## RESEARCH

**BMC Endocrine Disorders** 



# The association between the dietary inflammatory index during pregnancy and risk of gestational diabetes: a prospective cohort study and a meta-analysis

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## Abstract

Introduction To examine the association between dietary inflammatory index (DII) and risk of gestational diabetes mellitus (GDM).

Methods A prospective birth cohort study was conducted in Iran. During the first trimester of pregnancy, food intake was measured using a food frequency questionnaire. Each participant's DII score was calculated, and then, the Cox proportional hazard model was used to calculate the hazard ratio (HR) and 95% CI of GDM across the guartiles of DII. We systematically searched the literature to conduct a meta-analysis of observational studies (PROSPERO: CRD42022331703). To estimate the summary relative risk for the highest versus lowest category of DII, a randomeffects meta-analysis was performed. The certainty of evidence was assessed using the GRADE approach.

**Results** In the prospective cohort study (n = 635 pregnant mothers), the multivariable HRs of GDM for the third and fourth guartiles of DII were 2.98 (95%CI: 1.98, 6.46) and 2.72 (95%CI: 1.11, 6.63), respectively. Based on a meta-analysis of six prospective cohorts and a case-control study (1014 cases of GDM in 7027 pregnant mothers), being in the highest category of the DII was associated with a 27% higher risk of GDM (relative risk: 1.27, 95%CI:  $1.01, 1.59; I^2 = 50\%$ ; low certainty of evidence). A dose-response meta-analysis suggested a positive monotonic association between DII and GDM risk.

**Conclusions** Our prospective cohort demonstrated a positive correlation between GDM risk and the inflammatory potential of diet in the first trimester of pregnancy. The results need to be confirmed by larger cohort studies.

Clinical trial number Not applicable.

Keywords Dietary inflammatory index, Gestational diabetes mellitus, Inflammation, Iran

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## Introduction

The World Health Organization (WHO) defines gestational diabetes mellitus (GDM) as "any degree of glucose intolerance that manifests during pregnancy" [1]. The overall prevalence of GDM is increasing worldwide [2]. According to the current evidence, the prevalence of GDM ranges from approximately 6% in Europe to approximately 15% in China [3, 4]. The prevalence of GDM varies across the Middle East and North Africa region, including Iran. However, the total prevalence of GDM in Iran was reported in 7.6% of pregnancies [5].

Several adverse health consequences, such as an increased risk of preeclampsia during pregnancy [6] and higher future risk of type 2 diabetes [7], macrosomia, preterm birth, and comorbid conditions such as cardiovascular disease for both women and their children [8], linked to GDM. Maternal age, family history of diabetes, history of GDM, and history of macrosomia in infants [9], black race [10], overweight or obesity during pregnancy, and smoking [2] are risk factors for GDM. Evidence from epidemiological studies suggests that maternal inflammatory lifestyle factors such as overweight and obesity, as well as unhealthy dietary habits, either before or during pregnancy, may be associated with an increased risk of GDM [2, 11]. Low-grade systemic inflammation may trigger insulin resistance and thus be associated with a higher risk of developing GDM during pregnancy [12, 13].

The population-based Dietary Inflammatory Index (DII) is a new diet quality index developed based on the literature to assess the inflammatory potential of the diet [14]. The DII takes into account the effect of nutritional parameters on inflammatory markers such as C-reactive protein [15, 16], interleukin 6 [17, 18], and tumor necrosis factor-alpha [19]. Previous studies suggested that a diet with high inflammatory potential, represented by a higher DII value, may be associated with a higher risk of all-cause mortality, cardiovascular disease, and site-specific cancers [20, 21]. Elevated DII, indicating a more pro-inflammatory diet, may be associated with an increased risk of GDM in women who were obese before pregnancy, according to a prospective birth cohort study conducted in China [22]. However, there is limited data on the association between the inflammatory potential of diet and GDM in the Middle East [23]. We aimed to conduct a prospective cohort study to investigate the association between dietary inflammatory characteristics, as indicated by the inflammatory potential of diet, and GDM in Iranian women.

