# The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/intracytoplasmic sperm injection treatment increases the chance of pregnancy

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**Objective:** To investigate associations between preconception dietary patterns and IVF/intracytoplasmic sperm injection (ICSI) outcomes validated by biomarkers of the homocysteine pathway.
**Design:** Observational prospective study.
**Setting:** A tertiary referral fertility clinic at the Erasmus University Medical Centre, Rotterdam, The Netherlands.
**Patient(s):** One hundred sixty-one couples undergoing IVF/ICSI treatment.
**Intervention(s):** No interventions other than the Dutch governmental recommendation of folic acid.
**Main Outcome Measure(s):** Dietary patterns, blood and follicular fluid concentrations of folate, vitamin B12, vitamin B6, homocysteine, and fertilization rate, embryo quality, and pregnancy.
**Result(s):** In women, two dietary patterns were identified. The “health conscious–low processed” dietary pattern (variation explained 12.1%) was characterized by high intakes of fruits, vegetables, fish, and whole grains and low intakes of snacks, meats, and mayonnaise, and positively correlated with red blood cell folate ($\beta = 0.07$). The “Mediterranean” dietary pattern (variation explained 9.1%), that is, high intakes of vegetable oils, vegetables, fish, and legumes and low intakes of snacks, was positively correlated with red blood cell folate ($\beta = 0.13$), and vitamin B6 in blood ($\beta = 0.09$) and follicular fluid ($\beta = 0.18$). High adherence by the couple to the “Mediterranean” diet increased the probability of pregnancy, odds ratio 1.4 (95% confidence interval 1.0–1.9).
**Conclusion(s):** A preconception “Mediterranean” diet by couples undergoing IVF/ICSI treatment contributes to the success of achieving pregnancy. (Fertil Steril® 2010;94:2096–101. ©2010 by American Society for Reproductive Medicine.)

**Key Words:** Nutrition, Mediterranean diet, folate, vitamin B6, homocysteine, subfertility, reproduction

Subfertility is an increasing problem in the reproductive population of industrialized countries, primarily because of postponed childbearing (1). This problem is accentuated by unhealthy lifestyles, such as smoking, alcohol use, and malnutrition (2).

A nutritionally unbalanced diet characterized by low intakes of minerals and vitamins has been associated with adverse fertility outcomes (3). Especially the B-vitamins, folate, vitamin B6, and vitamin B12, are important because of their role in the homocysteine pathway (4–6). A deficiency of these vitamins may cause an accumulation of homocysteine concentrations, which can ultimately lead to hyperhomocysteinemia (3, 5–7). This biochemical derangement seems to be detrimental for reproductive outcome as elevated total homocysteine (tHcy) concentrations in follicular fluid have been inversely associated with IVF/intracytoplasmic sperm injection (ICSI) outcomes, that is, number of preantral follicles, retrieved oocytes, and embryo quality (8–10).

Thus, it seems biologically plausible that the homocysteine pathway is at least one of the intermediate mechanisms between nutritional intake and reproductive outcome. Given that most micronutrients are present in common food sources, such as fruit, vegetables, and cereals, we are interested in the impact of the overall diet on IVF/ICSI outcomes. Therefore, our aims were to identify patterns in food consumption that explain the largest proportion of variation, for example, dietary patterns, in women of subfertile couples undergoing IVF/ICSI treatment; validate these dietary patterns with biomarkers of the homocysteine pathway in blood and follicular fluid; and determine associations between the dietary patterns of the subfertile couples and IVF/ICSI outcomes.

