Review Article

The Effect of Dietary Protein Intake on the Risk of Gestational Diabetes

Lingling Chen,1 Shuli Du,2 Honghua Song,2 Jing Chen,1 Cuiting Lv,3 and Chunhui Li4

1Department of Obstetrics, Dezhou Women and Children’s Hospital, Dezhou 253000, China
2Department of Obstetrics, Laoling People’s Hospital, Dezhou 253600, China
3Department of Reproductive Medicine, The Fourth Hospital of Hebei Medical University (Hebei Tumor Hospital), Shijiazhuang 050000, China
4Neurosurgery, Affiliated Hospital of Hebei University, Baoding, Hebei 071000, China

Correspondence should be addressed to Cuiting Lv; lcting1@sina.com

Received 3 July 2022; Revised 20 October 2022; Accepted 26 October 2022; Published 14 December 2022

Academic Editor: Christophe Hano

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Background. The results of epidemiological studies on the association between dietary protein intake and gestational diabetes mellitus (GDM) are controversial. Thus, this systematic review and meta-analysis of cohort studies were established to attain comprehensive findings regarding the association between dietary protein and the risk of GDM.

Methods. Bibliographic databases including PubMed, Scopus, Web of Science, and Google Scholar were searched to discover papers related to dietary protein and the risk of GDM. The summary relative risks with 95% confidence intervals (CIs) were estimated through a random effect model for the analysis of the highest versus the lowest categories of dietary proteins.

Results. A significantly increased risk of GDM among women who consumed the highest amount of animal protein was observed (summarized risk estimate: 1.52; 95% CI: 1.07, 2.17; $I^2 = 50.8\%$). No significant associations were identified regarding vegetable protein (summarized risk estimate: 0.99, 95% CI: 0.80 to 1.23, $I^2 = 63.8\%$) and total protein (summarized risk estimate: 1.12; 95% CI: 0.88, 1.41; $I^2 = 35.4\%$).

Conclusion. This review revealed that total protein intake had no relationship with the risk of GDM, while animal protein increases this risk. Further larger prospective cohort studies are required to confirm our results.

1. Introduction

Gestational diabetes mellitus (GDM), one of the most common complications of pregnancy, is a defect in glucose metabolism during pregnancy created by diminished insulin secretion along with pregnancy-related insulin resistance [1]. GDM makes mothers and offspring susceptible to an elevated risk of cardiovascular disease, type 2 diabetes mellitus (DM), obesity, and metabolic syndrome after pregnancy and in adult life [2]. Therefore, finding modifiable contributors for GDM poses significant public health significance as it may be helpful to eliminate the unfavorable implications for both mothers and infants [3]. Known risk factors for GDM are older maternal age, family history of diabetes, obesity, and previous GDM [4, 5]. Some studies have indicated that dietary factors are modifiable determinants of GDM [6, 7].

Among dietary factors, dietary protein may play an important role in the development of GDM by a proposed mechanism of fatigue and failure of pancreas islets, through a decrease in glucose threshold of pancreas islets and therefore induction of more insulin secretion from these cells, which induce enhanced gluconeogenesis and increase plasma glucagon level [8]. Previous studies demonstrated that higher prepregnancy intake of animal protein was associated with increased GDM [9]. In other studies, only animal protein was associated with this risk, and vegetable protein decreased the risk of GDM [10,11]. However, another report on the American population declined any increased risk for GDM in even increased dietary animal proteins [12].
Observational studies indicated inconsistent results for the relation of total protein intake or different types of protein and sources of protein with GDM. Regarding the mentioned inconsistency, all the observed results in these studies were accumulated by meta-analysis approach to assessing the association between dietary protein intake including total and specific proteins as well as the source of proteins and GDM risk.

2. Methods

This study has adhered to the Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) Guideline [13].

2.1. Search Strategy. Two independent investigators systematically searched Scopus, Medline, Web of Knowledge databases, and Google Scholar search engine to explore the related articles published until October 2021. Relevant words such as dietary proteins or animal proteins, or vegetable protein or nuts or egg or meat, and gestational diabetes or diabetes pregnancy were used. Any restrictions such as language were not considered during the search process. The reference list of eligible articles and pertinent reviews were manually inspected to complete the search.

