Food & Function

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/d2fo03609f

Protein powder supplementation in early pregnancy and the risk of gestational diabetes mellitus: a prospective cohort study†

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Objective: Protein powder has attracted attention due to its possible adverse effects. We aimed to investigate the association of protein powder supplementation in early pregnancy with gestational diabetes mellitus (GDM) risk. *Methods*: We included 6897 participants with singleton pregnancies from a prospective birth cohort. Protein powder supplementation and GDM relationships were examined by unadjusted and multivariable analysis, 1 : 2 propensity score matching, and inverse probability weighting (IPW). A multinomial logistic regression model was used to further explore the effects of protein powder supplementation on the risk of GDM subtypes. *Results*: Overall, 14.6% of pregnant women (1010) were diagnosed with GDM. In the crude and multivariable analysis before propensity score matching, participants who had received protein powder supplements were more likely to have GDM than women who did not (OR, 1.39 [95% CI: 1.07–1.79]; OR, 1.32 [95% CI: 1.01–1.72]). Protein powder supplementation was significantly associated with a higher GDM risk on IPW analysis (OR, 1.41 [95% CI, 1.08–1.83]), propensity score matching analysis (OR, 1.40 [95% CI, 1.01–1.93]) and multivariable analysis adjusted for propensity score (OR, 1.53 [95% CI, 1.10–2.12]). In the multinomial logistic regression model, protein powder supplementation was only positively associated with the risk of GDM with isolated fasting hyperglycaemia (IFH) in the crude and multivariable models (OR, 1.87 [95% CI: 1.29–2.73]; OR, 1.82 [95% CI: 1.23–2.68]). *Conclusions*: Protein powder supplementation in early pregnancy is significantly associated with a greater risk of GDM, especially for GDM-IFH. Additional comparative studies are needed to validate these findings.

Received 23rd November 2022,
Accepted 22nd March 2023

DOI: 10.1039/d2fo03609f

rsc.li/food-function

Introduction

Gestational diabetes mellitus (GDM) is one of the most common pregnancy complications, which is defined as glucose intolerance of variable degrees with the onset or first recognition during pregnancy.[1] In the past two decades, the GDM prevalence has increased by over 30% globally.[2] In China, more than 2.9 million pregnant women are suffering from GDM, and the incidence is rapidly increasing.[3] GDM has long been associated with adverse outcomes for both maternal and offspring health.[4] Therefore, identifying the possible risk factors in early pregnancy is important for the early prevention of GDM.

Many risk factors, such as advanced maternal age, parity, obesity before pregnancy, excessive gestational weight gain, family history of diabetes and certain dietary nutrition, have been implicated in the development of GDM.[5] Recently, there has been growing interest regarding the effects of food intake and dietary supplementation in early pregnancy on GDM risk.[6] A meta-analysis of prospective studies indicated that pre-pregnancy intake of fried food, fast food, and red and processed meat was positively associated with the risk of GDM.[7] Moreover, iron supplementation, higher maternal vitamin B12 levels and dietary protein intake in early pregnancy are also significantly associated with GDM risk.[1,8,9] However, no studies have investigated the relationship between maternal protein powder supplementation in early pregnancy and GDM.

Over the past few years, consumption of over-the-counter protein powder supplements has become increasingly popular

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†Electronic supplementary information (ESI) available. See DOI: **https://doi.org/10.1039/d2fo03609f**

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among gym-goers as well as the public, including pregnant women. It is crucial for pregnant women to consume enough protein to support the growth and development of the fetus and to maintain maternal health.[10] Protein powder can be a convenient and quick source of protein for pregnant women who may have difficulty obtaining sufficient amounts from their diet alone. However, these pregnant women lacked knowledge about the correct use of protein powder supplements and often obtained them directly from sellers or through websites.[11] Furthermore, concerns regarding the safety of protein powder supplements are growing due to the reported presence of toxic agents.[12] Hence, more attention should be paid to the possible side effects of protein powder supplementation on human health, particularly in pregnant women.

In the current study, we used the binomial logistic regression model and propensity score model to examine the association between protein powder supplementation in early pregnancy and the risk of GDM in a Chinese birth cohort. Moreover, a multinomial logistic regression model was also used to determine which specific subtype of GDM was affected by protein powder supplementation.