## MATERIALS AND METHODS
### Study Population

The FOod, Lifestyle and Fertility Outcome project was designed to investigate the relationship between nutrition and lifestyle and IVF/ICSI outcome

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(11). In short, between September 2004 and January 2007 subfertile couples undergoing IVF/ICSI treatment at the Erasmus University Medical Centre, Rotterdam, The Netherlands, were invited to participate. Sixty-four percent (n = 161) of the couples were included in the analysis. Of the eligible 251 couples 15 couples dropped out because of oocyte donation, endometrioma, hydrosalpinx, medication error, or pregnancy before start of the treatment. Couples of whom no oocytes could be retrieved were also excluded (n = 20). Because lifestyle factors, including dietary patterns, are culturally determined, we excluded couples of non-European origin (n = 55) as well (12). Ethnicity was categorized into Dutch native, European other, and non-European according to the definitions of Statistics Netherlands (http://www.cbs.nl/en-GB/menu/methoden/begrippen/default.htm?ConceptID=315). The study protocol was approved by the Dutch Central Committee for Human Research and the medical ethical and institutional review board of the Erasmus University Medical Centre in Rotterdam. Participants provided written informed consent and the obtained materials and questionnaires were processed anonymously.

## Questionnaires

All participants filled out a general questionnaire that generated the following information: age, educational level, medical history, body mass index (BMI), ethnicity, medication use, smoking, folic acid, and vitamin use. All participants filled out a food frequency questionnaire (FFQ) to estimate food intake of the previous 4 weeks. This FFQ was developed by the division of Human Nutrition, Wageningen University, and validated for intake of energy, B-vitamins, and fatty acids (13, 14). The FFQ was provided on the day of oocyte retrieval or semen sample collection and returned on the day of embryo transfer.

## In Vitro Fertilization Procedure

We used three IVF stimulation treatments. Women were assigned either to one of two types of conventional ovarian stimulation, or a mild ovarian stimulation treatment as previously described (11). In all three regimens a single dose of 5,000 or 10,000 IU human chorionic gonadotropin subcutaneously (hCG, Pregnyl, NV Organon, The Netherlands) was administered to induce oocyte maturation as soon as the leading follicle reached a diameter of at least 18 mm and at least one additional follicle reached a diameter of 15 mm. Oocyte retrieval was performed 35 hours after hCG injection by transvaginal ultrasound-guided puncture of the follicles. Intravaginal luteal phase supplementation of 600 mg/day progesterone was started on the evening following oocyte pickup, and was continued for 12 days thereafter. On day 3 after oocyte pickup a maximum of two embryos was transferred.

## Follicular Fluid and Blood Sample Collection

During oocyte retrieval, follicular diameters were measured and monofollicular fluid from the largest follicle was aspirated from each ovary and collected separately (11). The oocytes were washed and transferred to a separate droplet of medium to monitor embryo quality. The monofollicular fluids were centrifuged for 10 minutes at 1,700 × $g$ to separate red blood cells (RBC), leucocytes, and granulosa cells. The samples were frozen without preservatives and stored at –20 °C until assayed. Venous blood samples were drawn on cycle day 2 before the first injection of recombinant FSH and on the day of hCG administration. At both time points folate, vitamin B6, vitamin B12, tHcy, and estradiol were determined. Baseline FSH levels were determined on cycle day 2 only (11).

We previously demonstrated that folate concentrations increase on average to 22.5 nmol/L when women of reproductive age use 250 $\mu$g folic acid daily for 4 weeks (16). A blood concentration above this value was therefore classified as regular folic acid use and below as no folic acid use.

## Endpoints of the Study

The primary endpoints of the study were the biomarker concentrations in blood and follicular fluid and the IVF/ICSI treatment outcomes fertilization rate, embryo quality, and positive pregnancy test. Fertilization was determined on day 1 after the IVF/ICSI procedure, and was calculated as the number of fertilized oocytes divided by the total number of oocytes retrieved. On day 3 postoocyte retrieval embryo quality scores were assigned ranging from 1 (best quality) to 5 (to poorest quality without transfer) (17). Pregnancy confirmation was assessed by a biochemical pregnancy test in urine 15 days after oocyte retrieval.

