Association between diet quality during preconception or pregnancy and adverse perinatal outcomes: a systematic review and meta-analysis

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September 24, 2021

Abstract

Background: Although women are encouraged to achieve good diet quality in preconception and pregnancy, the benefits on perinatal outcomes have not been established. Objective: To systematically review and quantify the association between diet quality and adverse perinatal outcomes. Search strategy: Medline, Embase, Food Science and Technology Abstracts and CINAHL were searched up to 5th March 2020. Selection criteria: Two authors independently screened, selected and coded relevant prospective cohort studies. Data collection and analysis: Thirty-three studies (315,431 participants) were included in the meta-analysis. Odds ratios and mean differences from individual studies were pooled using random-effects models. Main Results: The pooled results for the association between diet quality and excessive (OR: 0.91; 95 CI: 0.76, 1.10) or inadequate (OR: 0.90; 95 CI: 0.70, 1.17) gestational weight gain were not statistically significant. Women in the top tertile of diet quality scores during prepregnancy or pregnancy had a lower risk of gestational diabetes (OR: 0.77; 95 CI: 0.65, 0.90), hypertensive disorders of pregnancy (OR: 0.87; 95 CI: 0.83, 0.92), preterm birth (OR: 0.77; 95 CI: 0.66, 0.89), small for gestational age (OR: 0.88; 95 CI: 0.79, 0.99) and low birth weight (OR: 0.60; 95 CI: 0.37, 0.99) compared to those in the bottom tertile. No studies were found for delivery mode. Conclusions: Data from prospective cohort studies support the potential of improving maternal diet quality in the effort to prevent adverse perinatal outcomes. Funding: Canadian Institutes of Health Research HLT 151517, National Natural Sciences Foundation of China No. 81661128010 Keywords: Diet quality, perinatal outcomes.

Introduction

First 1000 days of life, including the prenatal period, offers a unique opportunity for the children and future generations to develop their ability to grow and prosper in society[1-3]. Mounting evidence from human and animal studies have shown that the maternal environment regulates embryonic epigenetic modulation and can predispose to later development of diseases[4,5]. Maternal nutrition in particular appears to be a key driver of epigenetic programming[3,5,6].

Although women in preconception and pregnancy have been advised to achieve a good quality of diet[7], little evidence was available on the benefits until the last few decades. The publication of the results of pregnancy and birth cohorts with high quality dietary data has facilitated the research on the health impacts of diet quality on perinatal adverse outcomes[8,9], including excessive/inadequate gestational weight gain, gestational

diabetes (GDM), hypertensive disorders of pregnancy (HDP), cesarean delivery, preterm birth, and extremes of birthweight.[10-15]

Several systematic reviews reported the associations between maternal dietary patterns and rates of GDM, HDP, preterm birth and fetal growth.[16-20] However, the validity of these studies has been limited by the inclusion of a single publication database[18], lack of a meta-analysis[16-18], and reporting of only a few of the relevant perinatal outcomes[19]. These reviews are also limited by the absence of registered or published protocols, which hinders the evaluation of a potential reporting bias.[21] Most importantly, the inclusion of studies using *a posteriori* dietary patterns[16-20] limits the relevance of these results to guide dietary interventions as they are data-driven and vary greatly between studies.

Diet quality, a relatively new concept, can be measured by scoring diet in terms of '*a priori* ' defined adherence to dietary guidelines or a specific pattern.[22,23] To date, no systematic review has evaluated the association between diet quality and adverse perinatal outcomes. The objective of this study is to synthesize the evidence and quantify the association between diet quality in preconception or pregnancy and perinatal adverse outcomes in prospective cohort studies.

Methods

This systematic review and meta-analysis was conducted following the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines[24]. A detailed description of the methodology has been published previously[25].

