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The Association Between History of Infertility and Dietary Practices: A Cross-Sectional Study Among Preconception Females

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ABSTRACT

Objective: To evaluate the extent to which a history of infertility is associated with adherence to specific diets among reproductive-aged females.

Design: Cross-sectional analysis.

Subjects: Between 2017–2023, 7,227 North American female pregnancy planners aged 21-45 years enrolled in PRESTO (Pregnancy Study Online), a preconception cohort study. Participants completed self-administered baseline questionnaires during preconception.

Exposure: Infertility history, defined as: 1) self-reported 12-month clinical infertility, 2) history of visiting a clinician for an infertility work-up, and/or 3) clinician-identified cause of infertility (e.g., ovulatory or tubal).

Main Outcome Measure: Adherence to specific diets, including vegetarian, vegan, Mediterranean, Paleo, Weight Watchers®, ketogenic, dairy free, gluten free, Atkins®, South Beach®, Zone®, raw foods, or other at baseline. Multivariable log-binomial regression models estimated the prevalence ratios (PRs) and 95% confidence intervals (CIs), adjusted for age, income, and body mass index (BMI).

Results: The percentage of participants with a history of infertility was 26% based on the 12-month clinical infertility definition, 30% based on visiting a physician for infertility evaluation, and 26% based on an infertility diagnosis following a physician visit. Overall adherence to any particular diet was low (4.6% vegetarian, 2.8% ketogenic, 1.7% Weight Watchers®, 1.4% Mediterranean, 1.3% vegan, 0.8% Paleo, and all other diets: <0.8%); 86.6% reported not adhering to any particular diet. A history of 12-month clinical infertility was associated with lower adherence to vegetarian (PR=0.78; 95% CI: 0.60-1.03), Paleo (PR=0.43; 95% CI: 0.19-0.98), and Weight Watchers® (PR=0.55; 95% CI: 0.34-0.91) diets. An infertility history involving a medical work-up was associated with a higher prevalence of adherence to a ketogenic diet (PR=1.56; 95% CI: 1.17-2.09). Participants whose infertility was attributed to ovulatory or tubal causes were nearly two times more likely to adhere to a ketogenic diet (PR=2.01; 95% CI: 1.38-2.94; PR=2.22; 95% CI: 1.09-4.49, respectively).

Limitations: The cross-sectional design cannot establish temporality or causality. Data on dietary patterns and infertility history were self-reported, which can introduce misclassification. Generalizability may be limited because participants were pregnancy planners not using fertility treatments; participants were also more likely to be non-Hispanic White and of higher socioeconomic status than the general population.

Conclusion: The ketogenic diet was more prevalent among females with an infertility history, while vegetarian, Paleo, and Weight Watchers® diets were less prevalent. These associations mirror the results of studies evaluating the reverse relationship, suggesting that some patients with infertility seek information for behavioral modifications via evidence-based medicine.

Keywords: cross-sectional studies; diet; infertility; females; preconception

INTRODUCTION

Infertility is defined as the inability to conceive either after 6 or 12 months of unprotected intercourse for females aged ≥ 35 or <35 years, respectively.[1] Current data on the prevalence of infertility in the United States (US) is inconsistent. Recent studies have estimated that the prevalence of 12-month infertility among US females aged 15-44 ranges between 8-15%.[2-3] Risk factors for female factor infertility include age, cigarette smoking, alcohol use, excessive weight gain or

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weight loss, sleep deprivation, and stress.[4-6] However, the experience of infertility can also affect behaviors and lifestyle choices.[7-8] For example, an increase in pregnancy attempt time was previously associated with a decrease in the following behaviors: caffeine intake, cannabis use, and vigorous exercise.[9] Consequently, behavioral modifications might alter outcomes among couples attempting conception, highlighting behavioral choices that may need emphasis during conception counseling.