2.2. Inclusion and Exclusion Criteria. Studies were eligible whenever they owned the following parameters: prospective cohort design, participants enrolled were females with pregnancy, and papers mentioned the risk outcomes including hazard ratio, odds ratio, and relative risk. Confidence interval was used as distribution determinate for the measurement of any statistical relationship between dietary total protein or major protein subclasses (animal or vegetable source) intake and the risk of GDM.

Other observational studies such as case-control or cross-sectional studies, unrelated articles, proceedings, unpublished nonpublished papers, secondary studies and review reports, and letter to the editors were excluded. Furthermore, studies that have reported risk estimates per intake of dietary protein as a percent of energy intake were excluded if they did not report the total amount of energy intake. Studies that reported the amount of protein intake before the pregnancy instead of during pregnancy were also excluded [14]. In addition, studies not reporting the main outcomes (RR, OR, and HR) for the risk of GDM in subjects with higher and lower protein intake were excluded [15].

Besides the strength of novelty, this study faces important limitations. These limitations should be mentioned in the interpretation of the results. The limited number of studies evaluating the association between dietary protein intake and the risk of GDM fulfilling the eligibility criteria for inclusion in the meta-analysis is the first important limitation. The second limitation is significant heterogeneity among the included studies. In the analysis of the results, subgroup analysis was applied to determine the sources of heterogeneity. The limited number of interventional studies in the field of study questions and using observational studies for data synthesis is another limitation. The observational studies may have some biases which prevent us to show any causal link between the level of dietary protein intake and the risk of GDM. The fourth limitation is the potential measurement errors that happen in dietary protein measurement. Different methods used for GDM diagnosis in different studies should also be mentioned as a limitation. The lack of covariates control in some studies is another limitation.

2.3. Quality Assessment. The risk of bias for each included article was evaluated via Newcastle–Ottawa Scale (NOS) tool [16]. Studies with a total NOS score of ≥7 were considered high-quality publications. Two authors estimated the quality of each study independently. A third party (Principal investigator) made a final decision in a case where there was disagreement.

2.4. Data Extraction and Abstraction. Two investigators individually extracted the willing information, and if they had paradoxical opinions, the third author resolved the problem. The following data were extracted: first author surname, publication date, the country where the study was performed, age (mean/range), follow-up period, sample size, number of GDM patients, measure and range of dietary protein intake, estimated risk (RR, HR, and OR) for each category of dietary protein intake, methods for identifying GDM, dietary measurement method, and variables adjusted for. When several risks estimated were reported, the greatest degree of covariates was chosen for control.

2.5. Statistical Analysis. Relative risks (RRs) reported in the included studies were adapted to be able to be compared applying the method of quartile comparison, which is explained in detail previously [17]. The determinants of distribution of the data like SE and SD were adapted by calculating the variants using the values stated in the main included study. Calculations were done based on the comparison of different levels of dietary protein groups. The random-effects model was used to join risk estimates (relative risks, hazard ratios, and odds ratios) and ninety-five percent confidence intervals. The random-effects model, also named the variance components model, is a method used on variables which follow random distribution. This hierarchical linear model presupposes the data to be originated from dissimilar populations which their dissimilarity is associated with the hierarchy. For the measurement of heterogeneity of included subjects, the I² as well as Cochrane Q models were applied as explained in details previously [18]. Control of funnel plots asymmetry was used to control publication bias [19]. The method of subgroup analysis was used for the identification and adjustment of the different source of bias with different factors including the population size and origin, techniques of nutritional measurement, weight, exercise level, and other variables. The effect of each study on the magnitude of the observed results was evaluated by the “sensitivity analysis” method. In this method, the analysis was performed repeatedly with the respective
omission of included investigations. STATA application was used for statistical analysis. The cut of point of 0.05 was used for significance level.

3. Results

The flow diagram of the literature search is seen in Figure 1. A total of 1872 unique articles were identified through an initial search, of which 1802 publications were excluded by assessing their eligibility based on inclusion and exclusion criteria in the screening of titles and abstracts. After removing unrelated papers, the full texts of a total of 35 publications were reviewed. In this stage, twenty-nine articles were excluded due to the following reasons: irrelevant articles (n = 19), cross-sectional studies (n = 3), case-control studies (n = 4), and studies with insufficient data (n = 3). Six cohort studies were finally included in the systematic review and meta-analysis [12, 20–24].

