The compliance to exercise, duration, timing, and type of exercise might greatly influence the outcomes. To best inform Obstetric guidelines, studies putting the previous parameters into consideration are warranted.

The strength of the current meta-analysis is that it is the first to compare different types of diets and define the time, intensity, duration, and frequency of exercise.

Limitations
The study limitations were including some observational studies, the limitations to the English language, and the significant heterogeneity observed.

Conclusion
The Dietary Approaches to Stop Hypertension, Alternate Healthy Eating Index diet, and Mediterranean Diet were effective in reducing gestational diabetes mellitus. The DASH diet showed superiority to the Mediterranean. Furthermore, the Alternate Healthy Eating Index diet was better than the DASH diet. Data regarding physical activity were conflicting. Early mild-moderate physical activity was effective, while late, moderate-vigorous exercise was not. Randomized control trials and genetic studies are needed for the individualization of dietary patterns.

Abbreviations
MedDiet: Mediterranean diet; DASH diet: Dietary Approaches to Stop Hypertension; AHEI: Alternate Healthy Eating Index diet; GDM: Gestational diabetes mellitus.

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Author contributions
Concept and design: AHA & RAA. Literature search: AHA & RAA. Data analysis: AHA. Manuscript drafting, revision, and before submission: AHA & RAA. Manuscript submission: AHA. All authors read and approved the final manuscript.

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Availability of data and materials
The data used in this manuscript are available upon request.

Declarations
Ethical approval and consent to participate
We did not include any article published by the authors.

Consent for publication
Not applicable.

Competing interests
The authors declare no conflict of interest.

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