Preconception Dietary Patterns and Associations With IVF Outcomes: An Ongoing Prospective Cohort Study

Shanshan Wu1,2†, Xudong Zhang1,2†, Xinyang Zhao1,2, Xinyao Hao1,2, Siwen Zhang1,2, Pingping Li1,2 and Jichun Tan1,2*

1 Department of Obstetrics and Gynecology, Center of Reproductive Medicine, Shengjing Hospital of China Medical University, Shenyang, China, 2 Key Laboratory of Reproductive Dysfunction Disease and Fertility Remodeling of Liaoning Province, Shenyang, China

There is a lack of research on preconception diet and reproductive outcomes conducted in the Chinese population using individual assessment. Between April 2017 and April 2020, 2,796 couples undergoing in vitro fertilization treatment were recruited in this ongoing prospective cohort, and 1,500 eligible couples were included in the final analysis. A validated semi-quantitative food frequency questionnaire was used to evaluate the maternal preconception diet. Other lifestyle factors, including smoking status, psycho-mental status, sleep quality, and physical activity, were also assessed. Five dietary patterns were identified using principal component analysis, namely “Fruits-Vegetables-Dairy-Eggs,” “Fish/Seafood-Animal blood,” “Tubers-Beans-Cereals,” “Puffed food-Candy-Bakery,” and “Dried Fruits-Organs-Rice.” After adjusting for multiple confounders, we detected that the women who are more inclined to the “Fruits-Vegetables-Dairy-Eggs” pattern and less adherent to the “Tubers-Beans-Cereals” were more likely to achieve normally fertilized eggs and transferable embryos. Regarding pregnancy outcomes, we observed that a lower “Puffed food-Candy-Bakery” score and a higher “Dried fruits-Organs-Rice” score were related to a higher likelihood to achieve biochemical pregnancy. In terms of pregnancy complications, an inverse association between “Fish/Seafood-Animal blood” and hypertensive disorders was observed. We further clustered the dietary patterns based on the proportion of food groups consumed and found that dairy intake was beneficial to embryo quality, while frequent rice consumption was associated with a higher risk of macrosomia. Notably, in the stratified analysis, we observed that the positive relationship between the “Fruit-Dairy-Vegetables-Eggs” score and normal fertilization and the inverse association of the “Fish/Seafood-Animal blood” score with hypertensive disorders during pregnancy were exhibited only among women with body mass index ≥25 kg/m². In conclusion, pre-treatment diets might be an important target for intervention to achieve a better reproductive outcome.

Keywords: preconception, dietary patterns, principal components analysis, cluster analysis, IVF
INTRODUCTION

Infertility is the inability to conceive within 12 months of regular, unprotected sexual intercourse (1), which has been recognized as a public health issue worldwide by the World Health Organization (WHO). The global disease burden of infertility has been increasing since 1999, estimated to affect about 10–15% of women of reproductive age (2–4). Although in vitro fertilization (IVF) treatment is a common alternative, the financial burden of treatment has deterred many couples (5). As a result, emerging scientific studies have been devoted to identifying modifiable factors which may affect human fertility, including diet, physical activity, stress, and lifestyle (6–9).

Studies on the relationship between micronutrients and fertility suggested that nutrition affects reproductive health (10–14), among which, folic acid and vitamin D are widely concerned. Compared with individual nutrients, the dietary pattern can represent the comprehensive effect of all foods consumed in one’s diet. Therefore, research on dietary patterns provides a broader view of food and nutrient intake and overcomes the methodological limitations of studying a single nutrient in food (15, 16). In addition, previous studies have suggested that dietary patterns are relatively stable from preconception to pregnancy (17). Several studies have reported that maternal dietary patterns may be associated with reproductive outcomes, such as ongoing pregnancy, pregnancy complications, preterm delivery, and neonatal defect (18–26). Thus, establishing a healthy habitual diet before pregnancy may be an important intervention target to improve reproductive health.

There are limited pieces of evidence on the association between dietary patterns and IVF outcomes (27–35). Among these studies, the “Mediterranean diet (MedDiet)” is a hot topic (29, 31, 33–35), while few studies focus on the analysis of diversified dietary patterns (27, 28, 30, 32). A study conducted by Vujkovic et al. recruited 161 couples undergoing IVF treatment and identified two dietary patterns by principal component analysis (PCA), namely “health conscious–low processed” and “Mediterranean” diet (28). It was reported that high adherence by the couple to the “Mediterranean” diet increased the probability of pregnancy (OR: 1.4, 95% CI:1.0–1.9). Another study conducted on the Rotterdam Periconceptional Cohort of 228 women with a singleton ongoing pregnancy revealed that periconceptional maternal adherence to a high fish and olive oil, low meat dietary pattern was positively associated with embryonic growth (32). Notably, the sample sizes of the abovementioned two studies were relatively limited, and other periconceptional lifestyle factors, such as psycho-mental status, sleep quality, and physical activity, have not been adjusted. Furthermore, most of the available studies were conducted in western countries, nevertheless, dietary habits are population-specific, and there are distinctive differences between Chinese and Western diets (36). Therefore, large-scale studies to explore the association between preconception diet and reproductive outcomes with adjustment of confounding bias introduced by varied lifestyle factors are warranted.

The major objective of this prospective cohort study is to assess the associations between preconception dietary patterns and reproductive outcomes following IVF treatment, ranging from embryonic development to pregnancy complications, in a large Chinese population. In this way, we may go a step further in giving proper advice on the dietary pattern for couples who prepare to have a child.

MATERIALS AND METHODS

Study Population

Data were obtained from couples recruited in an ongoing prospective cohort study, which was conducted at the reproductive center of a university in Shenyang, China. 2,796 couples were enrolled between April 2017 and April 2020. The inclusion criteria were as follows: (1) Chinese couples settled in the northeast of China; (2) willing to cooperate to complete the questionnaires across the gestational period; (3) intended to stay in the northeast of China for at least 3 years after delivery. All participants gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Shengjing Hospital of China Medical University (2017PS269K).

To investigate the effects of preconception dietary pattern on IVF outcomes, we only included the couples undergoing their first IVF treatment and excluded the couples: (1) using donor sperm or oocyte; (2) performing preimplantation genetic diagnosis (PGD) or preimplantation genetic screen (PGS); (3) women with pre-pregnancy diabetes. The flowchart of the selection process is presented in Figure 1.

IVF Procedures and Outcomes Assessment

The timeline of IVF treatment was previously described in detail (37–39). Briefly, the IVF process includes the following four steps: (1) controlled ovarian hyperstimulation (COH), (2) oocyte retrieval, (3) embryo transfer, and (4) pregnancy tests. Ovulation...
was triggered using human chorionic gonadotropin (hCG) when there were three or more dominant follicles (diameter ≥18 mm). After 34–36 h of hCG injection, oocyte retrieval was performed under the guidance of ultrasound.

The oocytes underwent IVF or intracytoplasmic in semination (ICSI) upon clinical indication. The number of oocytes with two pronuclei and good-quality embryos formed were evaluated by embryologists. The Peter system was used to evaluate the embryo quality on day 3 (40). Embryos with more than three cells and anucleate fragmentation <50% were classified as having transferable quality. Embryos with 6–10 cells and anucleate fragmentation <20% were identified as good-quality embryos. The possibility of normal fertilization, transferable, and good-quality embryos on day 3 were considered as embryonic developmental parameters.