## Materials and methods Persian birth cohort Participants

The current study was carried out as part of the Persian Birth Cohort (Prospective Epidemiological Research Studies in IRAN) [24]. The Persian Birth Cohort is a prospective cohort study conducted nationwide in five districts of Iran. Its aim is to advance knowledge and provide scientific evidence for the development of evidence-based national policies on various aspects of the developmental origins of health and disease [24]. Previous publications provided detailed information about study participants and recruitment procedures. Long story short, participants were selected from pregnant women living in the central Iranian city of Semnan. Pregnant women referred to Semnan health centers between 2018 and 2020 were invited to participate in this prospective cohort study. In addition, we placed advertisements on social and local media platforms as well as in medical clinics across the city to motivate women to participate in this prospective cohort study. Women of Iranian nationality who met the following criteria were included in the study: mothers who (1) were in the first trimester of pregnancy, regardless of their pregnancy history (including parity) or whether they had received fertility treatment; (2) had to have resided in Semnan for at least one year and intended to give birth in a Semnan hospital; and (3) pregnancies that ended in either cesarean section or vaginal delivery. Exclusion criteria included (1) birth of twins and (2) having any diagnosed endocrine or hormonerelated disorders such as thyroid disorders, polycystic ovary syndrome, diabetes, or adrenal gland disorders.

A total of 1024 women agreed to participate in the research. Of these, 635 pregnant women were eligible for the current study. Exclusions included mothers who did not complete dietary questionnaires in the first trimester (n = 293), mothers who dropped out of the study before completion and had incomplete information about the study results (n = 45), mothers whose total energy intake was less than 500 or more than 3500 kcal/day (n = 18) [25], mothers who smoked cigarettes (n = 23). Each participant received an explanation of the study protocol and signed an informed consent form. The Ethics Committee of Semnan University of Medical Sciences approved the protocol of the study (Code of Ethics: IR.SEMUMS.REC.1400.251).

## Assessment of dietary intake Nutritional intake evaluation

In this prospective cohort study, a 90-item food frequency questionnaire (FFQ) was developed and validated to assess participants' dietary intake during the first trimester of pregnancy [24]. Dietary assessments were conducted by trained interviewers who conducted faceto-face interviews. We collected information about the frequency of food consumption in the first trimester of pregnancy. The frequency of consumption of each food item in the FFQ included nine possible items, ranging from "never or less than once a month" to "six or more times per day." We then converted this information into grams per day using household measurements. We calculated total energy and nutrient intake using Nutritionist IV software modified for Iranian foods (version 7.0; N-Squared Computing, Salem, OR).

## Calculation of dietary inflammatory index

The DII score was calculated by multiplying the dietary inflammatory weights of 29 nutrients or foods [26]. We first adjusted food intake to total energy intake using the residual method. These values were then summed. To reduce the differences in dietary intake between individuals, the daily intake of macro- and micronutrients (protein, carbohydrates, total fat, polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFA), saturated fatty acids, cholesterol, n-3-fatty acids, required acids, n-6 fatty acids, iron, magnesium, selenium, zinc, caffeine,  $\beta$ -carotene, vitamin A, vitamin D, vitamin E, vitamin C, vitamin B6, vitamin B12, iron fumarite, folic acid, niacin, riboflavin, thiamine) were initially calculated. We did not include flavanones, isoflavones, thyme/oregano, anthocyanidins, rosemary, garlic, ginger, saffron, turmeric, trans fatty acids, benzophenon-3-ol, and tea in our calculation of the DII score because there was insufficient data on their consumption. We standardized energy-adjusted nutrient intake to the corresponding global mean and standard deviation. Finally, the DII score was calculated by adding all food parameter-specific DII scores. A more pro-inflammatory diet is indicated by higher DII values, whereas a more anti-inflammatory diet is indicated by lower (more negative) DII values.

#### Outcome assessment

GDM in our study is defined according to the American Diabetes Association (ADA) diagnostic criteria [27]. The diagnosis was made using a two-step approach: first, a 50-g (non-fasting) glucose challenge test, followed by a 100-g oral glucose tolerance test for those who screened positive. GDM was diagnosed if two or more of the following plasma glucose levels were met or exceeded: fasting blood sugar higher than 95 mg/dL, one-hour blood sugar higher than 180 mg/dL, two-hour blood sugar higher than 155 mg/dL, and three blood sugar hours greater than 140 mg/dL. Additionally, women who required pharmacological treatment for GDM were also considered to have GDM, with medical records and laboratory measurements used to confirm the diagnosis [27].