Methods

Study population

The present study was embedded in a prospective birth cohort study, which was conducted in Wuhan, China. Details of the cohort design have been described elsewhere.[13] A total of 11 320 pregnant women were recruited from September 2012 to October 2014, and each participant was required to complete a structured questionnaire at enrollment and provide urine and blood samples before delivery. Women without 75 g 2-hour oral glucose tolerance test (OGTT) data (n = 4299) were excluded. We further excluded women with missing data on demographic statistics (n = 115). Finally, 6897 women were included in the present study (Fig. 1).

Protein powder supplementation

Protein powder supplementation (yes/no) was defined through the question: "Did you take protein powder supplements during the first trimester?".

Ascertainment of GDM and GDM subgroups

The study participants received universal GDM testing by use of OGTT during pregnancy between 24 and 28 gestational weeks. According to the recommendations of the International Association of Diabetes and Pregnancy Study Groups (IADPSG),[14] GDM was diagnosed if fasting plasma glucose (FPG) was ≥5.1 mmol L^{-1} or 1 h postload plasma glucose (1hPG) was ≥10.0 mmol L^{-1} or 2 h postload plasma glucose (2hPG) was ≥8.5 mmol L^{-1}. Based on the results of the OGTT, GDM was further classified into the following three subtypes:[15] isolated fasting hyperglycaemia (GDM-IFH) group, with isolated FPG ≥5.1 mmol L^{-1}; isolated post-load hyperglycaemia (GDM-IPH) group, with isolated 1hPG ≥10.0 mmol L^{-1} and/or 2hPG ≥8.5 mmol L^{-1}; and combined hyperglycaemia

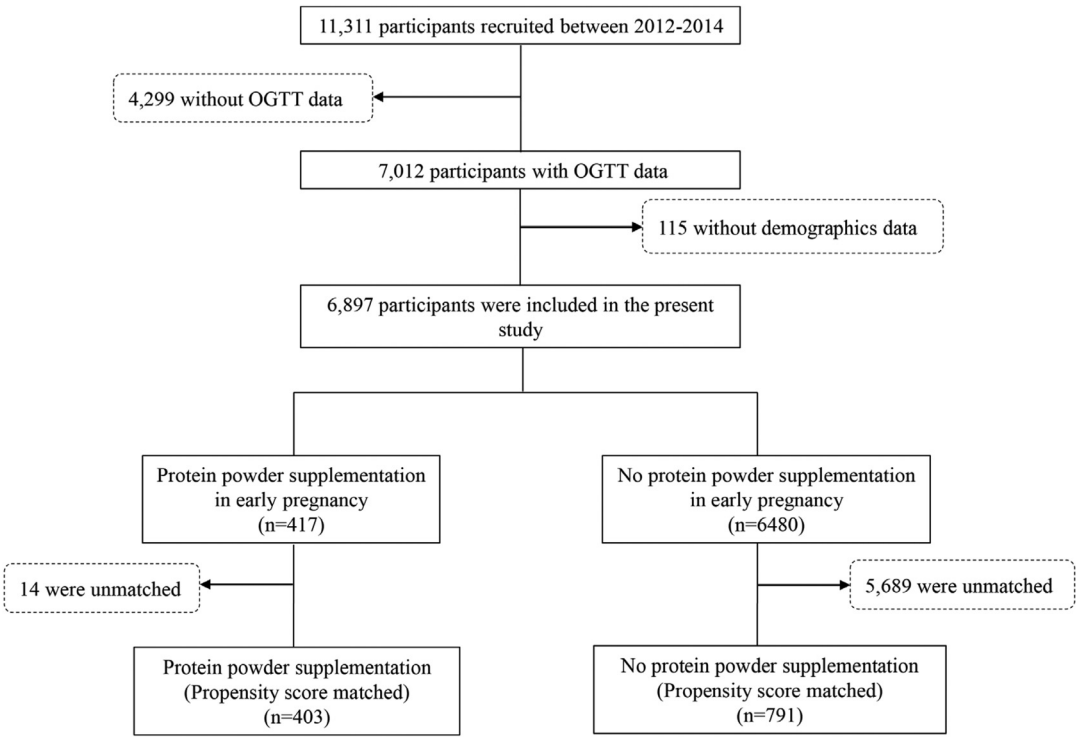

Fig. 1 Flowchart showing participant recruitment and classification for propensity score matching.

(GDM-CH) group, with both fasting and post-load glucose (either 1hPG or 2hPG or both) exceeding thresholds.