In general, one or two embryos were transferred on the third or fifth day after fertilization. A serum β-hCG level >30 mIU/mL on day 14 after embryo transfer was considered to indicate biochemical pregnancy. Intrauterine gestational sac confirmed by ultrasound 28 days after embryo transfer was considered clinical pregnancy. The pregnancy loss before the 12 gestational weeks (GWs) was defined as early abortion, while the miscarriage occurring after 12 GWs but before 18 GWs was defined as late abortion. Live birth was defined as the delivery of a live newborn, and preterm delivery was defined as delivery at 36+6 GWs or below. Neonatal birth weight <2,500 g was considered as low birth weight, while >4,000 g was considered as macrosomia. Gestational diabetes mellitus (GDM) was diagnosed during 24–28 GWs if the participant met at least one of the following criteria: (1) fasting plasma glucose ≥5.1 mmol/L, (2) 1-h plasma glucose ≥10.0 mmol/L, and/or (3) 2-h blood glucose >8.5 mmol/L. Hypertensive disorders during pregnancy include gestational hypertension, pre-eclampsia, eclampsia, chronic hypertension, and chronic hypertension with superimposed pre-eclampsia. Gestational hypertension was defined as the onset of high blood pressure (at least 140 mmHg systolic or 90 mmHg diastolic) without proteinuria on two occasions at least 4 h apart in an ordinarily normotensive pregnant woman after 20 GWs. Pre-eclampsia or eclampsia was defined as gestational hypertension with concurrent proteinuria.

**Questionnaire Collection**

In this ongoing prospective cohort, both male and female partners are required to complete a questionnaire (base-Q) with 284 items on dietary intake and lifestyle before commencing ovulation induction. Furthermore, the female partners with positive β-hCG test would complete (1) the first questionnaire (T1–Q) with 219 items on medication and lifestyle, complete at the day of the B-ultrasonic pregnancy test; (2) the second questionnaire (T2–Q) with 169 items on clinical and lifestyle information during 22–26 GWs; (3) the third questionnaire (T3–Q) with 185 items on pregnancy complications and lifestyle at 30–34 GWs. The timing of the collection of questionnaires is shown in [Supplementary Figure 1](https://example.com/Supplementary_Figure_1). Questions regarding the clinical information and IVF outcomes were obtained from electronic medical systems and completed by medical staff, while the information associating lifestyle and the dietary pattern was filled in by patients under the guidance of trained clinical staff. Internal quality control was carried out according to the audio recordings automatically obtained by the system to ensure credibility.

To explore the association between pre-treatment diet and IVF outcomes, the information on maternal lifestyle during the preconception period was extracted from base-Q. In detail, the base-Q is composed of four parts: dietary intake, micronutrient supplement, psycho-mental status assessment, and other lifestyle factors. At the end of the whole questionnaire, we designed three questions, which were repetitive with the body of the questionnaire, to preliminarily assess the retest reliability. Taking the answers in the main body of the questionnaire as the standard, if the number of correctly answered questions among these three questions is three, two, one, and zero, the reliability is assigned as 100, 67, 33%, and 0, respectively. The questionnaires with reliability below 67% were considered implausible and excluded, as shown in [Figure 1](https://example.com/Figure_1).

Preconception dietary intake assessment was based on a self-administered, semi-quantitative food frequency questionnaire (FFQ). Participants were required to recall their frequency of intake and portion size consumed during the past 12 months. The FFQ was derived and modified from the validated Chinese dietary FFQ from the Chinese Center for Disease Control and Prevention (41, 42), which was widely used in various studies (43–48). Previous studies suggested that the reproducibility and validity of the Chinese dietary FFQ were satisfactory and it can be used to classify the subjects according to their food consumption in 1 year (41, 42). The FFQ adopted in this study contains 48 questions covering 24 non-overlapping food groups, which are based on nutrients, common characteristics, and culinary use, and 18 non-quantitative questions regarding beverages and spicy food intake ([Supplementary Table 1](https://example.com/Supplementary_Table_1)). Frequency options include: (1) every day; (2) 4–6 times a week; (3) 1–3 times a week; (4) 1–3 times a month; (5) almost never/never. Amount per day or per times options include: (1) <25; (2) 25–50; (3) 50–100; (4) 100–150; (5) 150–200; (6) 200–300; (7) >300. Data were converted into weekly consumption by multiplying the frequency and serving per intake. The percentages of weekly intake of the food groups were calculated as consumption of each food divided by total consumption of all foods. Total energy intake for each participant was calculated based on [China Food Composition Tables](https://example.com/China_Food_Composition_Tables) (49).

The consumption of micronutrient supplementation (folic acid, multivitamins, vitamin A–E, calcium, and iron) was assessed by base-Q as well. The frequency options were set as described above. We listed the common brands of supplements on the market and the corresponding content of each tablet so that the subjects can recall their daily intake as much accurately as possible. Afterward, standardized daily intake of each supplementation weighted by frequency was figured out and treated as a continuous variable in further analysis.

The stress, anxiety, and depression status of participants were assessed by the perceived stress scale, self-rating anxiety scale, and self-rating depression scale, respectively. These scales have previously been applied and validated in a Chinese population in previous studies (50–53).
Other lifestyle factors include smoking, passive smoking, sleep quality, physical activity, and work intensity. Sleep quality was evaluated by the Pittsburgh sleep quality index, which has been used in the Chinese population (54, 55). Physical activity was evaluated by the Chinese version of the International Physical Activity Questionnaire, and weekly metabolic equivalents (METs) were figured out according to the method described in previous studies (56, 57). The levels of work intensity were categorized as (1) unemployed; (2) low (75% working time spent on sitting or standing, 25% activity); (3) moderate (25% sitting or standing, 75% activity with moderate intensity); (4) high (40% sitting or standing, 60% activity with high intensity) (58).

In the validation analysis of base-Q, 16 couples were randomly selected and invited to complete the same questionnaire twice over the study period with a time interval ranging from 15 days to 2 months. Intraclass correlation coefficients were higher than 0.60 (0.62–0.81), indicating moderate to good test-retest reliability (59).

**Covariates**

Potential covariates include factors related to human fertility and IVF outcomes confirmed in previous studies (8, 9, 50, 54, 60). Information on maternal age (continuous), pre-pregnancy body mass index (BMI, continuous), educational level (middle school or below, high school, vocational or technical college, undergraduate, or postgraduate), the type (primary or secondary), cause (unexplained, male factor, female factor, or both) and duration (continuous) of infertility, COH protocol (long, short, antagonist, or others), insemination technique used (IVF, ICSI, or both), and the stage and quality of embryos transferred were extracted from the medical records. Infertility is the inability to conceive within 12 months of regular, unprotected sexual intercourse (1). In this study, the endpoint of infertility duration evaluation was the date of oocyte retrieval.

Other covariates including preconception psycho-mental status (stress, anxiety, and depression) and lifestyle factors (smoking, passive smoking, sleep quality, physical activity, and work intensity) were derived from the base-Q, as the first questionnaire completed before IVF treatment. Smoking status was categorized as (1) current smoker; (2) former smoker; (3) non-smoker. Passive smoking status was treated as a rank variable according to the frequency of exposure (< once a week; ≥ once a week). Sleep quality and physical activity were treated as continuous variates. Work intensity was treated as a rank variable according to the categorization described above.

The confounders associated with the dietary pattern were also considered, such as the consumption of beverages (categorical), spicy food (categorical), and micronutrient supplement (continuous). In detail, due to non-quantitative data collection, the intake of beverages and spicy food were analyzed as rank variate and dichotomous variate (yes or no), respectively. The intakes of beverages were ranked based on the frequency (Never/Seldom: ≥ once a month; < once a week; ≥ once a week). Univariate associations of covariates with reproductive outcomes following IVF treatment are summarized in Supplementary Table 2.