## Assessment of other variables

Trained interviewers used structured questionnaires designed for use in Persian birth cohorts to collect data on study participants' characteristics [24]. Trained interviewers recorded details about age, medical history, education level, parental occupation, and family income. To assess the levels of physical activity, we used the International Physical Activity Questionnaire [28]. We divided study participants into two groups based on metabolic equivalent minutes per week (MET minutes/ week) [29]: (1) no or low physical activity (< 3000 MET minutes/week), and (2) moderate to high physical activity (>3000 min/week MET). Cohort interviewers measured height and weight at multiple time points during the pregnancy. Baseline weight was recorded using a digital scale set to the nearest 0.5 kg while mothers were comfortably dressed and not wearing shoes. In the second and third trimesters, pre-delivery weight measurements were taken following the same protocol. For our analysis, gestational weight gain was calculated by subtracting the mother's weight recorded during the first trimester from her last recorded weight immediately before delivery. To enhance accuracy, we accounted for gestational age by calculating the average weekly weight gain. This was done by dividing the total weight gain by the number of weeks between the first-trimester measurement and the last pre-delivery weight. Height was measured to the nearest 0.5 centimeters without shoes using a wall stadiometer, and the calculation of body mass index (BMI) consisted of dividing weight in kilograms by height in meters squared.

## Statistical analyses

We first calculated the DII for each participant and divided the participants into quartiles based on their DII values. Next, we summarized and compared the characteristics of participants across the DII quartiles using the ANOVA test for continuous variables and the  $\chi^2$  test for categorical variables. The associations between DII quartiles and the risk of GDM were assessed using Cox proportional hazard models, with hazard ratios (HR) and 95% confidence intervals (CI) estimated for each quartile. In the multivariable analysis, we adjusted for potential confounders, including age, education level, physical activity, weight gain during pregnancy, family income, marital status, pre-pregnancy BMI, energy intake, and histories of cardiovascular disease (CVD) and hypertension. The specific questions used to gather data on these variables can be found in Supplementary Text 1. All statistical analyses were conducted using SPSS software (version 22). A p-value of less than 0.05 was considered statistically significant.

## Systematic review and meta-analysis Literature search and study selection process

We searched PubMed, EMBASE, and Web of science to find potential eligible studies. Our search strategy included keywords related to dietary inflammatory index and GDM. We submitted the protocol of the review with PTOSPERO (CRD42022331703). The meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews of Interventions [30].

#### Study selection and eligibility criteria

We selected studies that (1) had an observational design, including prospective and retrospective cohort or casecontrol studies; (2) included pregnant women aged  $\geq$  18 years; (3) considered the DII as an exposure either before or during pregnancy; (4) considered GDM as an outcome; and (5) reported adjusted effect size (relative risk (RR), hazard ratio, odds ratio) with 95% confidence interval (CI) of GDM across all DII score categories.

## **Data extraction**

Two reviewers (HSF and NP) independently reviewed the full texts of the prospective eligible studies. The same two authors extracted the first author's name, study design, and name, country, number of participants and events, age range or mean age, techniques used to identify exposure and outcomes, level of statistical adjustment, and effect estimates provided. When disagreements arose, they were resolved by consensus.

## **Risk of bias assessment**

Risk of bias assessment was performed using the ROB-INS-I tool for observational studies [31]. Two reviewers (MH and MM) conducted risk of bias assessments independently and in duplicate. When disagreements arose, they were resolved by consensus.

## Data analysis

Our analysis of the relationship between DII and GDM risk involved calculating summary RRs and 95% CIs using random effects models (DerSimonian and Laird method) [32]. The hazard ratios were considered equivalent to RR [33]. When studies reported the odds ratio as an effect estimate, we converted the effect estimates into RR [34]. To determine the RR and 95% CI of GDM for the highest versus lowest category of DII, we performed a pairwise meta-analysis. We then conducted a dose-response metaanalysis using studies with sufficient information for analysis. We calculated the summary RR for a one-unit increase in DII in each study and then summarized the study-specific RRs using a random effects model. We also conducted a single-stage, weighted, mixed-effects doseresponse meta-analysis to test the possible dose-response relationship between the DII and GDM risk according to the method of Crippa and colleagues [35]. We assessed heterogeneity using the I<sup>2</sup> statistic and performed a  $\chi^2$  test for homogeneity [36]. Due to the small number of studies (n < 10), we did not conduct a subgroup analysis and did not assess the potential for publication bias [36]. The statistical software STATA, version 17.0, was used for the analyses.

## Grading the evidence

The updated Grading of Recommendations Assessment, Development, and Evaluations (GRADE) tool was used by AJ and SS-B to assess the certainty of the evidence [37, 38].

## Results

## Prospective cohort study

The baseline characteristics of participants in the quartiles of DII are presented in Table 1. A total of 635 participants were included in this study. Participants in the fourth quartile of DII were significantly older, had lower BMI values, and were less likely to experience nausea and use multivitamin during the current pregnancy than participants in the first quartile of DII. There were no significant differences in other characteristics between quartiles of DII.