Search strategy

Four databases of published literature (MEDLINE ALL (Ovid), Embase (Ovid), Food Science and Technology Abstracts (Ovid) and CINAHL (EBSCOHost)) were searched from database creation to the cut-off date of March 5th2020. Both medical subject headings and text keywords were used to develop a comprehensive search strategy with inputs from the whole research team including the health science librarian (LS)[26]. Two groups of keywords were used: 'preconception or pregnancy', and 'diet quality' (See Table S1 for detailed search terms used in OVID Medline). The reference lists of included studies and relevant review articles were screened to identify any additional studies. When eligible abstracts were identified, the title and authors were searched to determine if full-text articles had been published. Eligibility was limited to full-text articles published in scholarly peer-reviewed journals in English[27].

Study Selection

The primary outcome of this systematic review is excessive or inadequate gestational weight gain according to the NAM recommendations, and secondary outcomes include GDM, pre-eclampsia, preterm birth, delivery mode and birth weight. Studies were included if they met the following criteria: 1) Prospective cohort studies of women in the preconception period or pregnancy recruited from the general population. 2) Diet quality measured with pre-specified scoring scales and validated dietary assessment methods. 3) Assessment of the association between diet quality score and any of the systematic review outcomes. The publications identified with the search process were uploaded to the Covidence software. YY and IH independently screened the titles and abstracts. All references that met the inclusion criteria or those for which eligibility was uncertain were selected for full-text screening. Reasons for exclusion at the time of full-text screening were recorded. Any disagreements arising during the selection process were resolved by discussion with a third reviewer (LD). The process of study selection is reported using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram[28].

Data Management

YY, IH and YZ independently extracted information from the included studies using a predefined data coding sheet. Authors were contacted to obtain more information if related data was ambiguous or not included in the publications. In cohorts reporting different diet quality scores, the results based on the largest sample size were included in the meta-analysis to avoid sample overrepresentation. When diet quality measures

were provided on equal sample sizes, results for the diet quality score with the most items were included. In cohorts where diet quality was reported at different time points in pregnancy, second trimester measures were selected. For each of these decisions, sensitivity analyses were then performed using other reported results from the same cohort to test the robustness of the findings. For each study, results from the model adjusting for the most confounding variables were selected.

YY and IH independently assessed the quality and risk of bias of each included study with the Newcastle–Ottawa Scale (NOS)[29]. The sum of points was used to categorize overall study quality as either high (7-9), moderate (4–6) or low (0-3).

Statistical Analysis

Meta-analyses using random-effects models were conducted for each outcome. Adjusted mean differences (MD) and odds ratios (OR) were pooled for continuous and categorical outcomes, respectively. Different scales of reporting diet quality across studies, including one absolute unit increase, one SD increase, tertiles, quartiles, quintiles were transformed to calculate the effect size in the top tertile of diet quality scores compared with the bottom tertile using methodology reported in previous studies[19,30,31]. There are two assumptions for this method: 1) diet quality scores are normally distributed and 2) the associations with the outcomes are log-linear. In a normal distribution, the means of the top and bottom tertiles, quartiles, quintiles of are 2.18, 2.54, 2.80 SD apart, respectively. log ORs and SEs were multiplied by 2.18/SD, 2.18, 2.18/2.54, 2.18/2.80 for the transformation from 1 unit, 1 SD, quartile, quntile, respectively, to estimates in tertile. Heterogeneity was assessed using the I^2 statistic, Cochran's Q test (P-heterogeneity) and by visual inspection of the forest plots. Sources of heterogeneity were assessed by conducting subgroup analyses when there was a substantial amount of heterogeneity (I^2[?]75% or P-heterogeneity<0.05).

Sensitivity analyses were performed by excluding one study at a time to evaluate the influence of any individual study on the pooled estimate. The robustness of the estimates was also examined with sensitivity analyses excluding moderate- and low-quality studies. Publication bias was assessed by visual inspection of a funnel plot and Egger's test when at least 10 studies were included in the meta-analyses[32].

Data analyses were performed using R version 4.0.3 (R Project for Statistical Computing). Two-tailed P values were used and $P < .05$ was considered statistically significant.