Covariates

Data on maternal demographics, socioeconomic status, and lifestyle characteristics were obtained using a structured questionnaire before recruitment. Maternal age, educational level (≤9/10–12/13–15/≥16 schooling years), physical activity (never or rarely, 1–2 days per week, 3–4 days per week, 5–6 days per week, daily), smoking status (yes/no), passive smoking (yes/no), alcohol drinking (yes/no), working status (yes/no), multiparity (yes/no), gravidity (1/2/≥2) and family history of diabetes (yes/no) were included. The economic status was defined by the "perception of family economic resources", which is measured on a discrete scale with four categories (very good/good/normal/poor). Pre-pregnancy BMI was calculated using pre-pregnancy weight (kilograms) divided by height squared (meters squared). Gestational weight gain was calculated by subtracting pre-pregnancy weight from the weight at the time of admission for delivery. Information on nutritional supplementation (yes/no) in the first trimester (including calcium, multivitamins, iron and folic acid) was obtained from the questionnaire.

Statistical analyses

Frequencies and descriptive statistics were used to summarize participant baseline characteristics. Logistic regression models were used to estimate the association between protein powder supplementation and the risk of GDM. An initial multivariable logistic regression model included demographic factors, lifestyle and other nutritional supplements. In addition, to help account for the nonrandomized supplementation of protein powder, we used propensity score methods to reduce the effects of confounding.[16] The propensity score was calculated with a multivariable logistic regression model to establish each participant's probability of protein powder supplementation according to the baseline characteristics. The following variables were used to generate the propensity score: age, pre-pregnancy BMI, education level, economic status, smoking status, passive smoking, alcohol drinking, gestational weight gain, work during early pregnancy, multiparity, gravidity, physical activity, family history of diabetes, and supplement with calcium, multivitamins, iron and folic acid.

To construct the propensity score matching model, participants who did or did not use protein powder supplements were matched 1 : 2 in random order on the logit of the propensity scores using a "greedy nearest-neighbor" algorithm (maximum caliper distance, 0.01) using the MatchIt package in R.[17] Adequacy matching for no major imbalance of each baseline covariate was assessed by comparing distributions of propensity score (Fig. S1–S3†) and standardized mean differences (SMDs), which is more meaningful than calculating the *P*-values of *t*-tests.[18]

The primary analysis used inverse probability weighting (IPW). In the IPW analysis, the predicted probability from the propensity score model was used to calculate the stabilized IPW weight. Logistic models that used the IPW weights were reported. Next, we conducted a secondary analysis that used propensity score matching and another that included the propensity score as an additional covariate.

Subgroup analyses were conducted with the multivariable logistic regression model. Specified subgroups for analyzing the risk of GDM included age (≤29/30–35/>35), pre-pregnancy BMI (<18.5/18.5–24/>24), educational level (≤9/10–12/>13), physical activity during early pregnancy (yes/no), gravidity (1/2/≥3), parity (1/≥2), economic status (very good/good/normal/poor) and work during early pregnancy (yes/no). To test for significant differences in the effect size among subgroups, an interaction term was included in the main propensity score model for each subgroup.

Additional sensitivity analyses were performed to establish the robustness of our findings. First, a propensity score matched model was constructed according to 1 : 1 matching. Second, a propensity score matched model was constructed according to the caliper set to 0.1. Third, a propensity score matched model was constructed according to the full method or optimal method. Fourth, a propensity score-matched analysis was conducted when age (as a categorical variable) was used to generate the propensity score. Fifth, a propensity score matched model was constructed excluding participants with a family history of diabetes.

Finally, a multinomial logistic regression model was used to further explore the effects of protein powder supplementation on the risk of GDM subtypes.

All analyses were performed using R version 4.1.0. Two-side *P* values of less than 0.05 were considered statistically significant.