The baseline dietary intake of nutrients and food groups among quartiles of DII were indicated in Table 2.

The HRs (95% CI) of the incidence of GDM across quartiles of DII are shown in Table 3. In the crude model, those who were in the fourth quartile of DII, compared to the first quartile, were more likely to develop GDM [HR = 2.97, 95% CI = 1.44, 6.11; *P*-value = 0.003]. After adjusting for potential confounders (age, education, occupation, family income, marital status, physical activity, prepregnancy body mass index, energy intake, history of hypertension, and weight gain during current pregnancy), those in the third (HR: 2.98, 95%CI: 1.98, 6.46; *P* = 0.006) and fourth (HR: 2.72, 95%CI: 1.11, 6.63; *P* = 0.02) quartiles of DII had a higher risk of developing GDM during their current pregnancy.

## Meta-analysis

Through database searching, 28 records were identified for full-text assessment (Supplementary Fig. 1). After excluding 22 articles that did not meet our inclusion criteria, six articles were found to have sufficient data and met our inclusion criteria [22, 23, 39–42] (Table 4). Then, along with the results of the present study (Persian Birth Cohort), a total of seven observational studies with a total of 7027 pregnant mothers and 1014 cases of GDM, reporting the association between DII and the risk of GDM, were considered eligible for the analyses. Our meta-analysis included articles published between 2016 and 2021. One of the studies was a case-control study

Variable	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Р
Age (years)	28.3±5.10	28.4±5.02	28.3±4.87	29.8±5.05	0.02
Prepregnancy BMI (kg/m²)	$25.5 \pm 4.54$	$24.9 \pm 4.47$	$25.4 \pm 4.45$	$24.1 \pm 4.06$	0.01
Weight gain during current pregnancy (kg)	$13.2 \pm 5.36$	$13.5 \pm 4.83$	$13.4 \pm 5.16$	$13.7 \pm 4.49$	0.80
Having job with income (%)	28.1	24.7	22.5	24.7	0.63
University graduate (%)	4.5	4.4	5.8	4.4	0.23
Physical activity					0.60
Low (%)	24.5	24.7	26.3	24.5	
Moderate (%)	26.1	26.1	20.9	26.8	
History of CVD (%)	28.6	14.3	28.6	28.6	0.93
History of hypertension (%)	14.3	28.6	35.7	21.4	0.69
History of hypothyroidism (%)	21.6	30.6	20.7	27.0	0.32
History of hyperthyroidism (%)	14.3	14.3	28.6	42.9	0.66
Order of pregnancy (≥ 3, %)	20.8	17.6	16.3	22.7	0.21
Nausea during current pregnancy (%)	30.1	24.8	21.7	23.3	0.01
Multivitamin use during pregnancy (%)	22.9	41.4	14.3	21.4	0.006

Table 1 Characteristics of the participants in the Persian birth cohort study across categories of the dietary inflammatory index

Abbreviations: CVD, cardiovascular disease

[23], and the other studies, including the present study, were prospective cohort studies [22, 39–42].

In five studies, including the present study [22, 23, 41, 42], an FFQ was used for dietary assessment, while in the other two studies [39, 40], a three-day food diary was used. Included studies were from Iran [23, 41], the US [42], China [22], Ireland [40], and Finland [39]. Based

on the ROBINS-I tool, three studies were rated to have a serious risk of bias [39, 40, 42], and the other four studies, including the present study, were rated to have a moderate risk of bias [23, 41, 43] (Supplementary Table 1).

Of the studies, six studies, including the present study, reported information on the highest versus lowest category meta-analysis [22, 23, 39–41]. Being in the highest

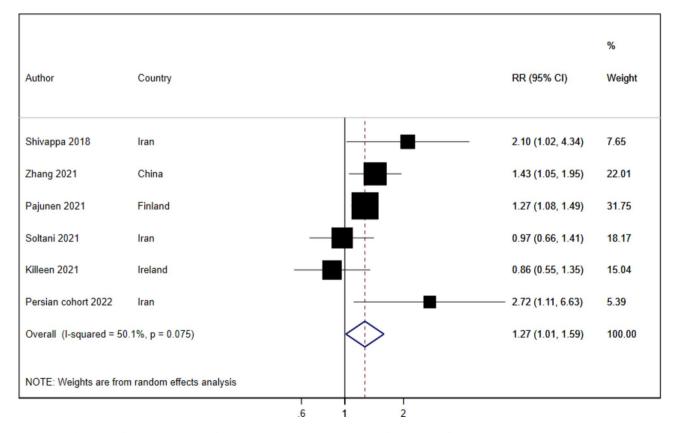


Fig. 1 The relative risk of gestational diabetes for the highest versus lowest category of the dietary inflammatory index