## Statistical Methods

All 195 food items from the FFQ data of all participants were classified into 22 food groups and adjusted for total energy intake (15, 18). This was followed by principal component analysis (PCA) applied on the energy-adjusted food groups of the women to construct overall dietary patterns by explaining the largest proportion of variation in the food group intake (19, 20). The two most prevalent dietary patterns were selected by rotating the solution with varimax method (21). Each woman was assigned two personal scores for the two respective factors, calculated as the product of the food group value and its factor loadings summed across foods. According to their personal score the group of 161 women was divided into tertiles and classified as low, intermediate, or high adherence to the respective dietary pattern. The strength of adherence indicates the resemblance of the woman's diet compared with the respective dietary pattern identified by PCA. To elucidate the relative contribution of each food group to the two dietary patterns Pearson's correlation coefficients ($r$) were calculated (Table 1).

The associations between other lifestyle characteristics and the identified dietary patterns are described in Table 2. Continuous variables with skewed distributions are displayed as median with range. Normally distributed variables are presented by mean and standard deviation. $P$-values were estimated from a linear regression model. Categoric variables are presented in frequencies and tested with chi-square test.

The associations between the dietary patterns and biomarkers are shown in Table 3. Because the biomarkers showed skewed distributions they are displayed as median with 95% confidence intervals (95% CI). $P$-values were estimated from a multivariable linear regression model in which logarithmically transformed biomarkers were chosen as the dependent variables, whereas dietary pattern, age, BMI, and vitamin use were included as covariates. Biomarkers in follicular fluid were adjusted for gram of protein to eliminate potential confounding of the oocyte maturation status. Statistically significant $\beta$-estimates are given in the text of the Results section.

Finally we investigated whether the couple's dietary pattern was associated with IVF/ICSI outcome parameters (data not shown). The personal scores for the two dietary patterns were now calculated for both the woman and man and analyzed as the couple's dietary pattern score by taking the average of these personal factor scores. Linear and logistic regression analyses were used in which fertilization rate, average embryo quality, and pregnancy were chosen as dependent variables. Covariates included woman's age, smoking, vitamin use, and type of fertility treatment. In the final regression model BMI, alcohol use and stimulation scheme were added as covariates. Statistical analysis was performed using SPSS 15.0 for Windows software (SPSS Inc, Chicago, IL).

# RESULTS

Two major dietary patterns are identified with PCA in 161 women. The first is labeled "health conscious–low processed," containing high intakes of fruits, vegetables, whole grains, fish, and legumes, but low intakes of mayonnaise, snacks, and meat products. The second dietary pattern, called "Mediterranean," comprises of high intakes of vegetable oil, fish, legumes, and vegetables but low intakes of snacks (Table 1). The "health conscious–low processed" and "Mediterranean" diet explain proportions of 12.1% and 9.1%, respectively, of the total variation in the nutritional intake of the women.

Table 2 depicts the general characteristics for women with low, intermediate, or high adherence to both diets. Women with high adherence to the "health conscious–low processed" diet show a lower BMI compared with women with low adherence. Women with high adherence to the "Mediterranean" diet are generally older, higher educated, consume more alcoholic drinks (e.g., wine), are more frequently of non-Dutch origin, and undergo more often IVF treatment.

An increase in RBC folate is observed among women with a high adherence to the "health conscious–low processed" diet ($\beta = 0.07$;

**TABLE 1**

**Characteristics of two dietary patterns in 161 women undergoing IVF/ICSI treatment, presented by correlation coefficients between dietary patterns and food groups.**