Results

Study selection, Characteristics, and Quality

The study selection process is shown in Figure 1. We identified 6113 unique publications from the databases and one from other sources. After title and abstract assessment, 98 publications were selected for full-text screening. A total of 34 articles met our eligibility and were included in this review, and 33 were included in meta-analyses.

As shown in Table S2, only two studies[33,34] were of moderate quality (NOS = 6) and all other studies were of high quality (NOS 7-9). The detailed characteristics of included studies are presented in Table S3. The sample sizes and study periods of the cohorts ranged from 41 to 72,072, and 1991 to 2017 respectively. All studies but one were conducted in pregnant women from the general population, with variable exclusion criteria related to maternal prepregnancy BMI, history of preterm birth, and maternal comorbidities. One study was conducted in pregnant women with obesity or history of GDM[35]. Four cohorts were conducted in Singapore[36], Malaysia[33], Mexico[37], and a French Caribbean island[38]. The other cohorts were conducted in high-income countries located in Europe, North America, and Oceania. Six studies used at least one self-reported outcome, while all other studies used valid assessments including medical records or standardized measurements. For dietary assessment, four[33,37,39,40]studies used dietary recalls, one[36] used both dietary recalls and food diaries, three[35,41,42] used non-validated FFQ, and the remainder of studies used a validated FFQ. Studies varied as to the timepoint and period of dietary assessment. Four studies[43-46] assessed diet in prepregnancy and other studies assessed diet during pregnancy. Diet quality was assessed using 22 different

scores, with versions of aHEI, HEI and MD scores most frequently assessed (Table S4). There was large variability of potential confounders included in the multivariable models across studies (Table S5).

Maternal Outcomes

Gestational Weight Gain

Six studies reported gestational weight gain according to NAM guideline as an outcome.[33,47-51] Pooled results demonstrated no statistically significant association between diet quality and excessive (OR: 0.91; 95 CI: 0.76, 1.10; I^2 = 59%; P-heterogeneity = 0.03; Figure 2) or inadequate gestational weight gain (OR: 0.90; 95 CI: 0.70, 1.17; I^2 = 80%; P-heterogeneity < 0.01; Figure S1). Results were consistent in the sensitivity analysis where the moderate quality study[33] was excluded (Table S6). Due to small number of studies, we were unable to detect the covariate that could explain the observed heterogeneity (Table S7).

Three studies reported gestational weight gain as a continuous outcome.[40,52,53] A Meta-analysis could not be performed because effect estimates were not available for one of the studies[52]. Rohatgi *et al.* found a strong association between HEI-2010 and GWG (p=0.0011), but no detailed effect estimates were reported[52]. Fulay *et al.* found that in women who were obese before pregnancy, each one-unit increment in the DASH diet score was associated with 0.19 (95% CI: 0.05, 0.34) kg higher GWG from the time of dietary assessment to delivery[53]. In a small study of 41 women, Grandy et al. did not find a statistically significant association between HEI-2010 and GWG[40].

GDM

Seven studies reported GDM as an outcome[34,35,43,44,47,54,55]. When results were pooled, pregnant women in the top tertile of diet quality scores had a lower risk of GDM compared with those in the bottom tertile (OR: 0.77; 95 CI: 0.65, 0.90; I^2 = 72%; P-heterogeneity <0.01; Figure 3). The results were consistent when the moderate-quality study[34] was excluded (Table S6). Subgroup analysis suggested that the association is stronger in studies with adjustment for education level (n=4, OR: 0.64; 95 CI: 0.56, 0.73; I^2 =0) than in those without adjustment for education level (n=3, OR: 0.91; 95 CI: 0.83, 0.99; I^2 =0). No heterogeneity between studies in each subgroup requiring further exploration was identified (Table S7).

HDP

Five studies reported HDP as an outcome[44,45,47,56,57]. When results were pooled, pregnant women in the top tertile of diet quality scores had a lower risk of preeclampsia compared to those in the bottom tertile (OR: 0.87; 95 CI: 0.83, 0.92; I^2 = 0%; P-heterogeneity = 0.67; Figure 4). All studies were of high quality (NOS score [?]7). (Table S2)

Delivery Mode

No studies evaluated the association between diet quality and delivery mode.