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lable 2 Dietar	v intake of the stud	iv participants across	categories of the dietar	v inflammatory index
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Variable	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Р
Energy (kcal/d)	1758±283	1688±313	1778±387	1810±686	0.36
Nutrients					
Carbohydrate (g/d)	$252 \pm 38.5$	$263 \pm 41.3$	$265 \pm 39.2$	$325 \pm 94.0$	0.01
Total fat (g/d)	$58.1 \pm 12.9$	$53.0 \pm 13.8$	$61.3 \pm 13.8$	77.1±24.4	0.01
Total protein (g/d)	$45.4 \pm 10.2$	$50.3 \pm 16.5$	$58.0 \pm 14.8$	$66.2 \pm 25.7$	0.02
Saturated fat (g/d)	17.2±4.33	$19.3 \pm 4.71$	$20.6 \pm 4.79$	$24.6 \pm 6.67$	0.001
PUFA (g/d)	$26.3 \pm 6.22$	21.8±6.14	$19.6 \pm 6.25$	18.0±6.34	< 0.001
MUFA (g/d)	$20.5 \pm 3.25$	$18.7 \pm 3.65$	$16.9 \pm 3.50$	$14.3 \pm 5.50$	< 0.001
Dietary fiber (g/d)	$20.5 \pm 2.57$	$18.7 \pm 2.54$	$16.2 \pm 2.99$	14.6±6.80	< 0.001
Vitamin C (mg/d)	$456 \pm 58.4$	$352 \pm 62.1$	272±81.2	$201 \pm 241$	< 0.001
Magnesium (mg/d)	$365 \pm 39.1$	$272 \pm 38.1$	$221 \pm 49.3$	$199 \pm 108$	< 0.001
Calcium (mg/d)	$530 \pm 252$	$623 \pm 271$	752±336	$931 \pm 458$	< 0.001
Zinc (mg/d)	$5.04 \pm 1.64$	$7.18 \pm 3.42$	$8.40 \pm 3.08$	$11.26 \pm 4.86$	< 0.001
lron (mg/d)	12.1±9.85	$21.6 \pm 30.1$	$24.7 \pm 25.3$	$38.3 \pm 38.5$	< 0.001
Copper (mg/d)	$0.78 \pm 0.23$	$1.08 \pm 0.22$	$1.34 \pm 0.26$	$1.81 \pm 0.78$	< 0.001
Vitamin A	425±233	$587 \pm 205$	753±239	1122±652	< 0.001
Vitamin E	$7.20 \pm 2.54$	$9.17 \pm 2.82$	$9.99 \pm 2.58$	$11.8 \pm 3.59$	< 0.001
Vitamin D	$1.39 \pm 1.19$	$2.28 \pm 1.54$	$2.78 \pm 2.21$	3.67±2.10	< 0.001
Vitamin K	$69.3 \pm 44.7$	88.5±38.6	$115 \pm 42.3$	$152 \pm 69.3$	< 0.001
Vitamin B1	$0.8 \pm 0.18$	$1.08 \pm 0.24$	$1.23 \pm 0.22$	$1.63 \pm 0.67$	< 0.001
Vitamin B2	$0.79 \pm 0.33$	$1.06 \pm 0.36$	$1.27 \pm 0.36$	1.71±0.63	< 0.001
Vitamin B3	$9.16 \pm 2.06$	$12.02 \pm 2.67$	$13.9 \pm 2.20$	$17.53 \pm 4.49$	< 0.001
Vitamin B6	$1.24 \pm 0.47$	$1.75 \pm 0.42$	$2.25 \pm 0.72$	$3.08 \pm 1.24$	< 0.001
Folate	$165 \pm 53.9$	$236 \pm 55.3$	$300 \pm 67.6$	$435 \pm 78.3$	< 0.001
Vitamin B12	$2.03 \pm 1.80$	$2.57 \pm 1.54$	$2.93 \pm 1.61$	$3.90 \pm 2.27$	< 0.001
Pantothenic Acid	$2.67 \pm 0.82$	$3.69 \pm 0.95$	$4.48 \pm 1.08$	$6.02 \pm 2.21$	< 0.001
Biotin	$24.5 \pm 7.14$	$32.7 \pm 9.32$	$34.7 \pm 8.55$	43.2±12.7	< 0.001
Food groups					
Grains (g/d)	$166 \pm 58.7$	173±64.9	$179 \pm 58.8$	$201 \pm 79.8$	< 0.001
Dairy (g/d)	223±177	273±182	313±203	413±301	< 0.001
Fruits (g/d)	423±118	396±146	$306 \pm 174$	$287 \pm 273$	< 0.001
Vegetables (g/d)	367±89.4	$292 \pm 77.2$	254±91.7	$212 \pm 140$	< 0.001
Legumes and nuts (g/d)	26.4±9.78	$23.2 \pm 10.1$	$21.4 \pm 10.6$	19.6±16.5	< 0.001
Red and processed meat (g/d)	9.43±8.33	12.1±8.68	14.1±9.50	15.8±12.5	< 0.001
Poultry (g/d)	6.83±6.68	8.82±6.66	$10.9 \pm 10.6$	12.3±11.9	< 0.001
Fish (g/d)	1.12±1.66	$1.57 \pm 2.43$	1.67±2.33	$2.32 \pm 2.50$	< 0.001
Egg (g/d)	$15.5 \pm 14.0$	23.4±29.0	$22.5 \pm 20.3$	28.7±21.7	< 0.001