**TABLE 1 | Demographic and clinical characteristics of the study population (N = 1,500).**

| Characteristics | Data |
|-----------------|------|
| Maternal age (years) | 32.09 ± 4.33 |
| BMI (kg/m²) | 23.35 ± 3.56 |
| Educational level: | |
| ≤ middle school | 332 (22.1%) |
| High school | 223 (14.9%) |
| Vocational/technical college | 296 (19.8%) |
| Undergraduate | 554 (36.9%) |
| Postgraduate | 95 (6.3%) |
| Infertility type: | |
| Primary infertility | 830 (55.3%) |
| Secondary infertility | 570 (44.7%) |
| Duration of infertility (years) | 3.81 ± 2.94 |
| Infertility cause: | |
| Unexplained | 61 (4.1%) |
| Male factor | 175 (11.7%) |
| Female factor | 823 (54.8%) |
| Both | 441 (29.4%) |
| COH protocol: | |
| Long agonist | 417 (27.8%) |
| Short agonist | 31 (2.1%) |
| Antagonist | 778 (51.9%) |
| Others | 274 (18.2%) |
| Insenmination method: | |
| IVF | 811 (54.1%) |
| ICSI | 466 (31.0%) |
| IVF + ICSI | 223 (14.9%) |
| Normally fertilized embryos | 8.48 ± 5.52 |
| Good-quality embryos on day 3 | 6.08 ± 4.39 |
| Transferable embryos | 4.28 ± 4.12 |
| Stage of embryos transferred: | |
| Cleavage | 1,009 (67.3%) |
| Blastocyst | 491 (32.7%) |
| Number of embryos transferred: | |
| One | 739 (49.3%) |
| Two | 761 (50.7%) |
| Quality of embryos transferred: | |
| Good-quality | 1,199 (79.9%) |
| Good-quality + non-good-quality | 123 (8.2%) |
| Non-good-quality | 178 (11.9%) |
| Biochemical pregnancy | 798 (53.2%) |
| Clinical pregnancy | 687 (45.8%) |
| Ectopic pregnancy | 18 (2.3%)a |
| Early abortion (< 12 GWs) | 88 (6.3%) |
| Late abortion (≥ 12 GWs) | 31 (2.1%)b |
| Live birth | 529 (35.3%)b |
| Preterm delivery | 73 (4.9%)b |
| Low birth weight | 51 (3.4%)b |
| Macrosomia | 40 (2.7%)b |
| Gestational diabetes mellitus | 90 (6.0%)b |
| Hypertensive disorders during pregnancy | 37 (2.5%)b |

Data were described as mean ± SD or N (%).

a The proportion was calculated as the number of cycles resulting in ectopic pregnancy divided by the number of cycles achieving biochemical pregnancy.

b 20 women in a state of ongoing pregnancy were excluded from the analysis.
### Statistical Analysis

Principal component analysis (PCA) with varimax rotation and k-means cluster analysis was used to extract dietary patterns (15). PCA is a data-driven technique that reduces the dimensions of the data and groups correlated variables to derive common components, in this case, dietary patterns (61). The number of factors reserved was based on the eigenvalue, factor interpretability, and the point at which the scree plot leveled off (Supplementary Figure 2). The coefficients of components describe the correlation between food groups and give interpretation to dietary patterns. We deemed those food items with coefficients ≥0.40 in each pattern to be important for the interpretability. The Bartlett test of sphericity and Kaiser-Mayer-Olkin test were used to test the applicability of analysis. Dietary pattern scores were assigned to reflect the adherence to each pattern for each participant. The scores were obtained by multiplying the coefficients by the corresponding standardized intake of each food group and summing it up. We divided the score of each pattern into quartiles (Q1-Q4) for further analysis and defined the lowest fourth as the reference.

K-means cluster analysis was performed on the percentages of weekly intake of the food groups, as described previously (25). We pre-specify the number of categories to be clustered, from 2 to 6, and determine the final number of mutually exclusive groups based on the actual meaning and interpretability of the results. In this way, all the participants were divided into different groups with an exclusive dietary pattern.

Descriptive statistics were used to describe the demographic, clinical, and lifestyle characteristics of each participant, shown as mean ± standard deviation (SD) for continuous variates or number (percentage) for categorical variates. Poisson regression with robust variance estimation was performed to explore the associations between the dietary patterns and the possibilities of normal fertilization, good-quality and transferable embryos formed on day 3, biochemical and clinical pregnancy, and live birth due to their high prevalence (62). Multivariable logistic regression was conducted to assess the effect of dietary patterns on the risks of early abortion, late abortion, preterm delivery, low birth weight, macrosomia, GDM, and hypertensive disorders during pregnancy. Tests for the linear trend were performed by using the median score in each quartile as a continuous variable. Only the covariates with a univariate association of

| Characteristics                                      | Data                               |
|------------------------------------------------------|------------------------------------|
| Smoking status:                                       |                                    |
| Current smoker                                       | 31 (2.1%)                          |
| Former smoker                                        | 104 (6.9%)                         |
| Non-smoker                                           | 1,365 (91.0%)                      |
| Passive smoking status:                              |                                    |
| < once a week                                         | 1,076 (71.7%)                      |
| ≥ once a week                                        | 424 (28.3%)                        |
| Perceived stress scale score:                         |                                    |
| 0–10                                                  | 317 (21.1%)                        |
| 11–20                                                 | 1,050 (70.0%)                      |
| >20                                                   | 133 (8.9%)                         |
| Anxiety status:                                       |                                    |
| No                                                    | 1,396 (93.1%)                      |
| Mild                                                  | 85 (5.6%)                          |
| Moderate                                              | 16 (1.1%)                          |
| Severe                                                | 3 (0.2%)                           |
| Depression status:                                    |                                    |
| Have symptoms of depression                           | 475 (31.7%)                        |
| No symptoms of depression                             | 1,025 (68.3%)                      |
| Sleep quality:                                        |                                    |
| Very good                                             | 855 (57.0%)                        |
| Fairly good                                           | 410 (27.4%)                        |
| Fairly bad                                            | 149 (9.9%)                         |
| Very bad                                              | 86 (5.7%)                          |
| Metabolic equivalents (min/week)                      | 1,180.81 ± 2,174.11                |
| Work intensity:                                       |                                    |
| Unemployed                                            | 988 (65.9%)                        |
| Low                                                   | 491 (32.7%)                        |
| Moderate                                              | 17 (1.1%)                          |
| High                                                  | 4 (0.3%)                           |
| Alcoholic beverages consumption                       |                                    |
| Never/Seldom                                          | 1,454 (96.0%)                      |
| ≥ Once a month; < once a week                         | 39 (2.6%)                          |
| > Once a week                                         | 7 (0.5%)                           |
| Tea consumption                                       |                                    |
| Never/Seldom                                          | 1,261 (84.1%)                      |
| ≥ Once a month; < once a week                         | 118 (7.8%)                         |
| ≥ Once a week; < everyday                             | 75 (5.0%)                          |
| Everyday                                              | 46 (3.1%)                          |
| Coffee consumption                                    |                                    |
| Never/Seldom                                          | 1,367 (91.1%)                      |
| ≥ Once a month; < once a week                         | 63 (4.2%)                          |
| ≥ Once a week; < everyday                             | 36 (2.4%)                          |
| Everyday                                              | 34 (2.3%)                          |
| Functional beverages consumption                      |                                    |
| Never/Seldom                                          | 1,458 (97.3%)                      |
| ≥ once a month; < once a week                         | 38 (2.5%)                          |
| > once a week; < everyday                             | 2 (0.1%)                           |
| Everyday                                              | 2 (0.1%)                           |
| Spicy food intake:                                    |                                    |
| Yes                                                   | 1,319 (88.0%)                      |
| No                                                    | 181 (12.0%)                        |
| Folic acid supplement (mg/month)                      | 4.80 ± 7.37                        |

Data were described as mean ± SD or N (%).
p < 0.2 were adjusted in final models (57), as shown in Supplementary Table 2.