Several studies have evaluated dietary factors as determinants of infertility.[10-11] A 2017 review of the literature on dietary intake and fertility supported the hypothesis that females who adhered to diets rich in fish, poultry, vegetables, and fruits had improved fertility outcomes.[11] In addition, a 2022 review of the literature on female dietary intake and in-vitro fertilization (IVF) outcomes, found evidence that adherence to a Mediterranean diet increased pregnancy chances during IVF.[12] A Mediterranean diet includes high amounts of whole grains, vegetables, fruits, nuts, legumes, and olive oil, and low to moderate intake of poultry, red meat, seafood, and dairy. Moreover, both a 2022 review of anti-inflammatory diets on fertility and a preconception cohort study of dietary intake on fecundability of females in North America and Denmark, including the cohort on which this report is based (i.e., PRESTO), indicated greater adherence to anti-inflammatory diets was associated with higher fertility. [13-14] Anti-inflammatory diets consisted of greater nutrient-dense food like vegetables and fruits and reduced processed foods and red meats. Furthermore, two preconception cohort studies in North America and Denmark found higher fecundability among couples that adhered to diets lower in glycemic load, added sugars, and carbohydrate-to-fiber ratios.[15]

There is limited research on how a history of infertility is associated with behaviors, including dietary choices. The goal of the current study was to evaluate the extent to which a history of infertility is associated with dietary patterns among reproductive-aged females. Using data from a North American preconception cohort study of pregnancy planners, we estimated the prevalence of certain diets among those with and without a history of infertility (self-reported 12-month clinical definition, visiting a doctor for infertility work-up, and identified causes of infertility).

METHODS

Study Population

Pregnancy Study Online (PRESTO) is an internet-based preconception cohort study of couples in the US and Canada attempting to conceive without the use of fertility treatment. PRESTO seeks to identify factors that may impact a couple's fecundability, and its methodology has been described in greater detail previously.[16] Enrollment began in June 2013 and is ongoing. Eligible participants identified as female and were aged 21-45 years, in a relationship with a male partner, and willing to participate in a 12-month study. Male partners were aged ≥21 years. Eligible participants completed a baseline questionnaire about socio-demographics, lifestyle, medical and reproductive history. The Institutional Review Board of Boston Medical Center approved the PRESTO study protocol (protocol number: H-31848).

Assessment of Exposure

Three questions were included on the baseline female questionnaire to assess a history of infertility. The first question was: "Have you ever tried for twelve months or more to become pregnant without becoming pregnant during that time?" Responses included "yes", "no", or "no, never tried to get pregnant before." Participants who responded "yes" were further prompted to report the age at which they experienced these difficulties. Participants who "never tried to get pregnant before" were not asked any further questions about their infertility history. However, participants who responded "yes" or "no" were asked: "Have you ever visited a doctor because of difficulty becoming pregnant?" Response options included "yes" or "no". Only participants who responded "yes" were asked: "Did the doctor identify a reason for your difficulties in becoming pregnant?" Participants who responded "no" were classified as unidentified factor infertility. Participants who responded "yes" were further prompted to answer what reason the doctor identified (check all that apply): cervical factor, tubal factor, ovulation factor, hormonal problems, your partner, or something else. Participants who identified ovulatory or hormonal problems were combined into one group. Participants who reported "something else," with a diagnosis that matched one of the previous factors were manually regrouped into the appropriate category. For example, reports of "polycystic ovary syndrome (PCOS)" were regrouped into "ovulation factor."

Assessment of Outcome

Starting in October 2017, the baseline questionnaire included questions about specific diets as follows: "Are you currently practicing this diet?" Participants selected from the following categories (check all that apply): Vegetarian, Vegan, Dairy free, Gluten free, Mediterranean, Paleo, Atkins®, South Beach®, Weight Watchers®, Zone®, Ketogenic, Raw Foods, Other.