Abbreviations: MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids

category of the DII score, as compared to the lowest category, was associated with a 27% higher risk of GDM (relative risk: 1.27, 95%CI: 1.01, 1.59;  $I^2 = 50\%$ , Fig. 1). Each one-unit increase in DII score was associated with a 7% higher risk (relative risk: 1.07, 95%CI: 0.94, 1.22;  $I^2 = 80\%$ ; n = 7 studies; Supplementary Fig. 2). Based on the information that was reported in four studies including the present study [22, 23, 41], the nonlinear dose-response meta-analysis indicated a positive monotonic association between DII score and risk of GDM ( $P_{nonlinearity} < 0.001$ ,  $P_{dose-response} < 0.001$ ; Fig. 2). Due to the very low number of studies, we did not perform subgroup analyses and did not assess the potential for publication bias. The certainty

of the evidence was rated low as assessed by the GRADE tool (Supplementary Table 2).

## Discussion

During the present cohort study of Iranian pregnant mothers, we observed a significant increase in the risk of developing GDM in women who consumed a highinflammatory diet in the first trimester of pregnancy. A meta-analysis of recent observational studies confirmed the results of the Persian cohort study and suggested lowcertainty evidence for a positive association between DII during early pregnancy and the risk of developing GDM. The dose-response meta-analysis suggested a positive

Quartile	Q1	Q2	Q3	Q4
DII score	-5.32 to -1.35	-1.35 to 0.21	0.21 to 1.51	1.51 to 4.69
Participants (n)	158	159	159	159
Person-week	5973	5919	5617	5672
Cases (n)	10	15	27	28
HR and 95% CI				
Crude	1	1.52 (0.68–3.38)	2.88 (1.39–5.96)	2.97 (1.44–6.11)
P-value		0.30	0.004	0.003
Multivariable adjusted*	1	1.70 (0.75–3.85)	2.98 (1.37-6.46)	2.72 (1.11–6.63)
P-value		0.20	0.006	0.02

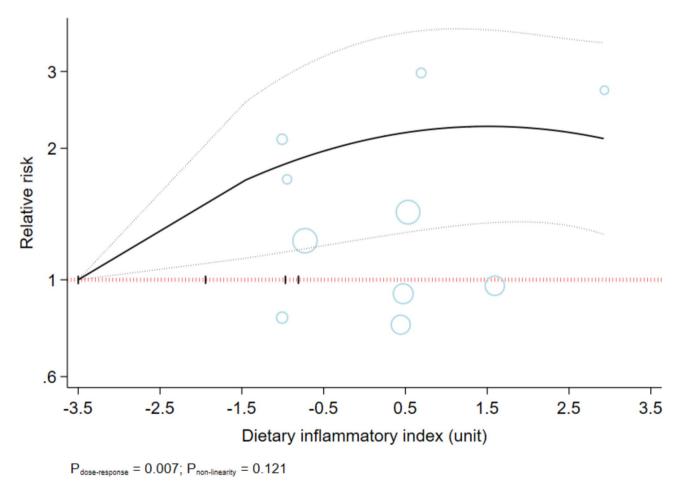
Table 3 The hazard ratio and 95%CI of gestational diabetes across categories of the dietary inflammatory index in the persian cohort study

\*Adjusted for age, education, occupation, family income, marital status, physical activity, prepregnancy body mass index, energy intake, history of hypertension and weight gain during current pregnancy

Abbreviations: DII, dietary inflammatory index; Q, quartile

monotonic association, with the risk of GDM increasing proportionally with the increase in DII score.