Given that maternal obesity has been widely reported to be associated with reproductive outcomes, including the success of IVF treatment, pregnancy complications, and even infant outcomes (63–65), we conducted stratified analyses based on pregnancy BMI categories (<25 kg/m²; ≥25 kg/m²) (29).

All statistical analyses were performed using SPSS version 22.0, and two-sided significance levels < 0.05 were considered to be statistically significant.

RESULTS

Demographic, Clinical, and Lifestyle Characteristics

Between April 2017 and April 2021, a total of 2,796 couples were recruited in our prospective cohort, among which, 1,500 couples were included in the analysis in this study after selection (Figure 1). The demographic and clinical characteristics of the study population are summarized in Table 1. The average age was 32.09 ± 4.33 years, and the average BMI was 23.35 ± 3.56 kg/m². Most women were non-smoker (91.0%), and 54.9% of couples sought IVF treatment due to the female factor alone. There were 798 women (53.2%) who achieved biochemical pregnancy, 687 (45.8%) achieved clinical pregnancy, of which, 529 women (35.3%) had a live newborn, while 20 women were still at the stage of ongoing pregnancy.

The information on lifestyle, psycho-mental status, beverage and spicy food consumption, and micronutrient supplement intake of the study population is presented in Table 2. Most women had a moderate perceived stress scale score and good sleep quality, without anxiety or depression.
TABLE 3 | Percentages (%) of weekly intake of 24 food groups assessed with a self-administered food frequency questionnaire across the four dietary patterns identified among 1,500 women in this prospective cohort.

| Food groups | Dietary patterns |
|-------------|-----------------|
|             | Fruits-Vegetables (n = 408) | Dairy (n = 280) | Rice (n = 232) | Varied (n = 580) |
|             | Mean  | SD    | Mean  | SD    | Mean  | SD    | Mean  | SD    |
| Rice        | 10.09 | 7.08  | 8.86  | 5.95  | 34.17 | 10.97 | 11.49 | 6.18  |
| Steamed wheaten foods | 4.63  | 4.53  | 4.61  | 4.32  | 6.53  | 4.05  | 7.18  | 3.73  |
| Coarse cereals | 1.70  | 2.64  | 1.68  | 2.51  | 1.55  | 3.28  | 3.06  | 3.95  |
| Chinese fried dough foods | 0.41  | 0.92  | 0.51  | 1.22  | 0.73  | 1.89  | 0.97  | 1.59  |
| Tubers       | 2.52  | 2.98  | 2.00  | 2.24  | 3.16  | 4.53  | 3.60  | 3.73  |
| Bean products | 2.11  | 2.69  | 2.21  | 2.76  | 2.24  | 2.51  | 3.58  | 3.90  |
| Soybean milk | 3.40  | 4.78  | 3.72  | 5.18  | 2.00  | 3.33  | 5.34  | 6.91  |
| Mushrooms    | 1.82  | 2.29  | 1.54  | 1.67  | 1.31  | 1.66  | 2.39  | 2.23  |
| Vegetables   | 18.82 | 9.46  | 9.70  | 5.07  | 12.61 | 8.35  | 10.11 | 5.64  |
| Fruits       | 25.42 | 9.64  | 14.28 | 6.72  | 11.28 | 7.32  | 11.31 | 5.32  |
| Dried fruits | 1.20  | 2.04  | 1.32  | 2.11  | 0.93  | 2.62  | 1.80  | 2.68  |
| Nuts         | 1.48  | 2.09  | 1.89  | 2.43  | 1.26  | 2.32  | 2.38  | 2.90  |
| Animal organs| 0.29  | 0.85  | 0.44  | 1.50  | 0.40  | 1.05  | 0.81  | 1.47  |
| Animal blood | 0.10  | 0.41  | 0.09  | 0.32  | 0.09  | 0.38  | 0.37  | 1.14  |
| Shrimp       | 1.73  | 2.29  | 1.85  | 2.50  | 0.97  | 2.14  | 2.24  | 3.02  |
| Fish         | 1.96  | 2.71  | 2.05  | 2.44  | 1.31  | 1.98  | 2.69  | 3.27  |
| Mollusks     | 0.17  | 0.60  | 0.24  | 0.59  | 0.09  | 0.32  | 0.57  | 1.30  |
| Shellfish    | 0.68  | 1.57  | 0.57  | 1.13  | 0.34  | 1.00  | 1.06  | 2.14  |
| Eggs         | 5.73  | 4.46  | 6.59  | 4.25  | 5.21  | 4.79  | 6.72  | 5.41  |
| Baked goods  | 2.52  | 3.42  | 3.89  | 4.18  | 2.01  | 3.26  | 4.04  | 4.62  |
| Candy/Chocolate | 0.97  | 1.88  | 1.33  | 2.69  | 0.94  | 1.68  | 1.98  | 2.94  |
| Puffed food  | 0.51  | 1.48  | 0.64  | 1.34  | 0.57  | 1.95  | 1.16  | 2.23  |
| Dairy        | 6.39  | 4.91  | 23.20 | 7.98  | 4.05  | 4.75  | 6.37  | 4.21  |
| Meat         | 5.36  | 4.94  | 6.79  | 5.42  | 6.42  | 6.46  | 8.86  | 8.05  |

*Percentage value (%) was calculated as the intake of the specific food group divided by total food intake. The highest mean values are underlined and bolded.

Dietary Patterns

Five dietary patterns were identified by PCA (Figure 2) and accounted for 44.3% of the total variance in the diet. The first dietary pattern was characterized by frequent intakes of fruit, vegetables, dairy products, and eggs. The second dietary pattern had higher intakes of seafood (including mollusks, shellfish, and shrimp), fish, and animal blood. The third dietary pattern was characterized by more frequent intakes of tubers, bean products, and coarse cereals. The fourth dietary pattern had higher intakes of puffed food, candy/chocolate, and baked goods. The fifth dietary pattern was characterized by frequent intakes of dried fruits, animal organs, and rice. Each dietary pattern was named after the food groups with a factor loading >0.5, therefore, the five patterns were named as “Fruit-Dairy-Vegetables-Eggs,” “Fish/Seafood-Animal blood,” “Tubers-Beans-Cereals,” “Puffed food-Candy-Bakery,” and “Dried Fruits-Organs-Rice,” respectively.

Moreover, we identified four clusters of dietary patterns from the cluster analysis (Table 3). The first cluster was characterized by higher intakes of fruits and vegetables, named “Fruits-Vegetables.” The second cluster had a higher consumption of dairy products and was named “Dairy.” The third cluster was the most frequently consumed rice, and the fourth had relatively higher consumption of varied food groups, named “Rice” and “Varied,” respectively.