| | Health conscious—low processed | Mediterranean |
|---|---|---|
| Explained variance | 12.1% | 9.1% |
| Alcoholic drinks | −0.15 | 0.13 |
| Breakfast cereals | 0.13 | −0.05 |
| Butter | 0.04 | −0.04 |
| Dairy products | −0.02 | 0.07 |
| Eggs | −0.02 | 0.16 |
| Fish and other seafood | 0.39[b] | 0.53[b] |
| Fruits | 0.62[b] | −0.07 |
| Legumes | 0.23[a] | 0.53[b] |
| Margarine | 0.15 | −0.17 |
| Mayonnaise and fatty dressings | −0.61[b] | −0.05 |
| Meat products | −0.23[a] | −0.15 |
| Nonalcoholic drinks | 0.19 | −0.11 |
| Nuts | −0.05 | 0.15 |
| Pasta, rice and refined grains | 0.03 | −0.10 |
| Potatoes | 0.03 | 0.04 |
| Sauces and condiments | 0.01 | 0.06 |
| Snacks | −0.49[b] | −0.30[b] |
| Soup | 0.13 | 0.07 |
| Sugar and confectionary | 0.02 | 0.19 |
| Vegetable oil | −0.14 | 0.75[b] |
| Vegetables | 0.45[b] | 0.57[b] |
| Whole grains | 0.43[b] | −0.02 |

*Note:* ICSI = intracytoplasmic sperm injection.
[a] *P* value <0.05.
[b] *P* value <0.01.

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$P$=.05) and "Mediterranean" diet ($\beta = 0.13$; $P$<.01) (Table 3). Furthermore, a high adherence to the "Mediterranean" diet is positively associated with vitamin B6 in blood ($\beta = 0.09$; $P$=.04) and follicular fluid ($\beta = 0.16$; $P$=.02).

Neither the "health conscious–low processed" nor the "Mediterranean" diet are associated with fertilization rate ($\beta = 0.00$, $P$=.44, $\beta = 0.00$, $P$=.31, respectively) and embryo quality ($\beta = -0.03$, $P$=.95, $\beta = 0.01$, $P$=.35, respectively). However, high adherence of the couple to the "Mediterranean" diet substantially increases the probability of pregnancy, odds ratio (OR) 1.4 (95% CI: 1.0-1.9). This association is not present in couples with high adherence to the "health conscious–low processed" diet, OR 0.8 (95% CI: 0.6–1.0). All ORs have been adjusted for the confounders age, BMI, smoking, alcohol use, IVF/ICSI treatment, and stimulation scheme. All associations are not significantly affected by the characteristics of the men, that is, age, BMI, smoking, and alcohol use (data not shown).

## DISCUSSION

This study demonstrates that Dutch subfertile couples with high adherence to the "Mediterranean" dietary pattern have a 40% increased probability of achieving pregnancy after IVF/ICSI treatment. The adherence to this diet is reflected by relatively high concentrations of folate and vitamin B6 in blood and follicular fluid. The "health conscious–low processed" dietary pattern was positively associated with RBC folate, but did not affect IVF/ICSI outcomes.

Labeling the extracted factors as the "health conscious–low processed" and "Mediterranean" dietary pattern is part of a continuing effort to achieve consistency in the use of dietary patterns in medical research. Northstone et al. (22) recently investigated dietary patterns during pregnancy in a large cohort study and identified a "health conscious," "traditional," and "processed" dietary pattern. Our first factor consists of high intakes of fruits, vegetables, fish, and whole grains and low intakes of snacks, meat, and mayonnaise, and resembles a combination of Northstones "health conscious" and "processed" diet, and was therefore labeled as "health conscious–low processed."

The second factor shares many features with the classical Mediterranean diet (23), defined by high intakes of vegetable oils, vegetables, fruits, nuts, fish, and legumes, low dairy intake, and moderate intake of alcohol. We examined the magnitude of comparability by scoring the factor to the 10-point Meditteranean diet scale as introduced by Trichopoulou et al. (23). Analysis revealed that women with high adherence to the second factor scored positively in 7 of 10 dietary criteria. This indicates good comparability with the traditional definition of "Mediterranean," justifying the labeling as the "Mediterranean" diet.

The two dietary patterns in our study show a remarkable overlap in foods, for example, high intakes of vegetables, fish, and legumes and low intakes of snacks. However, only the "Mediterranean" diet seems to increase the chance of pregnancy after IVF/ICSI treatment. There are two major differences between these two diets that may explain this finding.

