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Lack of a meaningful association between dietary patterns and in vitro fertilization outcome among Japanese women

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Abstract

Purpose: The purpose of this study was to examine whether preconception maternal dietary pattern is associated with in vitro fertilization (IVF) outcome among Japanese women.

Methods: This prospective study included 140 Japanese women who underwent conventional-IVF/intracytoplasmic sperm injection. The patients' diets during the previous month before egg retrieval were assessed with validated brief-type self-administered diet history questionnaire. Dietary patterns from 33 predefined food groups [energy-adjusted food (g/1000 kcal)] were extracted by factor analysis. The primary outcome measure was clinical pregnancy rate after IVF.

Results: Thirty-six women had confirmed clinical pregnancy. Three dietary patterns were identified: "Vegetable and seafood," "Western," and "Rice and miso soup." The "Vegetables and seafood" dietary pattern (high intakes of green and other vegetables, mushrooms, seasoning, fish, soy products, chicken, and potatoes) was not associated with clinical pregnancy ([odds ratio per one-quartile increase in dietary pattern: 0.94 (95% confidence interval: 0.67-1.32), *P* = 0.73]. This relationship was unaltered after controlling for potential confounders. Furthermore, no association was seen between the other two dietary patterns and clinical pregnancy.

Conclusions: The three maternal preconception dietary patterns identified revealed no meaningful association with IVF outcome in Japanese women. Further studies in various populations with different dietary patterns are needed to confirm these findings.

KEYWORDS
dietary habits, in vitro fertilization, infertility, Japanese, pregnancy

1 | INTRODUCTION

Worldwide, 48.5 million couples have infertility,[1] and more than 390 000 in vitro fertilization (IVF) cycles were performed in Japan in 2014.[2] A 2.07-fold increase in the number of IVF treatments has been noted from 2008 when the cycle-based registry was introduced.[2] Nevertheless, clinical pregnancy rates have not increased in Japan as well as in developed countries.[2,3] The main reason for this is that age is a major prognostic factor influencing the success rate of IVF,[2,3] which cannot be altered. As most patients undergoing IVF

treatment are willing to modify their lifestyle,[4] understanding the role of potentially modifiable lifestyle factors and their influence on IVF treatment could provide new insights for improving the rate of clinical pregnancy.

Among such lifestyle factors, there is a growing interest in the role of diet as a potentially modifiable factor that could influence the outcomes of IVF treatment. Several foods and nutrients such as whole grain,[5] dairy foods,[6] folate,[7,8] vitamin B$_6$,[9] vitamin B$_{12}$,[8] vitamin D,[10] omega-3 polyunsaturated fatty acids (PUFA),[11] and omega-6 PUFA [12] have been suggested to have beneficial effects on IVF outcomes. In addition to the effects of single nutrients or foods, the role of dietary pattern, which is able to explain the complex and confounding interactions between nutrients and foods,[13] in IVF outcomes has been recently examined. A study in the Netherlands calculated the Preconception Dietary Risk (PDR) score from the six main food groups (fruits, vegetables, meat, fish, whole wheat products, and fats) to evaluate the adherence to Dutch dietary recommendations and showed that a one-point increase in the PDR score in women undergoing IVF/intracytoplasmic sperm injection (ICSI) treatment was associated with a 65% increased chance of ongoing pregnancy.[14] In addition, another study used a statistical approach to identify dietary patterns in relation to IVF outcomes. A preconception Mediterranean dietary pattern of Dutch subfertile couples identified by principal component analysis showed a 40% increased probability of achieving pregnancy after IVF treatment.[15] However, to our knowledge, the relationship between dietary patterns and IVF outcomes has not been examined in Asian countries, including Japan, where dietary habits and lifestyle are different from those in Western countries. Thus, additional studies in regions with different food-cultural backgrounds might provide new insights into preconception diet in relation to outcomes of IVF.

The objective of the present prospective cohort study was to examine the association between preconception dietary patterns and IVF outcomes among 140 Japanese women undertaking IVF treatment at a private IVF clinic.