Dietary Patterns and Reproductive Outcomes

Modified Poisson regression models were used to assess the associations between the dietary patterns derived by PCA and the outcomes of IVF treatment. In terms of embryo development, positive dose-response relationships were observed between “Fruit-Dairy-Vegetables-Eggs” score and normal fertilization and transferable embryos formed (p for trend = 0.034 and 0.003, respectively) (Table 4). Specifically, women in the highest vs. lowest quartile of “Fruit-Dairy-Vegetables-Eggs” score had increased likelihoods to gain normally fertilized oocytes (adjusted RR: 1.04, 95%CI: 1.01–1.08) and transferable embryos (adjusted RR: 1.09, 95%CI: 1.04–1.14). In the contrast, we observed that a higher “Tubers-Beans-Cereals” score was associated with a lower possibility of normal fertilization (adjusted RR: 0.95, 95%CI: 0.92–0.98) and the formation of transferable embryos (adjusted
RR: 0.94, 95%CI: 0.90–0.98). Regarding pregnancy outcomes, we observed that women in the highest vs. lowest quartile of “Puffed food-Candy-Bakery” score had decreased probability to achieve biochemical pregnancy of 17% (95%CI:0.72–0.96) (Table 5). Moreover, the “Dried fruits-Organs-Rice” score was positively related to the likelihood to achieve biochemical pregnancy (adjusted RR: 1.20, 95%CI: 1.05–1.37 for Q3 vs. Q1). No significant relationship was observed between dietary patterns and the probability to gain good-quality embryos on day 3 and live birth (Tables 4, 5).

Multivariate logistic regression models were conducted to explore the effects of preconception dietary patterns on neonatal outcomes and pregnancy complications. We detected that the women who more adhere to the “Fish/Seafood-Animal blood” pattern might have a lower risk for hypertensive disorders during pregnancy (adjusted OR: 0.37, 95%CI: 0.14–0.99 for Q3 vs. Q1) (Table 6). No significant association was observed between preconception dietary patterns and the risk of early abortion, late abortion, preterm delivery, low birth weight, macrosomia, and GDM (Table 6, Supplementary Tables 3, 4).

Furthermore, we explore the relationship between the clusters of dietary patterns and reproductive outcomes taking “Fruits-Vegetables” as the reference group (Table 7). In modified Poisson regression models, we observed that women in the “Dairy” cluster had a higher possibility of the formation of transferable embryos (adjusted RR: 1.08, 95%CI: 1.03–1.13) and good-quality embryos on day 3 (adjusted RR: 1.07, 95%CI: 1.00–1.15) compared to women in the “Fruits-Vegetables” cluster. Moreover, in multivariate logistic regression models, women with a higher intake of rice were at a higher risk of delivering macrosomia (adjusted OR: 2.74, 95%CI: 1.02–7.35).

The results of stratified analyses revealed that the positive relationship between the “Fruit-Dairy-Vegetables-Eggs” score and normal fertilization and the inverse association of the “Fish/Seafood-Animal blood” score with hypertensive disorders during pregnancy were exhibited only among women with BMI ≥25 kg/m² (Supplementary Table 5). The associations between preconception diet and other reproductive outcomes were consistent across maternal pre-pregnancy BMI categories (data not shown).

**DISCUSSION**

In the present study, we used PCA to identify preconception dietary patterns in an ongoing prospective cohort, and then assessed the association between dietary patterns and reproductive outcomes. In terms of IVF intermediate and clinical outcomes, we detected that the women who are more inclined
TABLE 5 | Associations of the dietary patterns derived by principal component analysis with biochemical pregnancy, clinical pregnancy, and live birth.

| Dietary pattern | Biochemical pregnancy<sup>a</sup> | Clinical pregnancy<sup>a</sup> | Live birth<sup>b</sup> |
|-----------------|-----------------|-----------------|-----------------|
|                 | Adjusted RR | 95% CI | P<sub>for trend</sub> | Adjusted RR | 95% CI | P<sub>for trend</sub> | Adjusted RR | 95% CI | P<sub>for trend</sub> |
| Fruits-Vegetables-Dairy-Eggs | Q1 | Ref | – | 0.817 | Ref | – | 0.381 | Ref | – | 0.298 |
| Q2 | 0.96 | 0.85, 1.10 | | 0.90 | 0.78, 1.03 | | 0.86 | 0.72, 1.03 |
| Q3 | 1.01 | 0.89, 1.15 | | 0.92 | 0.80, 1.07 | | 0.84 | 0.70, 1.01 |
| Q4 | 1.00 | 0.87, 1.15 | | 0.91 | 0.78, 1.07 | | 0.88 | 0.73, 1.06 |
| Fish/Seafood-Animal blood | Q1 | Ref | – | 0.267 | Ref | – | 0.478 | Ref | – | 0.568 |
| Q2 | 1.00 | 0.88, 1.14 | | 1.01 | 0.86, 1.18 | | 1.12 | 0.92, 1.35 |
| Q3 | 0.91 | 0.79, 1.04 | | 0.96 | 0.82, 1.12 | | 1.07 | 0.89, 1.30 |
| Q4 | 0.94 | 0.83, 1.07 | | 0.96 | 0.82, 1.11 | | 1.09 | 0.90, 1.32 |
| Tubers-Beans-Cereals | Q1 | Ref | – | 0.334 | Ref | – | 0.413 | Ref | – | 0.611 |
| Q2 | 1.02 | 0.89, 1.16 | | 0.96 | 0.83, 1.12 | | 0.96 | 0.80, 1.16 |
| Q3 | 0.98 | 0.86, 1.12 | | 0.94 | 0.81, 1.11 | | 0.87 | 0.72, 1.06 |
| Q4 | 1.07 | 0.94, 1.23 | | 1.06 | 0.91, 1.23 | | 1.04 | 0.87, 1.25 |
| Puffed food-Candy-Bakery | Q1 | Ref | – | 0.019* | Ref | – | 0.113 | Ref | – | 0.053 |
| Q2 | 0.92 | 0.80, 1.04 | | 0.90 | 0.77, 1.06 | | 0.90 | 0.75, 1.09 |
| Q3 | 0.98 | 0.86, 1.10 | | 1.02 | 0.89, 1.18 | | 1.00 | 0.83, 1.19 |
| Q4 | 0.83 | 0.72, 0.96* | | 0.86 | 0.73, 1.01 | | 0.81 | 0.67, 0.96* |
| Dried fruits-Organs-Rice | Q1 | Ref | – | 0.048* | Ref | – | 0.398 | Ref | – | 0.680 |
| Q2 | 1.15 | 1.00, 1.32* | | 1.12 | 0.96, 1.31 | | 1.21 | 1.00, 1.47 |
| Q3 | 1.20 | 1.05, 1.37** | | 1.20 | 1.03, 1.40* | | 1.28 | 1.06, 1.54** |
| Q4 | 1.15 | 1.00, 1.33 | | 1.07 | 0.90, 1.26 | | 1.06 | 0.87, 1.30 |

<sup>a</sup>Models adjusted for age, coffee consumption, the supplement of folic acid and vitamin D, total energy, and the stage and quality of embryos transferred.

<sup>b</sup>Models adjusted for age, infertility type, stress, coffee consumption, the supplement of folic acid and vitamin D, total energy, and the stage and quality of embryos transferred. The bold values indicate statistical significance *P < 0.05, **P < 0.01.