The information from selected studies has been presented. Six cohort studies were included in the meta-analysis. The studies were published between 2008 and 2021, and they were conducted in the US [12,20,23], China [22,24], and Canada [21]. Women with GDM aged between 16 and 44 years old. A total of 23,270 pregnant women participated, 1193 of whom had GDM. Five studies used FFQ [12, 20, 21, 23, 24], and one used 24 h food recall [12]. The method of GDM diagnosis was an oral glucose tolerance test (OGTT) for five studies [12, 21–24] and physician diagnosis, glucose loading test, and urine screenings for one study [20]. All studies adjusted to age, four adjusted to energy intake, five adjusted to prepregnancy BMI, four adjusted to smoking, three adjusted to gestational weight gain, three adjusted to physical activity, and five adjusted to family history of diabetes. Three studies had high methodological quality (score ≥ 7) [20, 23, 24].

3.1. Meta-Analysis

3.1.1. The Association of Total Protein Intake and Risk of GDM. Five cohort studies were included in the meta-analysis [12,20,22–24]. When extreme categories were compared, no significant positive association was detected.
between total protein intake and risk of GDM (summarized risk estimate: 0.99, 95% CI: 0.80 to 1.23, I² = 63.8%) (Figure 2). Subgroup analysis found study location, sample size, dietary assessment tool, dietary evaluation time, adjustment to energy intake, smoking, physical activity, and family history of diabetes sources of heterogeneity. Furthermore, subgroup analysis showed that total protein consumption had a positive relationship with GDM in studies conducted in non-US countries, studies used a food recall questionnaire for dietary assessment, articles not controlled for energy intake, prepregnancy BMI, smoking, and family history of diabetes.

3.1.2. The Association between Animal Protein Intake and Risk of GDM. Five prospective studies examined the association between animal protein intake and risk of GDM [12, 20, 21, 23, 24]. In the meta-analysis comparing high vs. low animal protein intake categories, there was a significant association between animal protein intake and GDM (summarized risk estimate: 1.52; 95% CI: 1.07, 2.17; I² = 50.8%) (Figure 3). A significant positive association between animal protein intake and GDM was found in studies adjusted for prepregnancy BMI, smoking, and family history of diabetes.

3.1.3. The Association of Vegetable Protein Intake and Risk of GDM. Five cohort studies were included in the analysis of the high versus low intake of vegetable protein and risk of GDM [12, 20, 21, 23, 24]. Participants in the highest category of vegetable protein intake had not had an increased risk of GDM compared to participants with the lowest vegetable protein intake (summarized risk estimate: 1.12; 95% CI: 0.88, 1.41; I² = 35.4%) (Figure 4). Dietary assessment time, sample size, adjustment to physical activity, and gestational weight gain were sources of heterogeneity.

3.2. Sensitivity Analysis. Based on the sensitivity analysis results, no study had a significant impact on overall summary risk regarding the association of low vs. high total protein, animal and vegetable protein intake, and risk of GDM.

3.3. Publication Bias. The Egger test did not detect any evidence of publication bias for the association of total protein intake (P = 0.69), animal protein intake (P = 0.43), vegetable protein intake (P = 0.68), and risk of GDM. Furthermore, visual inspection of the funnel plot did not detect such findings.

4. Discussion

In this systematic review and meta-analysis of six cohort studies, a significantly higher risk of GDM was observed in relation to greater consumption of dietary animal proteins. However, no significant association was identified between total and vegetable protein intake and GDM risk. This is the first systematic review and meta-analysis that assess the relationship between dietary proteins and the risk of GDM. Our results regarding the significant positive association between animal protein intake and risk of gestational diabetes were compatible with previous findings of a large
updated meta-analysis on the association between meat protein intake and risk of diabetes in adults. They observed a 15–27% increased risk for processed and unprocessed meat, respectively [25]. The association was stronger in American population-based studies. In contrast to our results, Kurotani et al. did not reach any significant association.
between dietary animal protein intake and the risk of diabetes in women (in contrast to men) [26]. Supplemental iron intake in women is suggested as a potential explanation for this difference [27]. The detailed mechanisms of the effects of higher dietary animal protein intake on the risk of GDM are not completely understood. However, the observed association is biologically reasonable. It is suggested that the increased iron level released from heme in animal protein metabolism may be associated with this risk [27]. Iron is shown to be a potent prooxidant that may enhance oxidative damage to insulin-secreting cells in the pancreas [28]. The difference in policy on the intake of supplemental iron during pregnancy in different societies may explain part of the observed differences in the association between protein intake and the risk of GDM.