2 | MATERIALS AND METHODS

2.1 | Study population

Subfertile couples undergoing conventional-IVF(c-IVF)/ICSI and planning for fresh cleavage embryo transfer for the first time between November 2016 and December 2016 were invited to participate. In the clinic where this study was performed, female patients with tubal factor infertility (tubal obstruction, hydrosalpinx, or history of extrauterine pregnancy) undergo blastocyst transfer but not cleavage embryo transfer. The expected number of patients with fresh cleavage embryo transfer was 410. After the nurses confirmed the patient's IVF plan, a set of two self-administered questionnaires on dietary habits and general lifestyle was distributed to 304 women and collected before oocyte retrieval. All answered questionnaires were examined at least twice for completeness, and missing or

illogical data were confirmed by a doctor's interview. A total of 226 women (response rate 74.3%) completed questionnaires. Of these, 157 underwent cleavage embryo transfer. After we excluded 17 women [endometriosis, n = 12; male infertility requiring operation (percutaneous epididymal sperm aspiration or testicular sperm extraction), n = 1; non-Japanese origin, n = 1; non-domestic resident, n = 3], data on 140 women were used for the present analysis.

The present study was conducted according to the guidelines of the Declaration of Helsinki, and the study protocol was approved by the ethics and institutional boards of Kato Ladies Clinic (approval number: 16-12) and the University of Tokyo (approval number: 11355). Written informed consent was obtained from all participating women.

2.2 | Dietary assessment

Dietary habits during the previous month before egg retrieval were assessed using a brief-type self-administered diet history questionnaire (BDHQ).[16] BDHQ is a four-page structured questionnaire inquiring about the consumption frequency of selected foods commonly consumed in Japan, general dietary behavior, and usual cooking methods. Daily intake of foods (58 food items in total), energy, and selected nutrients was calculated using an ad hoc computer algorithm for BDHQ, which was based on the Standard Tables of Food composition in Japan.[17] The relative validity of the estimated intake from BDHQ was established in comparison with intakes assessed using 16-day semiweighed dietary records (DR) in a validation study of 92 Japanese men aged 32-76 years and 92 Japanese women aged 31-69 years. The median Spearman's correlation coefficient with DR for the 58 foods was 0.48 (range 0.22-0.83) in men and 0.44 (range 0.14-0.82) in women.[18] The median Pearson's correlation coefficient with DR for energy-adjusted intakes of the 42 nutrients was 0.56 (range: 0.41-0.63) in men and 0.54 (range: 0.45-0.61) in women.[19] A more detailed description of the methods used to calculate dietary intakes and the validity of the BDHQ has been published previously.[18,19]

2.3 | Dietary pattern

The dietary patterns in this study were identified by factor analysis using the FACTOR procedure in SAS software (SAS Institute, Inc., Cary, NC, USA). Before the factor analysis, the foods calculated from BDHQ (58 foods) were grouped on the basis of similarity of nutrient profiles or culinary usage of the foods; a total of 33 food groups were entered into the factor analysis after adjustment for total energy intake by the density method (g/1000 kcal).[20] The factors were rotated by orthogonal transformation (Varimax rotation function in SAS) to achieve a simpler structure with greater interpretability. The number of factors was determined by eigenvalues, scree plots, and the combinations of foods on the factors. A factor solution with three factors was found to be reasonable and meaningful. The proportion of variance explained by each factor was calculated by dividing the sum of the squares of the respective factor loadings by the number of variables. The factor scores for each pattern and for

TABLE 1 Factor-loading matrix for the three dietary patterns identified among the 140 Japanese women who participated in this IVF study[a]