To date, only two studies investigated the association between dietary patterns and IVF outcomes identifying individual patterns based on specific populations (28, 32). Vujkovic et al. (28) identified two dietary patterns namely “health conscious-low processed” and “Mediterranean” dietary patterns among 161 Dutch women (28). They revealed that a preconception “Mediterranean” diet, characterized by high intakes of vegetable oil, fish, legumes, and vegetables but low intakes of snacks, contributes to the success of achieving biochemical pregnancy (OR:1.4, 95%CI:1.0–1.9), which may in part support our finding of the inverse relationship between “Puffed food-Candy-Bakery” diet and biochemical pregnancy (adjusted RR:0.83, 95%CI:0.72–0.96). Interestingly, as reported by Vujkovic et al. (28), preconception “Mediterranean” diet could contribute to increases in blood folate concentration and vitamin B6 levels in both blood and follicular fluid. Folate and vitamin B6 have
Dietary pattern | Preterm delivery | Hypertensive disorders during pregnancy
--- | --- | ---
**Fruits-Vegetables-Dairy-Eggs**
Q1 | Ref | – | 0.921 | Ref | – | 0.276
Q2 | 0.67 | 0.34, 1.30 | 0.93 | 0.34, 2.53
Q3 | 0.71 | 0.36, 1.40 | 1.62 | 0.63, 4.17
Q4 | 0.90 | 0.44, 1.88 | 1.64 | 0.58, 4.85
**Fish/Seafood-Animal blood**
Q1 | Ref | – | 0.538 | Ref | – | 0.046*
Q2 | 0.75 | 0.39, 1.41 | 0.62 | 0.25, 1.52
Q3 | **0.32** | **0.14, 0.71*** | **0.37** | **0.14, 0.99***
Q4 | 0.80 | 0.43, 1.49 | 0.45 | 0.17, 1.17
**Tubers-Beans-Cereals**
Q1 | Ref | – | 0.556 | Ref | – | 0.689
Q2 | 0.98 | 0.51, 1.88 | 1.86 | 0.71, 4.85
Q3 | 0.49 | 0.23, 1.08 | 1.23 | 0.44, 3.50
Q4 | 1.31 | 0.66, 2.59 | 1.51 | 0.49, 4.64
**Puffed food-Candy-Bakery**
Q1 | Ref | – | 0.056 | Ref | – | 0.369
Q2 | 0.82 | 0.43, 1.55 | 0.92 | 0.37, 2.27
Q3 | 0.57 | 0.29, 1.12 | 0.89 | 0.36, 2.16
Q4 | 0.55 | 0.26, 1.14 | 0.59 | 0.19, 1.82
**Dried fruits-Organs-Rice**
Q1 | Ref | – | 0.382 | Ref | – | 0.648
Q2 | 0.96 | 0.48, 1.93 | 1.01 | 0.38, 2.69
Q3 | 1.15 | 0.59, 2.26 | 1.89 | 0.77, 4.63
Q4 | 1.33 | 0.65, 2.74 | 1.05 | 0.34, 3.29

*Models adjusted for age, BMI, educational level, smoking status, depression status, functional beverages consumption, multi-vitamins supplement, and total energy.

*Models adjusted for age, BMI, type and cause of infertility, physical activity, the supplement of vitamin A and vitamin D, and total energy. The bold values indicate statistical significance.

*P < 0.05; **P < 0.01.

been suggested to be beneficial to oocyte quality and embryonic development (66–68). However, no significant association of dietary patterns with fertilization rate and embryo quality was detected by Vujkovic et al. (28), which may be attributed to the limited sample size and the absence of adjustment for confounders associating diet and lifestyle. The Rotterdam Periconceptional Cohort (Predict) Study recruited 135 women with spontaneous pregnancy and 93 women who achieved pregnancies upon IVF/ICSI treatment. Three dietary patterns were identified in the Predict Study, “High vegetables, fruits and grain,” “High solid fat, snacks and sugars,” and “High fish and olive oil, low meat,” while no significant association between periconceptional maternal dietary pattern and first-trimester embryonic growth was observed in the IVF/ICSI subgroup (32). Besides limited sample sizes and differences in the statistical method used, the discordance between the results of these two studies and ours may also be attributed to differences in demographic characteristics and long-term dietary culture of western and eastern.

An epidemical study conducted among 644 women seeking infertility treatment in an agricultural region suggested that drinking three or more glasses of milk per day was negatively related to the risk of female infertility (OR: 0.3, 95% CI: 0.1–0.7) (69), which may partly support our findings of the beneficial effect of dairy intake on embryological parameters. However, the study on the correlation between maternal dairy intake and infertility treatment outcomes was limited. The Environment and Reproductive Health (EARTH) study by Afeiche et al. (70) reported that total dairy food consumption was positively correlated with live birth among women ≥35 years of age, while it was not related to ovarian response, embryological, or clinical pregnancy outcomes (70). Notably, the EARTH study recruited the women with multiple IVF cycles, on the contrary, only the women undergoing their first IVF cycle were included in the present study to avoid introducing bias, which may be a potential reason for inconsistent results.

Regarding pregnancy complications, we observed that the women who were more adherent to the “Fish/Seafood-Animal blood” pattern might have a lower risk for hypertensive disorders during pregnancy (adjusted OR: 0.37, 95% CI: 0.14–0.99). Several studies explored the effects of dietary patterns on pregnancy complications (19, 71, 72), however, to the best of our knowledge, there is a lack of study conducted on the IVF population with the same aim. Jarman et al. (19) explored the relationship of pre-pregnancy diet with pregnancy complications based on an ongoing prospective cohort in Canada and suggested that higher “healthy” pattern scores were associated with lower odds of developing gestational hypertension during pregnancy (adjusted OR: 0.6, 95% CI: 0.4–0.9) (19). In detail, the “healthy” pattern in Jarman et al.’s study referred to frequent intakes of vegetables, fruit, oils, brown pasta or rice, fish, tomatoes, and white pasta. Another longitudinal study conducted on the Danish National Birth cohort revealed a protective association of seafood diet with
gestational hypertension (OR:0.86, 95% CI: 0.77–0.95) and pre-eclampsia (OR:0.79, 95% CI: 0.65–0.97) (71). The results of these two studies were in accordance with ours, and hence remind us of the potentially important role of pre-conception fish/seafood intake in preventing hypertensive disorders during pregnancy. In addition, we detected that the women with frequent consumption of rice were at a higher risk of delivering macrosomia (adjusted OR: 2.74, 95%CI: 1.02–7.35) in this study. A study conducted by (72) based on the Norwegian Mother and Child Cohort Study included 65,904 pregnant women to explore the effect of dietary patterns in pregnancy on birth weight (72). Taking the high Western group with the highest intake of carbohydrates as the reference, (72) revealed a lower birth weight in the high prudent group with the lowest intake of carbohydrates. Combined with our findings, at any stage of pregnancy, from preconception to gestational period, excessive consumption of high glycaemic index carbohydrates may be detrimental. However, there is a lack of study assessing the correlation between the pre-pregnancy diet and the risk of macrosomia, hence, more studies are warranted to verify our results.

In stratified analyses, we detected that the effects of the preconception diet on fertilization and the risk of hypertensive disorders during pregnancy were not consistent across BMI categories. Previous studies have reported that BMI above the normal range was negatively associated with IVF outcomes (63, 73, 74). Therefore, we assumed that the protective effect of a healthier diet at the pre-treatment stage may be more significant for overweight and obese women.