Assessment of Covariates

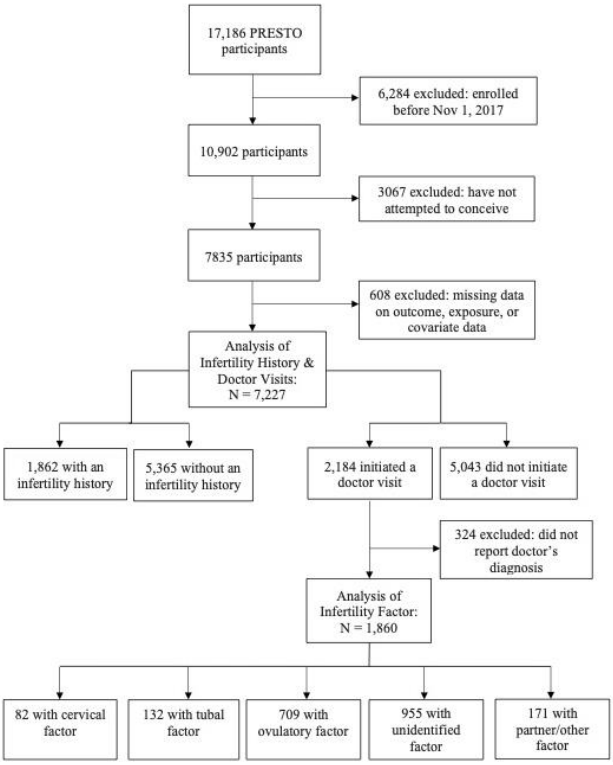
On the baseline female questionnaire, participants reported their age, household income, height, and weight. We calculated body mass index (BMI) by dividing weight (kg) by height squared (m^2).

Exclusion Criteria

Over the study period, 17,186 participants enrolled in PRESTO. We excluded 6,284 participants who enrolled before November 1st, 2017, the date we added dietary practices to the baseline questionnaire. Then, we excluded

3,067 participants who had not previously attempted to conceive. We also excluded participants with missing data on dietary practices (n=336), infertility history (n=2), or one or more covariates (n=270). The analytic population for the first two exposures (history of infertility and visiting a doctor for an infertility work-up) was 7,227. The analytic population for infertility factor diagnoses was smaller (n=1,860) because it was restricted to participants who visited a clinician for infertility (n=2,184). Of this subset, participants who did not report information about their infertility diagnosis (n=324) were excluded. Figure 1 presents a flow chart of the exclusion criteria.

Figure 1. Flowchart of Exclusion Criteria



Statistics and Data Analysis

We analyzed the 12-month clinical definition of infertility as a binary variable (yes vs. no). We further dichotomized participants reporting 12-month infertility according to whether they visited a doctor for infertility concerns (yes vs. no). The reference group comprised participants with no history of infertility (N=5,365). Finally, participants who visited a doctor for their infertility difficulties were analyzed based off the following categories: cervical, tubal, ovulatory, and unidentified factors. For the questions regarding doctor visits and infertility subtypes, the reference group comprised participants who responded "no" to a history of infertility and to visiting a doctor (N=4,491).

Most participants reported not adhering to any particular diet (86.6%). The most prevalent diets in the analytic study population were vegetarian (4.6%), ketogenic (2.8%), Weight Watchers® (1.7%), Mediterranean (1.4%), vegan (1.3%), and Paleo (0.8%). Fewer than 0.8% of participants adhered to a dairy-free, gluten-free, South Beach®, Atkins®, Zone®, raw foods, or "other" diet; thus, these participants were grouped together as "other diet" because of small numbers (n<70). We analyzed each dietary practice as a dichotomous outcome variable, using "no particular diet" as the reference group.

We fitted log-binomial regression models to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) for adherence to a particular diet comparing participants who did vs. did not meet criteria for each of the infertility history definitions. Our selection of confounders was based on a causal diagram and the literature on this topic. We conducted unadjusted and adjusted models. Adjusted models controlled for baseline age (<35 or ≥ 35 years), BMI (<25, 25-30, or ≥30 kg/m^2), and annual household income (≤100,000, 100,000-150,000, or ≥150,000 U.S. dollars).

RESULTS

Baseline Characteristics

The median age of cohort participants was 30 years (range 21-45), and median BMI was 27.4 kg/m^2 (range 15.0-72.7). Most participants self-identified as non-Hispanic White (81%), were <35 years of age (81%), and had BMI ≥25 kg/m^2 (62%). Most participants had higher education (64% with at least a college degree) and a household income greater than the median US income (57% with income ≥ $75,000). Most participants did not smoke on a regular basis (91%), consumed <7 drinks/week (89%) and took daily multivitamin/folate supplements (79%). About 74% of participants had at least one previous pregnancy while 50% of participants had given birth previously.