	Factor 1 Vegetables and seafood	Factor 2 Western	Factor 3 Rice and miso soup
Green and dark yellow vegetables	**0.72**	**0.27**	−0.02
Mushroom	**0.67**	**0.26**	−0.05
Seasonings	**0.65**	0.24	0.06
Fish	**0.63**	**−0.28**	0.07
Other vegetables	**0.56**	**0.34**	−0.07
Sea products	**0.53**	**−0.46**	0.03
Shellfish	**0.52**	**−0.38**	−0.20
Seaweeds	**0.51**	−0.11	0.22
Soy products	**0.45**	0.15	0.07
Chicken	**0.38**	**0.30**	0.17
Salad vegetables	**0.36**	**0.33**	**−0.31**
Potatoes	**0.28**	0.09	−0.23
Confectioneries	**−0.27**	0.03	−0.21
Soft drinks	**−0.34**	0.12	−0.10
Fats and oils	**0.29**	**0.47**	**−0.35**
Sugar	0.15	**0.47**	0.07
High fat milk	−0.04	**0.39**	−0.04
Black and Oolong tea	0.02	**0.35**	0.23
Red meats	0.02	**0.31**	−0.07
Fruit	0.21	0.23	0.12
Green tea	−0.03	0.23	−0.16
Eggs	0.13	0.19	−0.19
Pickled vegetables	0.09	0.18	−0.04
Low fat milk	0.00	−0.08	0.07
Alcoholic beverages	0.07	**−0.64**	−0.10
Cooked rice	**−0.38**	0.03	**0.74**
Miso soup	−0.07	0.02	**0.58**
Noodles	−0.09	−0.17	−0.21
Fruit and vegetable juice	−0.04	0.17	**−0.29**
Ice cream	−0.06	0.10	**−0.31**
Coffee	−0.10	0.00	**−0.34**
Processed meats	−0.09	−0.07	**−0.38**
Breads	−0.22	−0.08	**−0.48**
Percentage of variance	12.3%	7.5%	6.7%

[a]Absolute values <-0.25 or >0.25 are represented in bold.

each individual were determined by summing the intake of each food group weighted by the factor loading.[21] We used these scores to rank the subjects according to the degree to which they conformed to the dietary pattern. All data presented are from the Varimax rotation (Table 1).

2.4 | IVF procedure

Patients underwent oocyte retrieval in any of the four ways depending on the medical doctor's assessment of their situation: clomiphene-based minimal stimulated cycle, natural cycle, clomiphene and FSH-stimulated cycle, or letrozole-stimulated cycle. Oocytes were fertilized either by c-IVF or ICSI, and fertilized oocytes were cultured in vitro until embryo transfer. They underwent elective single cleavage embryo transfer. Details of minimal ovarian stimulation combined with elective single cleavage embryo transfer policy protocol have been described previously.[22,23] Embryo grading was performed according to Veeck's criteria.[24] ICSI was performed in the case of moderate/severe male factor infertility, oocytes that matured in vitro after egg retrieval, or a history of fertilization failure diagnosed by other fertility centers.

Clinical pregnancy was defined by detecting an intrauterine gestational sac by ultrasound scan approximately 21 days after egg retrieval.

2.5 | Assessment of confounding factors

We collected information on the patient's age, height, education level [<13 (high school or less), 13-14 (technical or professional school), or ≥15 years (university or more)], history of pregnancy, supplement usage, and smoking history through a self-administered questionnaire at first visit. Body weight was measured to the nearest 0.1 kg in light clothing without shoes on the day of egg retrieval by trained nurses. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

2.6 | Statistical methods

Descriptive data are presented as means [± standard deviation (SD)] for continuous variables and percentages of subjects for categorical variables. The values of nutrient and food intake were energy-adjusted using the density method (ie, percentage of energy for energy-providing nutrients and amount per 1000 kcal of energy for other nutrients and foods). The factor scores for each dietary pattern were categorized into quartiles, which were used for the comparison of nutrient intakes and other characteristic factors. Pearson's correlation coefficients were used to describe the relationships between nutrient intakes and each dietary pattern.

Logistic regression analysis was used to estimate both crude and multivariate odds ratios (ORs) and 95% confidence interval (CI) of clinical pregnancy for each quartile category of the dietary pattern. Multivariate ORs were calculated by adjusting for potential confounding factors, including age (years, continuous variable), BMI (kg/m^2, continuous variable), parity (0 or ≥1), education (<13, 13-14 or ≥15 years), smoking experience (yes or no), alcohol drinking (yes or no), and folate supplement use (yes or no), number of oocyte retrieved (n, continuous variable), and Veeck's criteria (1-5). Trends of association were assessed by a logistic regression model assigning consecutive integers (1-4) to the levels of the independent variables. All reported P-values were two-tailed, and a P-value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Dietary patterns

Three dietary patterns were identified. The factor-loading matrices for each dietary pattern are shown in Table 1 and each was labeled according to the food groups with high loadings. Factor 1, which loaded heavily with vegetables, fish, seafood, soy products, and chicken, was named the "Vegetable and seafood" pattern. Factor 2, with a high-positive loading for red meat, chicken, and oils and a high negative loading for seafood, was named the "Western" pattern. Factor 3, with a high-positive loading for rice and miso soup and a negative loading for confectionaries, was named "Rice and miso soup" pattern. Overall, the three dietary patterns accounted for 26.6% of the variance in food intake.