This is the first study to explore the effects of preconception dietary patterns on IVF outcomes ranging from embryo development to pregnancy complications in a Chinese population. Given the dramatic differences between western and eastern eating habits, a study using individual assessment of dietary patterns was necessary. In addition, several lifestyle factors including psycho-mental status, physical activity, and sleep quality were evaluated in this study using validated questionnaires and were adjusted in the final analyses, which might improve the accuracy and credibility of our results. Our findings revealed associations of preconception diet with reproductive outcomes following IVF treatment, including fertilization, embryo quality, and pregnancy complications, which may provide important clues for dietary guidance during preconception counseling. Moreover, our results preliminarily indicate that diet prior to pregnancy may be an important target for interventions to achieve a better reproductive outcome.

Inherent to the observational design of the present study, several limitations have to be acknowledged. First, the comparison with results from other studies is challenging...
due to the observational, data-driven approach of deriving dietary patterns. Although the FFQ used in this study was derived from a validated Chinese dietary FFQ and previous studies have suggested that it can be used to classify the subjects according to their food consumption in 1 year, there is still a potential measurement bias due to retrospective assessment, which may lead to misclassification. Moreover, 24 non-overlapping food groups classified in this study may be limited to cover habitual dietary intake. As for the statistical analyses, numerous statistical tests were conducted that may cause type-I error inflation and generate false-positive results. Notably, although significant, the effect sizes for fertilization and embryo quality were relatively small, therefore, the results are preliminary and their clinical relevance should be interpreted carefully. Furthermore, 41.4% of the male partner in this study had reproductive disorders, while their pre-treatment diets and lifestyles were not adjusted or discussed due to the limitation of data, hence, a more comprehensive study considering both male and female pre-treatment diets is warranted. In addition, the participants recruited in our ongoing prospective cohort were all from north-eastern China, thus a national, multicenter, large-sample-size study should be conducted to verify our findings. Finally, blood metabolomics testing might be conducive to obtaining a more accurate conclusion, and further studies to explore underlying mechanisms were necessary.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

REFERENCES

1. Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, De Mouzon J, Sokol R, et al. The international glossary on infertility and fertility care, 2017. Hum Reprod. (2017) 32:1786–801. doi: 10.1093/humrep/dex234
2. Sun H, Gong TT, Jiang YT, Zhang S, Zhao YH, Wu QJ. Global, regional, and national prevalence and disability-adjusted life-years for infertility in 195 countries and territories, 1990-2017: Results from a Global Burden of Disease Study, 2017. Aging (Albany NY). (2019) 11:10952–91. doi: 10.18632/aging.102497
3. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates on infertility prevalence and treatment seeking: Potential need and demand for medical care. Hum Reprod. (2009) 24:2380–3. doi: 10.1093/humrep/dep218
4. Datta J, Palmer MJ, Tanton C, Gibson LJ, Jones KG, Macdowall W, et al. Prevalence of infertility and help seeking among 15 000 women and men. Hum Reprod. (2016) 31:2108–18. doi: 10.1093/humrep/dew123
5. Adashi EY, Dean LA. Access to and use of infertility services in the United States: Framing the challenges. Fertil Steril. (2016) 105:1113–8. doi: 10.1016/j.fertnstert.2016.01.017
6. Buck Louis GM, Sapra KJ, Schisterman EF, Lynch CD, Maisog JM, Grantz KL, et al. Lifestyle and pregnancy loss in a contemporary cohort of women recruited before conception: The LIFE Study. Fertil Steril. (2016) 106:180–8. doi: 10.1016/j.fertnstert.2016.03.009
7. Gaskins AJ, Chavarro JE. Diet and fertility: a review. Am J Obstet Gynecol. (2018) 218:379–89. doi: 10.1016/j.ajog.2017.08.010
8. Hakimi O, Cameron L. Effect of exercise on ovulation. Sport Med. (2016) 47:1535–67. doi: 10.1007/s40279-016-0669-8
9. Ilacqua A, Izzo G, Emerenziani G, Pietro, Baldari C, Aversa A. Lifestyle and fertility: The influence of stress and quality of life on male fertility. Reprod Biol Endocrinol. (2018) 16:1–11. doi: 10.1186/s12958-018-0436-9
10. Chen Q, Feng Y, Yang H, Wu W, Zhang P, Wang K, et al. A vitamin pattern diet is associated with decreased risk of gestational diabetes mellitus in Chinese women: Results from a case control study in Taiyuan, China. J Diabetes Res. (2019) 2019:5232308. doi: 10.1155/2019/5232308
11. Øyen N, Olsen SF, Basit S, Leirgul E, Strøm M, Carstensen L, et al. Association Between Maternal Folic Acid Supplementation and Congenital Heart Defects in Offspring in Birth Cohorts From Denmark and Norway. J Am Heart Assoc. (2019) 8:e011615. doi: 10.1161/JAHA.118.011615
12. Patfoni A, Ferrari S, Viganò P, Pagliardini L, Papaleo E, Candiani M, et al. Vitamin D deficiency and infertility: Insights from in vitro fertilization cycles. J Clin Endocrinol Metab. (2014) 99:E2372–6. doi: 10.1210/jc.2014-1802
13. Rizk NJ, Rizk MS, Mohamed AS, Naguib YM. Attenuation of sleep deprivation dependent deterioration in male fertility parameters by vitamin C. Reprod Biol Endocrinol. (2020) 18:1–13. doi: 10.1186/s12958-020-0563-y
14. Schisterman EF, Sjaarda LA, Clemons T, Carrell DT, Perkins NJ, Johnstone E, et al. Effect of folic acid and zinc supplementation in men on semen quality and live birth among couples undergoing infertility treatment: a randomized clinical trial. JAMA - J Am Med Assoc. (2020) 323:35–48. doi: 10.1001/jama.2019.18714
15. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. (2002) 13:3–9. doi: 10.1097/00041433-200202000-00002

AUTHOR CONTRIBUTIONS

JT and SW: conceptualization. SW: methodology and writing–original draft preparation. SW and XZhan: formal analysis. XZZhao, XH, SZ, and PL: investigation. JT: resources and funding acquisition. PL: data curation. All authors contributed to the article and approved the submitted version.

FUNDING

This research was funded by National Key Research and Development Program (2018YFC1004203), Major Special Construction Plan for Discipline Construction Project of China Medical University (3110118033), Shengjing Freelance Researcher Plan of Shengjing Hospital of China Medical University, National Natural Science Foundation of China (82071601/61873257), Key Research and Development Program of Liaoning Province (2018020222), and Central Government Special Fund for Local Science and Technology Development (2020JH6/1050006).