The DII is a newly developed, priori-defined diet quality index that focuses on the inflammatory potential of the diet and was therefore used in the present study to assess whether there is an association between a pro-inflammatory diet during early pregnancy and the risk of GDM. Previous studies have shown that higher intakes of some pro-inflammatory nutrients such as total fat, cholesterol, and heme iron [44–47], as well as pro-inflammatory foods or food groups such as red and processed meat and eggs during pregnancy, were associated



**Fig. 2** Dose-response association between the dietary inflammatory index and risk of gestational diabetes (P<sub>nonlinearity</sub> <0.001, P<sub>dose-response</sub><0.001; n=4 cohorts). Solid line represents the summary relative risk and dashed lines represent 95%CI. Circles are category-specific effect estimates in the included studies with the sizes of the circles proportional to inverse of the standard error. Small vertical black lines are baseline category in each study

Year Shivappa, 2018 Hospi Iran case-c Killaon 2001 Dropo	Study design	Par-	Mean	Dietary	Dietary assess-	Effect size (highest	Adjustments
		ticipants/ cases	age, year	assessment tool	ment timetrame	compared to the lowest category)	
	Hospital-based case-control	388/122	29	FFQ	One year before the interview	OR: 2.10 (1.02–4.34)	Age, energy, gestational age, exercise, BMI, history of diabetes, history of exposure to smoking and history of supplemental intake.
	Prospective cohort	394/57	32.5	3-day food diaries	Early pregnancy (14–16 weeks) and late pregnancy (28 weeks)	RR: 0.86 (0.55–1.35)	Maternal age at recruitment, ethnicity, economic advantage, smoking, study group, and maternal BMI (over 30 kg/m2)
Pajunen, 2021 Prospec Finland cohort	Prospective cohort	351/81	31.3	3-day food diaries	Early pregnancy	RR: 1.28 (1.08–1.49)	Pre-pregnancy BMI and original trial intervention groups
Sen, 2021 Pre-bir US study	th cohort	1808/96	32	FFQ	First and second trimesters	RR: 0.78 (0.65–0.95) per one-unit increase	Maternal prepregnancy BMI, education, age, parity, race/ethnicity, smok- ing during pregnancy, and household income.
Soltani, 2021 Prospec Iran cohort	Prospective cohort	812/231	30	FFQ	Weeks 8 and 16 of pregnancy	RR: 0.97 (0.66–1.41)	Physical activity, education occupation status, family number, history of stillbirth, history of preterm delivery, history of cesarean, history of abortion), pregnancy number (≤2/≥3) and baseline-BMI, maternal weight gain
Zhang, 2021 Prospec China cohort	Prospective cohort	2639/347	√ 13	FFQ	First trimester	RR:1.43 (1.05–1.95)	Age at enrollment, prepregnancy BMI, education level, average personal income, family history of diabetes, smoking and drinking habits, parity, pregnancy exercise, total energy intake, gestational week at FFQ, weight gain before GDM diagnosis, and multivitamin supplement use
Persian cohort, 2022 Prospective Iran cohort	ective t	635/80	29	FFQ	First trimester	RR: 2.72 (1.11–6.63)	Age, education, occupation, family income, marital status, physical activ- ity, prepregnancy body mass index, energy intake, history of hypertension and weight gain during current pregnancy

with a higher risk of developing GDM [46, 48–50]. Regarding dietary patterns, existing evidence suggests the need for the adoption of healthy dietary patterns [11, 51], or greater adherence to a priori defined low-inflammatory diet quality indices such as the Mediterranean [52, 53] or the Dietary Approaches to Stop Hypertension (DASH) [54] during pregnancy may be associated with a lower risk, and, in contrast, greater adherence to unhealthy dietary patterns such as Western dietary patterns with strong inflammatory properties during pregnancy may be associated with a higher risk of GDM [11].

Consistent with our results, a study by Shin et al. conducted in the United States found that adherence to a diet high in refined grains, fats, and added sugars and low in fruits and vegetables was associated with an increased risk of GDM during pregnancy [55]. A systematic review of 21 observational studies also found that diets rich in whole grains, vegetables, fruits, and fish and low in refined grains, red and processed meats, and high-fat dairy products may have a protective effect against GDM [56].