First, when comparing differences in food intakes, the high intake of vegetable oils in the "Mediterranean" diet is outstanding. Vegetable oils are generally rich in linoleic acid and belong to the family of $n-6$ fatty acid molecules, which can only be obtained by the diet. They are precursors of different prostaglandins, important for the initiation of the menstrual cycle, growth, and development of preantral follicles and ovulation. Prostaglandins are also involved in the maintenance of pregnancy by optimizing endometrial receptivity (24–27). This may imply that a higher intake of linoleic acid perhaps positively affects the implantation of the fertilized ovum.

The second difference between the two dietary patterns is found in their effect on the biomarkers of the homocysteine pathway. Both diets increase folate concentrations, but the "Mediterranean" diet shows an additional rise in vitamin B6 in blood and follicular fluid. Vitamin B6 is a versatile coenzyme involved in many biochemical pathways. Research has shown that giving vitamin B6 to subfertile women increases reproductive performance, that is, a 40% increased chance of conception and a 30% lower risk of miscarriage early in pregnancy (28). The positive association between vitamin B6 and the success of IVF/ICSI treatment is herewith in line.

Thus, this study has provided novel insights in the relationship between dietary patterns and IVF/ICSI outcomes, in which vitamin B6 and fatty acids may play an important role. Further research, however, is needed to validate the current findings and investigate optimal dosage effects before any dietary preparation can be generally recommended.

Self-reported dietary assessment methods are susceptible to measurement errors, where habitual energy intake tends to be underestimated (29). However, we consider it unlikely that these measurement errors would have produced false associations.