3.2 | Associations of dietary patterns with subject characteristics

Baseline characteristics according to the quartile of each dietary pattern are shown in Table 2. The subjects in the highest quartile of the "Western" pattern were less likely to be alcohol drinkers and had a higher energy intake (both $P < 0.05$). The subjects in the highest quartile of the "Rice and miso soup" pattern were more likely to be young ($P = 0.05$). In contrast, no difference was seen across the quartile categories of the "Vegetable and seafood" pattern.

3.3 | Associations of dietary patterns with nutrient intakes

Mean energy-adjusted nutrient intakes for the lowest (Q1) and highest (Q4) quartiles of each dietary pattern and Pearson's correlation coefficients are shown in Table 3. Across the distribution of each dietary pattern, there were differences in patterns of nutrient intake. The "Vegetable and seafood" pattern was positively correlated with protein, total fat, omega-3 polyunsaturated fatty acid (PUFA), omega-6 PUFA, dietary fiber, and all vitamins examined. The "Western" dietary pattern was positively correlated with total fat, omega-6 PUFA, dietary fiber, and folate and was negatively correlated with vitamins D and B_{12}. The "Rice and miso soup" pattern was positively correlated with carbohydrate but negatively correlated with total fat.

3.4 | Associations of dietary patterns with clinical pregnancy

Thirty-six women (25.7%) had confirmed clinical pregnancy in this study. The associations between the three dietary patterns and the rate of clinical pregnancy are shown in Table 4. No association was found between any of the three dietary patterns and clinical pregnancy. These associations did not change even after adjustments for potential confounding factors including age, parity, education level,

TABLE 2 Characteristics of the 140 Japanese women who participated in the IVF study[a,b]

	Total (n = 140)	Factor 1: Healthy		Factor 2: Western		Factor 3: Rice and miso soup	
		Q1 (n = 35)	Q4 (n = 35)	Q1 (n = 35)	Q4 (n = 35)	Q1 (n = 35)	Q4 (n = 35)
Age (years)	37.0 ± 4.2	36.7 ± 4.1	36.7 ± 3.9	37.9 ± 4.4	37.2 ± 4.5	38.4 ± 4.1	37.3 ± 4.4*
Age of husband (years)	38.6 ± 5.2	37.8 ± 4.2	38.0 ± 4.4	38.8 ± 5.3	38.1 ± 6.1	40.1 ± 5.1	38.3 ± 5.9
Energy intake (kcal/d)	1508 ± 377	1599 ± 295	1423 ± 328	1630 ± 434	1357 ± 317*	1483 ± 346	1407 ± 340
BMI (kg/m^2)	21.1 ± 2.9	20.8 ± 3.6	21.2 ± 2.1	21.5 ± 2.6	21.0 ± 1.8	21.5 ± 3.2	20.9 ± 2.4
Education (%)							
<13 years	12 (8.6)	4 (11.4)	2 (5.7)	3 (8.6)	5 (14.3)	3 (8.6)	5 (14.3)
13-14 years	49 (35.0)	10 (28.6)	12 (34.3)	15 (42.9)	12 (34.3)	14 (40.0)	13 (37.1)
≥15 years	79 (56.4)	21 (60.0)	21 (60.0)	17 (48.6)	18 (51.4)	18 (51.4)	17 (48.6)
Parity of 1 or more	31 (22.1)	8 (22.9)	6 (17.1)	10 (28.6)	7 (20.0)	12 (34.3)	4 (11.4)
Smoking experience (%)	28 (20.0)	8 (22.9)	8 (22.9)	11 (31.4)	6 (17.1)	8 (22.9)	4 (11.4)
Alcohol drinker (%)	83 (59.3)	22 (62.9)	20 (57.1)	26 (74.3)	17 (48.6)**	18 (51.4)	20 (57.1)
Folate supplement user (%)	86 (61.4)	16 (45.7)	22 (62.9)	20 (57.1)	21 (60.0)	23 (65.7)	24 (68.6)
Number of oocytes retrieved (n)	1.96 ± 1.30	2.03 ± 1.64	1.63 ± 0.88	2.17 ± 1.93	1.83 ± 0.95	2.03 ± 1.01	1.74 ± 1.07
Veeck's criteria of embryo							
1	31 (22.1)	9 (25.7)	5 (14.3)	9 (25.7)	7 (20.0)	10 (28.6)	5 (14.3)
2	37 (26.4)	6 (17.1)	14 (40.0)	9 (25.7)	9 (25.7)	8 (22.9)	10 (28.6)
3	70 (50.0)	20 (57.1)	14 (40.0)	16 (45.7)	18 (51.4)	17 (48.6)	20 (57.1)
4	2 (1.4)	0 (0)	2 (5.7)	1 (2.9)	1 (2.9)	0 (0)	0 (0)
5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