Several mechanisms may explain the above results of the present study and other prospective cohort studies. Excessive consumption of dietary sugar, an inflammatory dietary component, is associated with excessive energy intake and obesity, an important risk factor for GDM [57]. In addition, fasting blood glucose levels and insulin resistance may be increased by a high intake of rapidly absorbed carbohydrates in pro-inflammatory sugar-sweetened beverages [54, 55]. Additionally, diets high in whole grains, low in glycemic index, and low in simple sugars, such as the DASH or Mediterranean diet, may slow the body's glucose absorption and consequently reduce the need for insulin [58]. In addition, consumption of PUFAs and MUFAs in vegetable oils can improve glucose tolerance [59]. There is evidence that consumption of whole grains, an important anti-inflammatory dietary component, may reduce levels of systemic inflammatory markers that play a key role in diabetes risk [60]. According to previous studies, pro-inflammatory dietary components can trigger chronic systemic inflammation, which in turn can increase insulin resistance and plasma glucose levels [61–63]. Certain anti-inflammatory dietary components associated with DII, such as vitamin C, fiber, and carotenoids, may reduce the risk of GDM and improve insulin sensitivity due to their anti-inflammatory properties and biological antioxidant capacity [56, 64– 67]. The gut microbiota of pregnant women is another possible hypothesis [68]. Immune homeostasis is modulated by the gut microbiota [69]. Diet composition affects the balance of gut microbiota, which regulates insulin resistance and inflammation. Furthermore, diet influences intestinal inflammation either directly or indirectly by altering gut bacteria [70].

Our study has several important strengths, such as using a prospective observational design with a priori defined protocol, including a wide range of information from validated questionnaires, conducting a meta-analysis of observational studies, and assessing the certainty of evidence using the GRADE approach. In addition, we are not aware of any previous systematic literature review on the association of the DII and GDM. Thus, by incorporating the results of the present cohort study, we performed a systematic literature review to present a balanced understanding of the association between adherence to a diet with high inflammatory potential and risk of GDM. However, some potential limitations are unavoidable and need to be considered in future studies. First, the conclusion of the present study is based on observational studies and therefore cannot prove a causal relationship between DII during early pregnancy and GDM risk. However, results from randomized trials suggested that greater adherence to low-inflammatory diets such as the Mediterranean diet may reduce the risk of GDM [71, 72]. Further studies are needed to assess whether adopting a low-inflammatory diet can reduce the risk of GDM. Second, due to the observational design of the studies, the potential impact of unmeasured confounders as well as remaining confounders should be considered. Third, of the seven studies included in the meta-analysis, three studies were from Iran, which limits the generalizability of the results due to indirectness. Additionally, as almost all studies included in the present meta-analysis were small studies, there is a possibility of publication bias in this meta-analysis, which in turn may result in an overestimated effect estimate. This underscores the importance of interpreting the findings with caution and highlights the need for further research that addresses these limitations. Therefore, further large-scale cohort studies are needed to determine the association between the inflammatory potential of diet during early pregnancy and GDM risk.

## Conclusion

Our prospective cohort study of Iranian mothers found that a diet with higher inflammatory potential during early pregnancy may be associated with a higher risk of GDM. A meta-analysis of seven observational studies confirmed this finding and presented low-certainty evidence of a positive association between DII during pregnancy and GDM risk. However, due to the small number of studies included in the meta-analysis and the small sample size, larger cohort studies are required to confirm the results.

## Abbreviations

BMIBody mass indexDIIDietary inflammatory indexFFQFood frequency questionnaire

GDM	Gestational diabetes
GRADE	Grading of recommendations assessment, development, and
	evaluation (GRADE) approach
MET	Metabolic equivalents
MUFA	Monounsaturated fatty acids
PUFA	Polyunsaturated fatty acids
	, ,

## **Supplementary Information**

The online version contains supplementary material available at https://doi.or g/10.1186/s12902-025-01852-0.

Supplementary Material 1

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## Author contributions

HSF, NP, and AE contributed to the data gathering, literature search, data extraction, and manuscript drafting. AJ contributed to the study conception, data extraction, data analysis, and manuscript drafting. MMK and SSB contributed to study conception and data analysis. SS-B and MMK critically revised the manuscript. All authors have read and approved the final manuscript. SSB had primary responsibility for final content.

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#### Data availability

All data indicated and analyzed for this study are available by request to the corresponding author.

## Declarations

#### Ethical approval and consent to participate

This study was conducted in accordance with the guidelines set forth in the Declaration of Helsinki, and all procedures involving participants in the research study were approved by the Ethics Committee of Semnan University of Medical Sciences (Code of Ethics: IR.SEMUMS.REC.1400.251). Written informed consent was obtained from all subjects/patients. The protocol of the study was explained to all participants, and all participants provided signed informed consent.

### **Consent for publication**

Not applicable.

## **Competing interests**

The authors declare no competing interests.

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