## TABLE 2

**General characteristics of the 161 women undergoing IVF/ICSI treatment.**

| | Low (n = 54) | Health conscious—low processed intermediate (n = 54) | High (n = 53) | *P* value | Low (n = 54) | Mediterranean intermediate (n = 54) | High (n = 53) | *P* value |
|---|---|---|---|---|---|---|---|---|
| Age (y), median (range) | 34.2 (23.2– 43.7) | 35.6 (23.7–41.8) | 36.4 (26.6– 41.6) | .06 | 35.2 (23.2– 43.7) | 33.9 (23.7–40.6) | 37.2 (29.3– 42.1) | < .01 |
| BMI (kg/m$^2$), median (range) | 24.1 (16.1– 33.7) | 23 (18.1–36.3) | 22 (18–29.8) | .03 | 23.5 (18.5– 36.3) | 22.8 (18.1–34.4) | 22.3 (16.1– 29.8) | .34 |
| Educational level, n (%) | | | | | | | | |
| Low | 9 (17) | 5 (9.3) | 5 (9.4) | | 6 (11.1) | 7 (13.2) | 6 (11.3) | |
| Intermediate | 24 (45.3) | 23 (42.6) | 22 (41.5) | | 30 (55.6) | 25 (47.2) | 14 (26.4) | |
| High | 20 (37.7) | 26 (48.1) | 26 (49.1) | .15 | 18 (33.3) | 21 (39.6) | 33 (62.3) | .03 |
| Cause of subfertility, n (%) | | | | | | | | |
| Male factor | 19 (35.2) | 20 (37) | 18 (34) | | 20 (37) | 24 (44.4) | 13 (24.5) | |
| Female factor | 11 (20.4) | 10 (18.5) | 10 (18.9) | | 13 (24.1) | 4 (7.4) | 14 (26.4) | |
| Male and female factor | 6 (11.1) | 3 (5.6) | 2 (3.8) | | 4 (7.4) | 5 (9.3) | 2 (3.8) | |
| Unexplained | 18 (33.3) | 21 (38.9) | 23 (43.4) | .79 | 17 (31.5) | 21 (38.9) | 24 (45.3) | .07 |
| Ethnicity, n (%) | | | | | | | | |
| Dutch European | 48 (88.9) | 46 (85.2) | 41 (77.4) | | 47 (87) | 49 (90.7) | 39 (73.6) | |
| Other European | 6 (11.1) | 8 (14.8) | 12 (22.6) | .26 | 7 (13) | 5 (9.3) | 14 (26.4) | .04 |
| Smoking, n (%) | | | | | | | | |
| Yes | 5 (9.3) | 6 (11.1) | 2 (3.8) | | 4 (7.4) | 4 (7.4) | 5 (9.6) | |
| No | 49 (90.7) | 48 (88.9) | 50 (96.2) | .32 | 50 (92.6) | 50 (92.6) | 47 (90.4) | .89 |
| Alcohol use (units/week), median (range) | 0.9 (0–17) | 1.5 (0–32.2) | 1.1 (0–18.3) | .44 | 0.3 (0–13.4) | 0.7 (0–32.2) | 2.1 (0–18.3) | .02 |
| Folic acid supplements, n (%) | | | | | | | | |
| Yes | 42 (77.8) | 39 (72.2) | 43 (81.1) | | 38 (70.4) | 44 (81.5) | 42 (79.2) | |
| No | 12 (22.2) | 15 (27.8) | 10 (18.9) | .50 | 16 (29.6) | 9 (16.7) | 11 (20.8) | .33 |
| Vitamin supplements, n (%) | | | | | | | | |
| Yes | 24 (44.4) | 29 (53.7) | 25 (47.2) | | 23 (42.6) | 26 (48.1) | 29 (54.7) | |
| No | 30 (55.6) | 25 (46.3) | 28 (52.8) | .61 | 31 (57.4) | 28 (51.9) | 24 (45.3) | .45 |
| Energy intake (kJoule/d), mean (SD) | 8083 (2198) | 7649 (2146) | 8614 (3537) | .21 | 8040 (1922) | 8087 (2234) | 8212 (3707) | .86 |
| Endocrinology | | | | | | | | |
| FSH, cycle d, median (range) (U/L) | 8.2 (4.2–18.5) | 7.5 (4.1–30.3) | 8.1 (0.4–14.1) | .20 | 8.1 (4.5–30.3) | 7.6 (2.4–18.4) | 8.6 (0.4–18.5) | .53 |
| Estradiol, cycle day 2 (pmol/L) | 142 (72–273) | 132 (63–338) | 145.5 (41–443) | .17 | 138.5 (49–338) | 141.5 (68–307) | 140 (41–443) | .78 |
| Duration of subfertility, median (range) | 33 (9–115) | 40 (3–135) | 36 (6–121) | .94 | 41.5 (3–135) | 36 (10–121) | 34 (6–115) | .52 |
| Percentage of fertilized oocytes, mean (SD) | 0.7 (0.3–1) | 0.6 (0.1–1) | 0.6 (0.2–1) | .68 | 0.6 (0.1–1) | 0.7 (0.2–1) | 0.6 (0.2–1) | .22 |
| Biochemical pregnancy, n (%) (per started treatment) | 14 (34.1) | 10 (26.3) | 11 (26.2) | .66 | 11 (25) | 13 (32.5) | 11 (29.7) | .75 |
| Stimulation scheme, n (%) | | | | | | | | |
| PO2-150 | 40 (75.5) | 35 (68.6) | 36 (70.6) | | 34 (63) | 36 (73.5) | 41 (78.8) | |
| PO5-150 | 6 (11.3) | 4 (7.8) | 7 (13.7) | | 8 (14.8) | 3 (6.1) | 6 (11.5) | |
| DLP225 | 7 (13.2) | 12 (23.5) | 8 (15.7) | .95 | 12 (22.2) | 10 (20.4) | 5 (9.6) | .09 |
| Fertilization method, n (%) | | | | | | | | |
| IVF | 32 (66.7) | 33 (68.8) | 38 (76) | | 30 (61.2) | 28 (60.9) | 45 (88.2) | |
| ICSI | 16 (33.3) | 15 (31.3) | 12 (24) | .31 | 19 (38.8) | 18 (39.1) | 6 (11.8) | < .01 |

*Note:* ICSI = intracytoplasmic sperm injection; BMI = body mass index. Crude *P* values are shown.