ACKNOWLEDGMENTS

The authors sincerely thank the staff of the Reproductive Center of Shengjing Hospital for their support.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.808355/full#supplementary-material
16. Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? Am J Clin Nutr. (2001) 73:1–2. doi: 10.1093/ajcn/73.1.1

17. Crozier SR, Robinson M, Godfrey KM, Cooper C, Inskip HM. Women’s dietary patterns change little from before to during pregnancy. J Nutr. (2009) 139:1956–63. doi: 10.3945/jn.109.109579

18. Yang J, Kang Y, Cheng Y, Zeng L, Yan H, Dang S. Maternal dietary patterns during pregnancy and congenital heart defects: a case-control study. Int J Environ Res Public Health. (2019) 16:2937. doi: 10.3390/ijerph16122937

19. Jarman M, Mathe N, Ramazani F, Pakesreht M, Robson PJ, Johnson ST, et al. Dietary patterns prior to pregnancy and associations with pregnancy complications. Nutrients. (2018) 10:1–15. doi: 10.3390/nu10070914

20. Wen L, Ge H, Qiao J, Zhang L, Chen X, Kilby MD, et al. Maternal dietary patterns and risk of gestational diabetes mellitus in twin pregnancies: a longitudinal twin pregnancies birth cohort study. Nutr J. (2020) 19:1–12. doi: 10.1186/s12977-020-00529-9

21. Bao W, Bowers K, Tobias DK, Olsen SF, Chavarro J, Vaag A, et al. Preparation low-carbohydrate diet pattern and risk of gestational diabetes mellitus: a prospective cohort study. Am J Clin Nutr. (2014) 99:1378–84. doi: 10.3945/ajcn.113.082966

22. Zhou X, Chen R, Zhong C, Wu J, Li X, Li Q, et al. Maternal dietary pattern characterised by high protein and low carbohydrate intake in pregnancy is associated with a higher risk of gestational diabetes mellitus in Chinese women: a prospective cohort study. Br J Nutr. (2018) 120:1045–55. doi: 10.1017/S0007114517000156

23. Englund-Ogge L, Brantsater AL, Sengpiel V, Haugen M, Birgisdottir BE, Myhr E, et al. Maternal dietary patterns and preterm delivery: Results from large prospective cohort study. BMJ. (2014) 348:1–18. doi: 10.1136/bmj.g1446

24. He JR, Yuan MY, Chen NN, Lu JH, Hu CY, Mai WB, et al. Maternal dietary patterns and gestational diabetes mellitus: a large prospective cohort study in China. Br J Nutr. (2015) 113:1292–300. doi: 10.1017/S0007114515000707

25. Lu MS, He JR, Chen Q, Lu J, Wei X, Zhou Q, et al. Maternal dietary patterns during pregnancy and preterm delivery: a large prospective cohort study in China. Nutr J. (2018) 17:1–10. doi: 10.1186/s12977-018-0377-3

26. Chen X, Zhao D, Mao X, Xia Y, Baker PN, Zhang H. Maternal dietary patterns and pregnancy outcome. Nutrients. (2016) 8:1–26. doi: 10.3390/nu80606531

27. Vujkovic M, De Vries JH, Dohle GR, Bonsel GJ, Lindemans J, MacKlon NS, et al. Associations between dietary patterns and semen quality in men undergoing IVF/ICSI treatment. Hum Reprod. (2009) 24:1304–12. doi: 10.1093/humrep/dep624

28. Vujkovic M, De Vries JH, Lindemans J, MacKlon NS, Van Der Spek PJ, Steegers EAP, et al. The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/intracytoplasmic sperm injection treatment increases the chance of pregnancy. Fertil Steril. (2010) 94:2096–551. doi: 10.1016/j.fertnstert.2009.12.079

29. Karayannis Di, Kontogianni MD, Mendorou C, Mastrominas M, Yiannakouris N. Adherence to the Mediterranean diet and IVF success in couples undergoing IVF. Am J Obstet Gynecol. (2019) 220:567.e1–567.e18. doi: 10.1016/j.ajog.2019.02.004

30. Ricci E, Bravi F, Noli S, Somigliana E, Cipriani S, Castiglioni M, et al. Mediterranean diet and outcomes of assisted reproduction: an Italian cohort study. Am J Obstet Gynecol. (2019) 221:627.e1–627.e14. doi: 10.1016/j.ajog.2019.07.011

31. Lv N, Brown JL, Chinese American Family Food Systems: Impact of Western Influences. Nutr J. (2020) 19:1–5. doi: 10.1186/s12977-020-00529-9

32. Wu S, Wang M, Deng Y, Qiu J, Zhang X, Tan J. Associations of toxic and essential trace elements in serum, follicular fluid, and seminal plasma with in vitro fertilization outcomes. Ecotoxicol Environ Saf. (2020) 204:110695. doi: 10.1016/j.ecoenv.2020.110695

33. Wu S, Zhang Y, Wu X, Hao G, Ren H, Qiu J, et al. Association between exposure to ambient air pollutants and the outcomes of in vitro fertilization treatment: a multicenter retrospective study. Environ Int. (2021) 153:106544. doi: 10.1016/j.envint.2021.106544

34. Zhang X, Wu S, Hao G, Wu X, Ren H, Zhang Y, et al. Prolonged cryopreservation negatively affects embryo transfer outcomes following the elective freeze-all strategy: a multicenter retrospective study. Front Endocrinol (Lausanne). (2021) 12:1–11. doi: 10.3389/fendo.2021.709648

35. Lu MS, He JR, Chen Q, Lu J, Wei X, Zhou Q, et al. Maternal dietary patterns during pregnancy and preterm delivery: a large prospective cohort study in China. Nutr J. (2018) 17:1–10. doi: 10.1186/s12977-018-0377-3

36. Chen X, Zhao D, Mao X, Xia Y, Baker PN, Zhang H. Maternal dietary patterns and pregnancy outcome. Nutrients. (2016) 8:1–26. doi: 10.3390/nu80606531

37. Vujkovic M, De Vries JH, Dohle GR, Bonsel GJ, Lindemans J, MacKlon NS, et al. Associations between dietary patterns and semen quality in men undergoing IVF/ICSI treatment. Hum Reprod. (2009) 24:1304–12. doi: 10.1093/humrep/dep624

38. Vujkovic M, De Vries JH, Lindemans J, MacKlon NS, Van Der Spek PJ, Steegers EAP, et al. The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/intracytoplasmic sperm injection treatment increases the chance of pregnancy. Fertil Steril. (2010) 94:2096–551. doi: 10.1016/j.fertnstert.2009.12.079

39. Karayannis Di, Kontogianni MD, Mendorou C, Mastrominas M, Yiannakouris N. Adherence to the Mediterranean diet and IVF success rate among non-obese women attempting fertility. Hum Reprod. (2018) 33:494–502. doi: 10.1093/humrep/dey003

40. Twigt JM, Bolhuis MEC, Steegers EAP, Hammiche F, Van Inzen WG, Laven JSE, et al. The preconception diet is associated with the chance of ongoing pregnancy in women undergoing IVF/ICSI treatment. Hum Reprod. (2012) 27:2526–31. doi: 10.1093/humrep/des157

41. Kermack AJ, Lowen P, Wellstead SJ, Fisk HL, Montag M, Cheong Y, et al. Effect of a 6-week “Mediterrean” dietary intervention on in vitro human embryo development: the Preconception Dietary Supplements in Assisted Reproduction double-blinded randomized controlled trial. Fertil Steril. (2019) 113:260–9. doi: 10.1016/j.fertnstert.2019.09.041

42. Parisi F, Rousian M, Huijgen NA, Koning AHJ, Willemse SP, de Vries JHM, et al. Periconceptional maternal ‘high fish and olive oil, low meat’ dietary pattern is associated with increased embryonic growth: the Rotterdam periconceptional cohort (Predict) study. Ultrasound Obstet Gynecol. (2017) 50:709–16. doi: 10.1002/uog.17408

43. Sun Z, Lin Y, Liu L, Zou C, Zou X, Fu L, et al. Mediterranean diet improves embryo yield in IVF: A prospective cohort study. Reprod Biol Endocrinol. (2019) 17:1–7. doi: 10.1186/s12958-019-0520-9

44. Gaskins AI, Nassan FL, Chiu YH, Arvizu M, Williams PL, Keller MG, et al. Dietary patterns and outcomes of assisted reproduction.
Preconception Diet Affects IVF Outcomes

Wu et al.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Wu, Zhang, Zhao, Hao, Zhang, Li and Tan. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.