Baseline characteristics of participants, overall and by history of infertility, are shown in Table 1. Participants with an infertility history tended to be older, have lower educational attainment and household income, lower intakes of alcohol and daily multivitamins/folate supplements, lower gravidity and parity, and greater BMI than those without an infertility history. They were also more likely to have experienced menstrual irregularities than those without a history of infertility. The racial and ethnic distribution of those with and without a history of infertility was generally similar.

Table 1. Baseline characteristics of participants by infertility history, PRESTO (2017-2023)[a]

Characteristic	Total	12-month infertility		Identified cause of infertility			
		No	Yes	Cervical	Tubal	Ovulation	Unidentified
N	7,227	5,365	1,862	82	132	709	955
Age at baseline, years (median, range)	30 (21-45)	30 (21-43)	31 (21-45)	31 (21-40)	31 (21-42)	30 (21-45)	31 (21-45)
Highest level of education (%)							
<High-school degree	1.4	0.8	3.1	0.0	3.0	1.8	1.9
High-school degree	7.8	5.3	14.9	13.4	12.1	10.3	10.4
Some college / Vocational	26.7	22.2	39.9	32.9	39.4	37.4	32.5
College degree	30.5	32.9	23.4	28.1	23.5	26.1	26.6
Graduate degree	33.6	38.8	18.7	25.6	22.0	24.4	28.7
Household income, U.S. dollars (%)							
<50,000	24.5	18.2	42.5	34.2	34.1	32.2	30.9
50,000-99,999	34.8	34.6	35.2	29.3	36.4	40.6	35.3
100,000-149,999	23.7	26.9	14.3	18.3	18.2	17.5	19.5
≥150,000	17.1	20.2	8.0	18.3	11.4	9.7	14.4
Race/Ethnicity (%)							
Non-Hispanic White	80.6	83.0	73.6	73.0	78.8	78.4	76.0
Hispanic	7.9	7.1	10.2	9.8	6.8	7.8	10.0
Non-Hispanic Black	4.8	3.4	8.9	11.0	8.3	7.3	6.5
Non-Hispanic Asian	1.8	1.9	1.7	1.2	2.3	1.4	2.4
Non-Hispanic American Indian, Alaskan Native, or Indigenous	0.4	0.3	0.6	1.2	0.0	0.4	0.6
Multi-racial or other race	4.5	4.3	5.1	4.9	3.8	4.7	4.6
BMI, kg/m^2 (median, range)	27.4 (15.0–72.7)	26.4 (15.0-67.7)	31.4 (16.0-72.7)	29.2 (17.4-65.8)	27.3 (16.0-52.5)	33.0 (15.0-71.3)	28.3 (16.5-66.1)
≤18.5 (%)	1.5	1.3	1.9	1.2	4.6	1.1	1.7
18.5-24.9 (%)	36.4	40.7	24.0	31.7	37.1	21.0	32.9
25.0-29.9 (%)	23.2	24.9	18.3	19.5	19.7	16.2	21.1
≥30.0 (%)	38.9	33.1	55.8	47.6	38.6	61.6	44.2
Current regular smoker[b] (%)	8.8	5.8	17.5	11.0	11.4	13.0	11.8
Alcohol intake, drinks/week (%)							
< 7	89.1	88.2	91.8	91.5	90.2	93.0	91.1
≥ 7	10.7	11.6	8.0	7.3	9.1	6.8	8.7
Daily supplement use[c] (%)	78.9	83.4	66.2	76.8	73.5	74.8	75.8
Gravidity (%)							
0	25.4	23.5	30.9	25.6	28.0	32.4	24.8
1	34.4	38.1	23.9	19.5	25.0	24.5	25.0
≥2	40.1	38.4	45.2	53.7	47.0	43.0	50.1
Parity (%)							
0	50.5	49.7	52.9	56.1	54.6	53.7	51.5
1	32.5	34.2	27.4	25.6	32.6	28.9	31.4
≥2	17.0	16.1	19.6	17.1	12.9	17.3	17.0
Menstrual irregularity (%) [d]	21.6	16.0	37.7	42.7	25.8	61.0	24.8