[a]Values are means ± SD for continuous variables and number of subjects (%) for categorical variables.
[b]A linear trend test and a Mantel-Haenszel chi-square test were used for continuous and categorical variables, respectively: *$P < 0.05$, **$P < 0.01$.

TABLE 3 Nutrient intakes for the lowest (Q1) and highest (Q4) quartiles of the three dietary patterns identified for the 140 Japanese women who participated in the IVF study

Nutrient[a,b]	Total (n = 140)	Factor 1: Vegetables and seafood			Factor 2: Western			Factor 3: Rice and miso soup		
		Q1 (n = 35)	Q4 (n = 35)	Pearson r [3]	Q1 (n = 35)	Q4 (n = 35)	Pearson r [3]	Q1 (n = 35)	Q4 (n = 35)	Pearson r [3]
Protein (% of energy)	15.5 ± 2.5	13.3 ± 1.9	18.0 ± 2.3***	0.76	15.3 ± 3.2	16.2 ± 2.0	0.10	15.6 ± 2.2	15.9 ± 3.0	−0.01
Fat (% of energy)	28.5 ± 5.4	25.5 ± 5.9	31.0 ± 4.6***	0.38	25.3 ± 4.7	32.0 ± 4.9***	0.49	31.3 ± 4.6	26.1 ± 6.4***	−0.47
n-3 PUFA	1.4 ± 0.4	1.1 ± 0.3	1.8 ± 0.4***	0.79	1.5 ± 0.5	1.5 ± 0.3	−0.02	1.5 ± 0.3	1.5 ± 0.5	−0.14
n-6 PUFA	6.1 ± 1.3	5.3 ± 1.1	6.7 ± 1.3***	0.43	5.3 ± 1.1	7.0 ± 1.2***	0.48	6.6 ± 0.9	6.0 ± 1.5	−0.28
Carbohydrate (% of energy)	52.1 ± 7.4	56.5 ± 7.9	48.3 ± 6.5***	−0.52	50.5 ± 8.7	50.8 ± 6.5	0.15	49.2 ± 6.5	54.9 ± 9.3**	0.38
Dietary fiber (g/1000 kcal)	7.0 ± 1.9	5.4 ± 1.0	8.8 ± 1.6***	0.68	6.3 ± 2.1	8.3 ± 1.7***	0.40	7.0 ± 1.7	7.2 ± 2.0	0.02
Vitamin D (µg/1000 kcal)	6.5 ± 3.6	4.1 ± 1.8	9.5 ± 4.4***	0.69	8.8 ± 5.1	5.3 ± 2.1***	−0.42	6.3 ± 2.9	6.8 ± 4.5	0.02
Vitamin B_6 (mg/1000 kcal)	0.7 ± 0.2	0.6 ± 0.1	0.9 ± 0.1***	0.87	0.7 ± 0.2	0.8 ± 0.1	0.04	0.7 ± 0.2	0.7 ± 0.2	−0.04
Vitamin B_{12} (mg/1000 kcal)	4.8 ± 2.4	3.3 ± 1.3	6.8 ± 3.0***	0.68	6.5 ± 3.3	4.3 ± 1.7***	−0.46	5.0 ± 1.9	4.8 ± 2.7	−0.03
Folate (µg/1000 kcal)	194 ± 67	137 ± 34	249 ± 56***	0.65	170 ± 60	247 ± 71***	0.33	205 ± 67	193 ± 74	−0.10