Infant Birth Outcomes

Preterm Birth

Eight studies reported preterm birth as an outcome[36,38,42,46,53,56,58,59]. When results were pooled, pregnant women in the top tertile of diet quality scores had a lower risk of preterm birth compared to those in the bottom tertile (OR: 0.77; 95 CI: 0.66, 0.89; I^2 = 16%; P-heterogeneity = 0.30; Figure 5). All studies were of high quality (NOS score [?] 7) (Table S2). In the study of Saunders et al.[38], prepregnancy BMI was found to be a strong effect modifier and the protective effect of good diet quality on preterm birth was stronger in overweight/obese women.

Birth Weight Extremes

SGA and LBW

Six[47,48,60-63] and five[37,46,59,61,62] studies reported SGA and LBW as outcomes, respectively. When results were pooled, women in the top tertile of diet quality scores had a lower risk of SGA (OR: 0.88; 95 CI: 0.79, 0.99; I^2 = 5%; P-heterogeneity = 0.39; Figure S2) and LBW (OR: 0.60; 95 CI: 0.37, 0.99; I^2 = 23%; P-heterogeneity = 0.27; Figure S3) compared to those in the bottom tertile. All studies were of high quality (NOS score [?]7) (Table S2).

LGA and Macrosomia

Six[47,48,60-63] and three[59,61,62]studies reported LGA and Macrosomia as outcomes, respectively. Pooled results for the association between diet quality and LGA or Macrosomia were not statistically significant (Women in the top tertile as compared to bottom tertile. For LGA, OR: 0.90; 95 CI: 0.71, 1.15; I^2 = 59%; P-heterogeneity =0.03; Figure S4. For Macrosomia, OR: 1.12; 95 CI: 0.69, 1.81; I^2 = 33%; P-heterogeneity =0.22; Figure S5.). All studies were of high quality (NOS score [?]7) (Table S2).

Birth Weight as a Continuous Variable and Birth Weight for Gestational Age Z-score

Nine[36,39-41,61,63-66] and three[60,62,63] studies reported birth weight as a continuous variable and birth weight for gestational age z-score as outcome measures, respectively. Pooled results for the associations were not statistically significant (women in the top tertile compared with the bottom tertile. For birth weight, beta: -7.8; 95 CI: -56.0, 40.5; I^2 = 79%; P-heterogeneity <0.01; Figure S6. For birth weight for gestational age z-score, beta: 0.0; 95 CI: -0.1, 0.2; I^2 = 74%; P-heterogeneity =0.02; Figure S7.). All studies were of high quality (NOS score [?]7) (Table S2).

Sensitivity Analyses

The pooled estimates were similar with the omission of one study at a time, or with the inclusion of different dietary scores from the same cohort (Table S6).

Discussion

Main Findings

This review identified 34 prospective cohort studies reporting the association between maternal diet quality and adverse perinatal outcomes, 33 of which were included in the meta-analyses.

Interpretation

The results of this study are consistent with the association of healthy dietary patterns in pregnancy with lower odds of GDM[17,20], HDP[17,20], preterm birth[16,19,20] and SGA[19] reported in previous systematic reviews. These results highlight the potential benefits of a healthy diet on the regulation of glycaemia and systemic inflammation through the consumption of low glycemic-index foods and micronutrients[3,67]. We found no significant association between diet quality and excessive/inadequate gestational weight gain, LGA/macrosomia, and birthweight as a continuous variable. These results concord with previous research suggesting that energy intake, rather than diet quality, is the main driver of gestational weight gain and fetal growth[67]. No study evaluating the association of diet quality with delivery mode was identified. Only two cohorts (four studies) included measures of dietary quality in prepregnancy, which limited our ability to draw conclusions on subgroup analyses in prepregnancy. Studies were all of moderate or good quality and sensitivity analyses revealed consistent findings with the exclusion of moderate quality studies.