Results

Characteristics of the study population

Of a total of 6897 participants, we identified 417 participants with protein powder supplementation and 6480 without protein powder supplementation in the full unmatched cohort. The distribution of the participants' baseline characteristics according to protein powder supplementation is shown in Table 1, both in the unmatched and propensity score matched analytic samples. In the unmatched sample, protein powder supplementation differed according to the age, pre-pregnancy BMI, work status, gravidity, family history of diabetes and use of dietary supplements (calcium, multivitamins, iron and folic acid). The odds ratios (ORs) with 95% confidence intervals (CIs) for protein powder supplementation according to all the variables included in the propensity-score model are shown in Table S1.† The *C*-statistic of the propensity score model was 0.71, which indicated that substantial differences existed between the protein powder supplementation group and the non-protein powder supplementation group. In the 1 : 2 matched analytic sample, 403 participants received protein powder supplements and 791 did not receive them. The included covariates were all well balanced between with

Table 1 Characteristics of the population using or not using protein powder supplements, before and after propensity-score matching

Characteristic	Unmatched population			Propensity-score-matched population		
	Protein powder supplementation (N = 417)	No protein powder supplementation (N = 6480)	SMD	Protein powder supplementation (N = 403)	No protein powder supplementation (N = 791)	SMD
Age at delivery (years)	29.26 ± 3.61	28.42 ± 3.43	0.238	29.07 ± 3.46	28.94 ± 3.57	0.037
Pre-pregnancy BMI (kg m^{-2}), %			0.10			0.043
<18.5	101 (24.2)	1374 (21.2)		99 (24.6)	191 (24.1)	
18.5–24	272 (65.2)	4330 (66.8)		261 (64.8)	515 (65.1)	
24–28	40 (9.6)	658 (10.2)		39 (9.7)	80 (10.1)	
>28	4 (1.0)	118 (1.8)		4 (1.0)	5 (0.6)	
Education level (schooling years), %			0.189			0.079
≤9	42 (10.1)	591 (9.1)		40 (9.9)	71 (9.0)	
10–12	90 (21.6)	1092 (16.9)		85 (21.1)	148 (18.7)	
13–15	274 (65.7)	4432 (68.4)		267 (66.3)	553 (69.9)	
≥16	11 (2.6)	365 (5.6)		11 (2.7)	19 (2.4)	
Economic status, %			0.054			0.068
Very good	3 (0.7)	52 (0.8)		3 (0.7)	6 (0.8)	
Good	82 (19.7)	1288 (19.9)		79 (19.6)	148 (18.7)	
Normal	326 (78.2)	5071 (78.3)		316 (78.4)	632 (79.9)	
Poor	6 (1.4)	69 (1.0)		5 (1.2)	5 (0.6)	
Smoking (yes), %	2 (0.5)	36 (0.6)	0.011	2 (0.5)	3 (0.4)	0.018
Passive smoking (yes), %	185 (44.4)	3290 (50.8)	0.033	90 (22.3)	169 (21.4)	0.023
Alcohol drinking (yes), %	12 (2.9)	135 (2.1)	0.051	12 (3.0)	21 (2.7)	0.02
Gestational weight gain at delivery (kg)	17.61 ± 5.18	17.24 ± 4.90	0.074	17.64 ± 5.18	17.57 ± 4.89	0.015
Work during early pregnancy (yes), %	185 (44.4)	3290 (50.8)	0.129	180 (44.7)	355 (44.9)	0.004
Multiparity (yes), %	51 (12.2)	663 (10.2)	0.063	47 (11.7)	71 (9.0)	0.088
Gravidity, %			0.141			0.081
=1	217 (52.0)	3783 (58.4)		212 (52.6)	446 (56.4)	
=2	107 (25.7)	1560 (24.1)		104 (25.8)	195 (24.7)	
>2	93 (22.3)	1137 (17.5)		87 (21.6)	150 (19.0)	
Physical activity during pregnancy, %			0.045			0.087
Never or rarely	48 (11.5)	679 (10.5)		44 (10.9)	94 (11.9)	
1–2 days per week	35 (8.4)	598 (9.2)		34 (8.4)	69 (8.7)	
3–4 days per week	29 (7.0)	478 (7.4)		28 (6.9)	51 (6.4)	
5–6 days per week	6 (1.4)	95 (1.5)		5 (1.2)	4 (0.5)	
Daily	299 (71.7)	4630 (71.5)		292 (72.5)	573 (72.4)	
Family history of diabetes (yes), %	4 (1.0)	10 (0.2)	0.108	1 (0.2)	1 (0.1)	0.028
Calcium supplement use (yes), %	302 (72.4)	3411 (52.6)	0.418	289 (71.7)	572 (72.3)	0.013
Multivitamin supplement use (yes), %	333 (79.9)	3946 (60.9)	0.425	319 (79.2)	632 (79.9)	0.018
Iron supplement use (yes), %	189 (45.3)	1740 (26.9)	0.392	179 (44.4)	349 (44.1)	0.006
Folic acid supplement use (yes), %	367 (88.0)	5335 (82.3)	0.160	353 (87.6)	686 (86.7)	0.026

BMI: body mass index and SMD: standardized mean difference.

and without protein powder supplementation in the propensity score matched samples (SMD all < 0.1).