[a]All nutrients were energy-adjusted using the density method.
[b]Mean ± SD (all such values). Significance level with the first quartile (Q1) of each dietary pattern by Dunnett's t test: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

TABLE 4 Association between dietary pattern and clinical pregnancy among the 140 Japanese women who participated in the IVF study

	Clinical pregnancy/ total (n)	Clinical pregnancy[a]				
			Crude		Adjusted[b]	
		Rate (%)	OR	95% CI	OR	95% CI
Factor 1: Vegetables and seafood						
Q1	12/35	34.3	1.00	Reference	1.00	Reference
Q2	7/35	20.0	0.48	(0.16-1.42)	0.46	(0.14-1.53)
Q3	6/35	17.1	0.40	(0.13-1.22)	0.42	(0.13-1.43)
Q4	11/35	31.4	0.88	(0.32-2.38)	0.90	(0.30-2.69)
OR per 1-category increase[c]			0.94	(0.67-1.32)	0.97	(0.67-1.39)
P for trend			0.73			0.85
Factor 2: Western						
Q1	8/35	22.9	1.00	Reference	1.00	Reference
Q2	11/35	31.4	1.55	(0.53-4.48)	1.90	(0.58-6.24)
Q3	11/35	34.4	1.55	(0.53-4.48)	1.38	(0.41-4.61)
Q4	6/35	17.1	0.70	(0.21-2.28)	0.84	(0.23-3.11)
OR per 1-category increase [c]			0.91	(0.65-1.28)	0.92	(0.63-1.36)
P for trend			0.60			0.69
Factor 3: Rice and miso soup						
Q1	6/35	17.1	1.00	Reference	1.00	Reference
Q2	13/35	37.1	2.86	(0.94-8.71)	1.78	(0.53-5.94)
Q3	12/35	34.3	2.52	(0.82-7.75)	1.98	(0.58-6.77)
Q4	5/35	14.3	0.81	(0.22-2.93)	0.72	(0.18-2.93)
OR per 1-category increase [c]			0.94	(0.67-1.32)	0.94	(0.63-1.40)
P for trend			0.73			0.74

[a]All values are mean and 95% CIs in parentheses.
[b]Adjusted for age, BMI, parity, education, smoking experience (yes or no), alcohol drinker (yes or no), and folate supplement use (yes or no).
[c]Values are ORs and 95% CIs in parentheses, indicating the change in one category of dietary pattern.

smoking habits, and alcohol drinking habits. Among the potential confounders examined, the common factors that were strongly related to the rate of clinical pregnancy were age (OR = 0.81, 95% CI: 0.72-0.91) and Veeck's criteria of embryo quality (OR = 0.44, 95% CI: 0.27-0.71). With advanced age, the probability of clinical pregnancy decreased by 20%.

4 | DISCUSSION

To our knowledge, the present study is the first to examine the association between dietary patterns and IVF outcome among non-Western women. In this prospective study of 140 Japanese women undergoing IVF, we identified three dietary patterns: "Vegetable and seafood," "Western," and "Rice and miso soup." No meaningful associations were found between these dietary patterns and clinical pregnancy rate before and after adjustment for age, parity, education level, smoking habits, and alcohol drinking habits.

Several studies have examined the relationship between diet and IVF outcome; however, most of these studies have focused on single nutrients and foods.[5-12] Notably, a recent diet and medical issues study examined diet as a multidimensional exposure.[13] With regard to the association between diet and IVF, only one previous study used a statistical approach.[15] In the study of 161 couples undergoing IVF/ICSI treatment in the Netherlands, two dietary patterns: the "health conscious-low processed" and the "Mediterranean" dietary pattern were identified. The couples with high adherence to the "Mediterranean" dietary pattern, characterized by high intakes of vegetable oils, vegetables, fruits, nuts, fish and legumes, and low dairy intake, had a 40% increased probability of achieving pregnancy