Strengths and Limitations

This is the first systematic review evaluating and synthesizing the associations between maternal diet quality and adverse perinatal outcomes. The rigorous search and screening strategies employed, as well as the prospective registration and publication of our protocol limit the possibility of reporting bias. This review has several limitations. The exclusion of non-English publications, of abstracts, and of other grey literature could lead to publication bias. Publication bias could not be formerly assessed due to the limited number of studies reporting each specific outcome (less than 10 for any outcome). Some of the included studies reported diet quality measured with different tools and/or at different timepoints. A single measure had to be selected

to conduct the meta-analysis which could influence the results of the analysis. However, this is unlikely as sensitivity analyses conducted using other measures from the same cohorts provided similar estimates. These results are derived from observational studies and therefore no conclusions can be made on causal inference. The interpretation of these results is also limited by the variability in study populations, dietary scores, reported outcomes, and adjustment of confounding factors across studies. The vast majority of cohorts were conducted in high-income countries and therefore these results cannot be applied to middle and low-income countries. Twenty-two different dietary scores were used in the identified studies. The components of each diet quality score vary according to the underlying dietary recommendations, but they included similar adequacy components (vegetables, fruit, fish, nuts and unsaturated fats), and moderation items (added sugars and saturated fats). The robustness of the meta-analysis results in the sensitivity analyses including different diet quality scores measured in the same population is also reassuring as to the comparability of these scores. In the majority of studies, diet was appraised using an FFQ. While the use of FFQs has been associated with recall bias and classification errors, this is likely to bias results towards the null hypothesis. Studies reported variable outcome sets, which limited the number of results available for each outcome. While most studies used validated measurements or medical registration for outcome measurements, others relied on self-reporting. Misclassification related to self-reporting could have diminished the strength of the associations. In studies reporting GDM as an outcome, diet before 24 weeks of pregnancy was measured in six studies[35,43,44,47,54,55], but the timing of dietary assessment and recall period were not reported in the last study[34]. While we cannot exclude reverse causation due to measure of diet after implementation of dietary interventions in the last study, this would be expected to bias results towards the null hypothesis. While the results accounting for the most confounders were used in the meta-analysis, adjusted factors varied greatly between studies, and we cannot exclude the possibility of unaccounted confounding factors.

Conclusion

The results of this systematic review and meta-analysis demonstrate that good diet quality in pregnancy is associated with lower odds of GDM, HDP, preterm birth, and SGA/LBW. These findings support the potential of interventions based on dietary guidelines in preconception and pregnancy to help decrease the adverse perinatal outcomes. Long term follow-up of these cohort studies will be critical to establish the correlation between maternal diet quality and childhood growth trajectories.

Identified knowledge gaps include studies in middle and low-income countries, the association of maternal diet quality in preconception with perinatal outcomes, and the association of maternal diet quality with delivery mode.

DECLARATION

Author contribution

YY was the guarantor of the review. YY, WS, OF, IM, WF and LD contributed to the conception of the research question. YY, IH, WS, CF and DAF contributed to the development of search strategies, eligibility criteria and methodology for data synthesis. YY, YZ and IH worked in duplicate to screen the articles, extracting informations and assessing risk of bias. YY and IH analysed the data and drafted the results. YY, IH, WS, LD, WF, OF, IM, CF, YZ and DAF contributed to drafting of the paper and provided approval for the version submitted for publishing.

Funding statement & Disclosure of interests

This research project is sponsored jointly by the Canadian Institutes of Health Research (CIHR) (Grant HLT 151517) and the National Natural Science Foundation of China (NSFC) (Grant No. 81661128010). All authors declare no conflict of interest in conducting this review.

Acknowledgment

The authors would like to thank Lindsey Sikora (librarian) for counselling in developing the searching strategies. We also thank Dr Jean-Patrice Baillargeon and Dr Zhuoyu Wang for critical reviews and suggestions

in formulating the systematic review.

Ethical statement

No ethical approval was needed because this study used data from previous published studies and no primary data was collected.

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