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## TABLE 3

**Biochemical determinants of the homocysteine pathway in blood and follicular fluid in women undergoing IVF/ICSI treatment.**

| | Folate RBC (nmol/L) | Folate (nmol/L) | vitamin B6 (nmol/L) | vitamin B12 (pmol/L) | tHcy ($\mu$mol/L) |
|---|---|---|---|---|---|
| Health conscious—low processed | | | | | |
| Blood | | | | | |
| Low (n = 32) | 1,553 (488–2,461) | 32.1 (9.8–82.4) | 78.5 (43–231) | 316.4 (74–1,856) | 9.7 (6.1–75.3) |
| Intermediate (n = 25) | 1,149 (531–3,116) | 38 (11.7–82.3) | 75 (51–173) | 325 (140–724) | 9.2 (5.5–37) |
| High (n = 28) | 1,672 (783–3,611) | 37 (15.8–119.5) | 81 (46–250) | 301.5 (143–863) | 8.4 (5.8–12.6) |
| P value[a] | .05 | .09 | .33 | .55 | .72 |
| Follicular fluid | | | | | |
| Low (n = 36) | | 29.9 (7.3–84.4) | 68 (17.5–310) | 192.5 (59–3,695) | 6.3 (3.8–70.2) |
| Intermediate (n = 32) | | 32.7 (8.9–199.6) | 86.4 (14.5–310) | 247 (122.5–31,013) | 6.6 (3.3–27.2) |
| High (n = 39) | | 35.5 (12.5–190) | 84 (22.5–310) | 208.5 (87.5–1,672.5) | 6.1 (3.6–14) |
| P value[b] | | .23 | .97 | .59 | .72 |
| Mediterranean | | | | | |
| Blood | | | | | |
| Low (n = 27) | 1,078 (531–,3293) | 32.6 (11.7–119.5) | 72 (50–231) | 297 (74–724) | 10.1 (6.1–75.3) |
| Intermediate (n = 27) | 1,462 (488–2,244) | 33.9 (9.8–108.5) | 79 (43–173) | 333 (183–688) | 8.9 (5.5–18.3) |
| High (n = 31) | 1,665 (909–3,611) | 37.3 (17.1–92) | 89 (43–250) | 353 (140–1,856) | 8.7 (5.8–12.9) |
| P value[a] | <.01 | .28 | .04 | .14 | .48 |
| Follicular fluid | | | | | |
| Low (n = 34) | | 30.5 (8.9–199.6) | 70.5 (14.5–310) | 205.7 (59–31,013) | 6.3 (3.3–70.2) |
| Intermediate (n = 37) | | 32.3 (7.3–69) | 74 (17.5–310) | 195.5 (104–4,199) | 6.4 (3.8–15.5) |
| High (n = 36) | | 35.3 (12–190) | 91.5 (22.5–310) | 230 (87.5–2,959) | 6.2 (3.6–14) |
| P value[b] | | .14 | .02 | .89 | .20 |

*Note:* BMI = body mass index; RBC = red blood cell.
[a] Adjusted for age, BMI, and use of vitamin supplements.
[b] Adjusted for age, BMI, use of vitamin supplements, and total protein in follicular fluid.

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Because of the prospective study character, exposure determinants were measured before the outcomes were known. Therefore, energy and nutritional intake is unlikely to be differentially underreported or differently reported between couples with and without successful IVF/ICSI treatment.

The findings from this Dutch subfertile study group cannot be equally generalized to the reproductive population because couples seeking fertility treatment generally have a higher age and education. These results should also not be extrapolated to non-Europeans for which studies in different ethnic populations are required.

In conclusion, a high adherence to the “Mediterranean” dietary pattern by the couple may improve the chance of pregnancy after IVF/ICSI treatment. These findings are important with regard to the development of nutritional interventions to further improve fertility treatment and success rates.

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