after IVF treatment. However, couples with higher adherence to the "health conscious-low processed" dietary pattern, which contained high intakes of fruits, vegetables, whole grains, fish, and legumes, and low intakes of mayonnaise, snacks, and meat products, had a 20% decreased probability of pregnancy. These two dietary patterns in this previous study showed a remarkable overlap in foods, but the authors suggested that the "Mediterranean" dietary pattern was associated with a higher pregnancy rate because of the differences in fatty acids and vitamin B_6 between the two dietary patterns. In the "Mediterranean" pattern, there was a notably high intake of vegetable oils that were rich in omega-6 PUFA, including linoleic acids. Linoleic acids are the precursors of prostaglandins, which are involved in follicle development, corpus luteum function, and embryo implantation.[25-27] Moreover, high adherence to the "Mediterranean" pattern was positively associated with vitamin B_6 in the blood and follicular fluid, in addition to red blood cell folate. Vitamin B_6 is considered to increase pregnancy rate because vitamin B_6-dependent coenzyme participates in the metabolism of amino acids, lipids, nucleic acids, and glycogen, which are essential for reproduction.[9] This mechanism was considered to positively affect placentation and embryo implantation. However, a high concentration of folate was also noted in the "Mediterranean" pattern, and folic acid and vitamin B_6 reduce homocysteine concentration.[28] Consequently, inflammation was controlled, which was considered one of the reasons for the positive association between the "Mediterranean" pattern and pregnancy rate.[9] In the present study, omega-6 PUFA intake was positively correlated with both the "Vegetable and seafood" and "Western" patterns. With regard to vitamin B_6 and folate, strong positive correlations were observed only in the "Vegetable and seafood" pattern. This tendency was similar in the relationship of the "Mediterranean" and "health conscious-low processed" patterns with nutrient intake; however, neither the "Vegetable and seafood" pattern nor the "Western" pattern was associated with clinical pregnancy. We do not know the reason for the difference in the results between these studies, but it should be noted that the relationships of blood and follicle fluid concentration were not equal to those of nutrient intake.

Although we initially considered that a healthy dietary pattern with a high intake of fruit and vegetables, as well as abundant nutrients, might alter IVF outcomes, we could not find an association between dietary pattern and clinical pregnancy rate. The "Vegetable and seafood" pattern was highly correlated with folate, vitamin B_6, vitamin B_{12}, vitamin D, omega-3 PUFA, and omega-6 PUFA, and these have been reported to be beneficial for IVF treatment.[7-12] However, we did not observe a meaningful association between the "Vegetable and seafood" dietary pattern and clinical pregnancy rate. The reason for this is unclear; however, two possibilities may be considered. One was that the effect of a combination of promising nutrients was negated by other strong factors, such as age. Another possibility was that our study was too underpowered, because of the small sample size, to identify modest effect differences, although our number of participants was similar to that of a previous study of 161 couples undergoing IVF.[15]

The major strength of the present study includes its prospective design and comprehensive information regarding confounding factors. However, it had several limitations. First, the study population was not a representative sample of Japanese IVF patients. The present study was performed in a private clinic and the patients lived in relatively close proximity to this clinic; thus, our results might not be generalizable. Second, although a validated dietary assessment questionnaire was used, misreporting of self-reported food intake is a measurement error that is associated with underreporting rather than overreporting.[29] To minimize the effect of underreporting, we used energy-adjusted values. Third, we did not examine the influence of paternal factors, such as diet and lifestyle. There are some reports suggesting that a healthy diet can improve semen quality and fecundability rates in men.[30] Fourth, we obtained information about folate supplement usage but not about its dosage. Fifth, we did not gain social and economic information for ethical reason. Finally, although an adjustment of known potential confounders was performed, unknown or poorly measured confounding factors may have existed.

In conclusion, the three maternal preconception dietary patterns identified in this prospective study revealed no meaningful association with IVF outcomes among Japanese women. Dietary patterns may not be absolute factors influencing pregnancy outcomes in Japanese women undergoing IVF. Further studies in various populations with different dietary patterns are needed to confirm these findings.

DISCLOSURES

Conflict of interest: Miki Sugawa, Hitomi Okubo, Satoshi Sasaki, Yuko Nakagawa, Tamotsu Kobayashi, and Keiichi Kato declare that they have no conflict of interest. *Human rights statements and informed consent*: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and its later amendments. Informed consent was obtained from all patients for being included in the study. *Animal studies*: This article does not contain any studies with animal subjects performed by any of the authors.

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