Association of protein powder supplementation with the GDM risk

Among the 6897 participants included in the analysis, 1010 (14.6%) women were diagnosed with GDM. In the crude and multivariable analysis before propensity score matching, women who had received protein powder supplements were more likely to have GDM than were participants who did not (OR, 1.39 [95% CI: 1.07–1.79]; OR, 1.32 [95% CI: 1.01–1.72]). Additional three propensity-score analyses, including the IPW, matching and adjusted for propensity score, yielded similar results with the ORs and 95% CI being 1.41 (1.08–1.83), 1.40 (1.01–1.93) and 1.53 (1.10–2.12), respectively (Table 2). In the subgroup analyses of an unmatched cohort, the adverse effects of protein powder supplementation on the GDM risk were consistent across all subgroups examined, and no modification effects were observed (Table S2†). Multiple additional sensitivity analyses are presented in Table 3. The results did not differ materially from the main analyses when 1 : 1 matching was used, when the caliper was set to be 0.1, when full and optimal matched methods were used, when the propensity score was generated using age (as a categorical variable), or when the analyses were limited to women who had no family history of diabetes.

The effects of protein powder supplementation on the risk of GDM subtypes

To further explore which type of GDM was affected by protein powder supplementation, a multinomial logistic regression model was constructed. As shown in Table 4, protein powder supplementation was positively associated with the risk of GDM-IFH both in the crude and multivariable models (OR, 1.87 [95% CI: 1.29–2.73]; OR, 1.82 [95% CI: 1.23–2.68]). Nevertheless, there was no significant association between

Table 2 Association between protein powder supplementation and the risk of GDM in the crude analysis, multivariable analysis, and propensity-score analysis

Analysis	GDM
No. of events/no. of population at risk (%)	
Protein powder supplement use	79/417 (18.9)
No protein powder supplement use	931/6480 (14.4)
Crude analysis OR (95% CI)	1.39 (1.07–1.79)
Multivariable analysis OR (95% CI)[a]	1.32 (1.01–1.72)
Propensity-score analyses OR (95% CI)	
With inverse probability weighting[b]	1.41 (1.08–1.83)
With matching[c]	1.40 (1.01–1.93)
Adjusted for propensity score[d]	1.53 (1.10–2.12)

[a] The odds ratio from the multivariable logistic regression model, with adjustment for age, pre-pregnancy BMI, education level, economic status, smoking, passive smoking, alcohol drinking, gestational weight gain, work during early pregnancy, multiparity, gravidity, physical activity, family history of diabetes, and supplement with calcium, multivitamins, iron and folic acid. The analysis included all participants. [b] The primary analysis with an odds ratio from the multivariable logistic regression model with the same covariates with inverse probability weighting according to the propensity score. The analysis included all the participants. [c] The odds ratio from a multivariable logistic regression model with the same covariates with matching according to the propensity score. The analysis included participants (403 who used protein powder supplements and 791 who did not). [d] The odds ratio from a multivariable logistic regression model with the same covariates, with additional adjustments for the propensity score. The analysis included all the participants.

protein powder supplementation and the risk of GDM-IPH and GDM-CH. The analysis between protein powder supplementation and different time-point plasma glucose levels of OGTT showed similar results, that is, protein powder supplementation was only associated with increased FPG, but not 1hPG and 2hPG (Table S3†).

Discussion

To the best of our knowledge, this is the first study to investigate the relationship between protein powder supplementation and the risk of GDM in a cohort study. In this analysis involving a large cohort of pregnant women in China, we found that protein powder supplementation during early pregnancy was associated with significantly higher risks of GDM. More specifically, FPG and GDM-IFH were affected more by protein powder supplementation. These findings provide supportive evidence for policymakers to draw more attention to using protein powder supplements during early pregnancy.

It is difficult to compare our findings with those of previous studies due to the scarcity of research in this field. Recently, a small, case-control study involving 49 GDM pregnant women and 77 healthy pregnant women conducted in China reported a higher prevalence of GDM in subjects using protein powder supplementation in comparison with those who did not use it.