Different rationales are suggested for the difference between the observed results for the risk of GDM by animal and vegetable proteins. The first one is the presence of other nutrients such as cholesterol in red meat as the main source of animal protein in different dietary patterns. However, even studies that controlled this confounding factor reached a positive association between animal protein consumption and the risk of GDM. The difference in amino acids present in animal and vegetable proteins is another potential explanation for the observed difference in their effect on GDM risk. A large body of evidence showed different effects of amino acids in glucose metabolism in the liver, muscles, and pancreas [29]. For example, branched-chain amino acids which are associated with the increased risk of insulin resistance are found to be increased markedly in participants receiving animal proteins, but not in vegetable proteins [30, 31]. Apart from branched-chain amino acids phenylalanine and tyrosine, which are more in animal proteins, also were shown to be associated with the risk of diabetes in an investigation using a metabolomics approach [32]. Further studies are needed to elucidate the underlying mechanism by which dietary protein intake may be associated with pathways involved in the development of GDM.

Some studies provide evidence regarding the contribution of dietary iron intake to the risk of gestational diabetes [33–35]. It is shown that increased iron is able to activate oxidative stress pathways in different parts of the body including the pancreas [36, 37]. The oxidative damage to the pancreatic β-cells can be attributed to decreased insulin secretion and subsequent insulin resistance [38, 39]. There is accumulative evidence to support this hypothesis. Studies suggest a lower risk of diabetes in subjects with regular blood donation [40–42]. Multiple studies showed a significant association between indicators of body iron storage such as ferritin and risk of insulin resistance [43, 44]. It seems that different sources of dietary iron may cause dissimilar risks of insulin resistance [45]. Although epidemiologic studies support the increased risk of GDM in pregnant women with higher heme iron intake, multiple investigations failed to show this association with nonheme iron intake and iron supplementation during pregnancy [46]. It is suggested that the difference in the bioavailability of these two types of iron may be the source of the observed different effects [47]. Another explanation for the difference in the risk of GDM by heme and nonheme iron intake is the difference in baseline iron level [34].

It is supposed that patients receiving iron supplementation has lower baseline iron compared to the patients receiving higher heme iron. This discrepancy in baseline iron storage can cause a lower final level of total body iron storage in patients receiving nonheme iron supplementation during pregnancy, which can explain their lower risk of GDM.

In conclusion, this systematic review and meta-analysis of cohort studies showed a significant relationship between dietary animal protein intake and the risk of GDM in pregnant women. However, it failed to show any significant association between total and vegetable protein intake and the risk of GDM (Figure 5). More prospective cohort and interventional studies with larger study populations are needed to better show the relationship between protein intake and GDM. Other studies on involved pathways in the observed association are also needed to elucidate the underlying mechanisms.

The observed results provide evidence for the encouragement of pregnant women or women preparing for pregnancy to change a part of their dietary protein from animal proteins like the meat to vegetable proteins like nuts. This advice can be promoted by obstetricians, midwives, and nutritionists delivering preconception and antenatal care.

**Data Availability**

The data are available on request.

**Conflicts of Interest**

The authors declare that there are no conflicts of interest.

**Authors’ Contributions**

Lingling Chen, Shuli Du, and Honghua Song gathered data and reviewed the literature. Jing Chen analysed the data.
Cuiting Lv designed, supervised, and wrote the first draft of the paper. All authors critically revised the paper and approved the final version of the manuscript.

Acknowledgments

The authors want to thank Hebei Medical University for its support. The authors also thank Dr. Chunhui Li for his support in the study design, supervision, and fund absorption.

References