Table 3 Sensitivity analyses of the association between protein powder use and the risk of GDM

Analysis strategy	No protein powder supplementation		Protein powder supplementation		Measure of association (95% CI)
	All participants	GDM (%)	All participants	GDM (%)	
According to 1 : 1 matching	403	54 (13.4)	403	75 (18.6)	1.48 (1.01–2.17)
According to the caliper set to 0.1[a]	822	119 (14.5)	412	78 (18.9)	1.38 (1.00–1.88)
According to the full method[b]	5566	794 (14.3)	404	75 (18.6)	1.34 (1.02–1.74)
According to the optimal method[c]	834	120 (14.4)	417	79 (18.9)	1.39 (1.02–1.90)
According to the age categories[d]	786	106 (13.5)	402	75 (18.7)	1.47 (1.06–2.03)
Excluding participants with a family history of diabetes	784	112 (14.3)	398	76 (19.1)	1.41 (1.02–1.94)

[a] Matching using a caliper width of 0.1 of the standard deviation of the logit of the propensity score. [b] "Full" method matched samples consist of matched sets, where each matched set contains a processing unit and one or more controls (or a control unit and one or more processing units). [c] "Optimal" matching finds matching samples with the smallest average absolute distance between all matching pairs. [d] Age was categorized by <18.5, 18.5–24, 24–28, >28 in the propensity score matching.

Table 4 Association between protein powder supplementation and the risk of GDM subgroups in a multinomial logistic regression model

Protein powder supplementation	n[a]	GDM-IFH		GDM-IPH		GDM-CH	
		Case (%)	OR (95% CI)	Case (%)	OR (95% CI)	Case (%)	OR (95% CI)
No	6456	289 (4.5)	Ref	463 (7.2)	Ref	155 (2.4)	Ref
Yes	416	33 (7.9)	**1.87 (1.29–2.73)**[b]	31 (7.5)	1.10 (0.75–1.61)[b]	14 (3.4)	1.48 (0.84–2.59)[b]
			1.82 (1.23–2.68)[c]		1.00 (0.68–1.48)[c]		1.42 (0.79–2.54)[c]

[a] Participants who did not have glucose measurements at all three OGTT time points were not included. [b] Crude model. [c] Multivariable model with adjustment for age, pre-pregnancy BMI, education level, economic status, smoking, passive smoking, alcohol drinking, gestational weight gain, work during early pregnancy, multiparity, gravidity, physical activity, family history of diabetes, and supplement with calcium, multivitamins, iron and folic acid.

This report has not yet been fully peer-reviewed, but the results are posted to the MedRxiv website for public comment.[19] However, several studies have demonstrated that short-term high-protein diets improve glucose homeostasis in healthy adults and in individuals with diabetes.[20–22] The amount of protein consumed 6 hours before meals is one of the most important features for postprandial glycaemia prediction in pregnant women with GDM.[23] Furthermore, a randomized clinical trial found that consumption of whey protein powder shortly before breakfast could increase the early prandial and late insulin secretion and reduce postprandial glycaemia in type 2 diabetic patients.[24] The divergence may stem from the non-quantitative assessment of dietary supplement use. There is evidence that regular high doses of protein powder supplementation in addition to whole food proteins may actually be harmful.[25] Thus far, the impact of chronic and without professional guidance use of protein powder supplementation on human physical health is still unknown. Fortunately, more researchers have attempted to determine the potential adverse effect of a diet with indiscriminate use of protein powder supplements.[11,26]

We are not aware of the direct evidence regarding biological mechanisms underlying the adverse effects of protein powder supplementation on the risk of GDM. However, some of the recent evidence may offer a possible explanation. On the one hand, excessive use of protein powder supplements could cause a high protein intake, which might be associated with a higher risk of GDM. A multiethnic Asian cohort study indicated that higher intake levels of both animal and vegetable protein were associated with a higher risk of GDM in Asian women.[8] Additionally, a high protein and low carbohydrate dietary pattern in pregnancy was also linked to a higher risk of GDM in a Chinese prospective cohort study.[27] On the other hand, it has been found that many protein powders contained heavy metals (lead, arsenic, cadmium, and mercury), bisphenol-A, pesticides, or other contaminants with links to health conditions.[28] Previous studies have suggested that heavy metals, bisphenol-A and pesticides are all potential risk factors for GDM.[29–31] However, further research is needed to examine whether the association between protein powder supplementation and GDM risk is due to protein itself or other components within the protein powder supplements.

In the present study, we identified that protein powder supplementation mainly affected GDM subtypes with abnormal fasting glucose, which was consistent with the relationship between other exposures and GDM subtypes.[32,33] Some recent studies have indicated that individuals with isolated impaired fasting glucose and isolated impaired glucose tolerance have different insulin sensitivity characteristics of the liver and muscle.[34,35] Individuals with isolated impaired fasting glucose primarily manifest hepatic insulin resistance and relatively normal muscle insulin sensitivity.[36] Given that protein is an important modulator of glucose metabolism, a high protein diet may impact glucose homeostasis by promoting insulin resistance and increasing gluconeogenesis. However, the specific pathophysiological mechanism needs to be confirmed by further studies.

As the best approach to inform the effectiveness of a new intervention or treatment, the randomized control trial design could minimize unmeasured confounding and bias in observational studies.[37] Similarly, we have tried to minimize possible confounding using various analytic approaches in our observational cohort. In the main analysis, there was a significant association between protein powder supplementation and the risk of GDM in a multivariable regression model with inverse probability weighting according to the propensity score. Several other propensity-score approaches and multiple sensitivity analyses were also performed, which showed similar results. The findings were also consistent in subgroup analyses. In addition, the effects of protein powder supplements on the risk of GDM could be attributed to other dietary coexisting supplements. However, in the current study, the association between supplemental protein powder intake and GDM risk remains significant even after additional adjustments for the intake of multivitamins and other dietary supplements.

Several limitations of our study should be acknowledged. First of all, although potential confounding was accounted for by conducting a propensity analysis, we cannot completely exclude the possibility of residual confounding owing to the observation design. Considering the limitation of possible confounding variables, a well-designed randomized controlled trial is needed to confirm the adverse effects of protein powder supplementation. Second, because quantitative data on protein powder supplementation were not collected, information regarding the duration and frequency of protein powder supplement use is limited. Third, due to the weight gain in early pregnancy being unavailable, the data in this study were substituted with the weight gain over the entire pregnancy. Fourth, the influence of dietary protein intake (including major dietary protein sources and dietary patterns of protein intake) was not considered.

In conclusion, in this large birth cohort study we found that the risk of GDM was significantly higher in pregnant women with early protein powder supplementation than without supplementation. A well-designed randomized controlled trial is needed to determine the possible detriment of protein powder supplementation in early pregnancy.

Abbreviations

GDM	Gestational diabetes mellitus
OGTT	Oral glucose tolerance test
IADPSG	International Association of Diabetes and Pregnancy Study Groups
FPG	Fasting plasma glucose
1hPG	1 h postload plasma glucose
2hPG	2 h postload plasma glucose
IFH	Isolated fasting hyperglycaemia
IPH	Isolated post-load hyperglycaemia
CH	Combined hyperglycaemia
SMD	Standardized mean difference
IPW	Inverse probability weighting

OR Odds ratio
CI Confidence interval

Ethics approval and consent to participate

The current study was approved by the ethics committee of Tongji Medical College, Huazhong University of Science and Technology (number [2012]14) and the Wuhan Women and Children Medical and Healthcare Center (number 2010009). Written informed consent was obtained from all participants.

Data and material availability

The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions

Meng Yang: conceptualization, methodology, data curation, formal analysis, validation, funding acquisition, and writing – original draft; Zhongqiang Cao: data curation, project administration, visualization, and writing – review and editing; Jieqiong Zhou: project administration, visualization, and writing – review and editing; Jiuying Liu: validation and writing – review and editing; Yuanyuan Zhong: validation and writing – review and editing; Yan Zhou: validation and writing – review and editing; Xiaonan Cai: validation and writing – review and editing; Linling Yu: validation and writing – review and editing; Liqin Hu: validation and writing – review and editing; Han Xiao: supervision, validation, visualization, and writing – review and editing; Aifen Zhou: supervision, validation, visualization, and writing – review and editing.

Conflicts of interest

The authors declare that they have no competing interests.

Acknowledgements

This study was supported by the Wuhan Municipal Health Commission (no. WG21D06), the Top Medical Young Talents (2019) of Hubei Province, and the Central Guidance on Local Science and Technology Development Fund of Hubei Province (no. 2022BGE261).

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