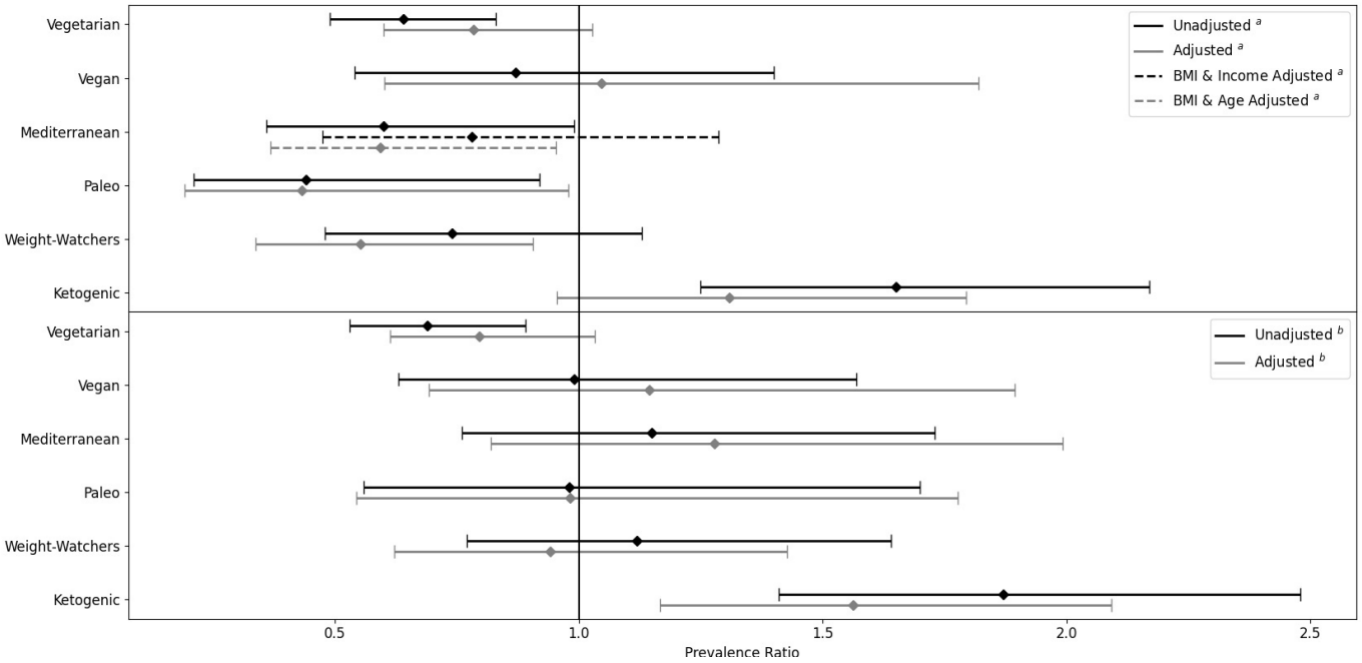
a 7,227 participants include those with and without an infertility history. Only participants with an infertility history who visited a doctor for infertility work-up reported an infertility diagnosis (n=1,860). Participants with an infertility factor diagnosis were able to report more than one factor.
b Defined as smoking on a regular basis at least one cigarette per day
c Defined as daily use of prenatal vitamins, multivitamins, and/or folate supplements
d Menstrual cycle irregularity was defined as an inability to predict next periods the last few years

Finally, 1,860 participants visited a doctor and received a diagnosis regarding the cause of their infertility (Table 1). Of this subset, most participants reported ovulatory factor (35%) and unidentified factor (51%) as causes. Age, ethnicity, educational attainment, household income, daily use of multivitamins and/or folate supplements, and alcohol consumption were not appreciably different across cause-specific infertility groups. Participants with ovulatory factor were more likely to have obesity and menstrual cycle irregularities when compared with participants reporting other causes of infertility.

Infertility History and Dietary Practices

A history of 12-month infertility was associated with a lower prevalence of adherence to Paleo (PR=0.43; 95% CI: 0.19-0.98), Weight Watchers® (PR=0.55; 95% CI: 0.34-0.91), and vegetarian (PR=0.78; 95% CI: 0.60-1.03) diets. Due to a lack of model convergence for adjusted models of Mediterranean diet, we ran reduced adjusted models controlling for age and BMI, which demonstrated a 40% decrease in prevalence of adherence to the Mediterranean diet in participants with infertility history (PR=0.59; 95% CI: 0.37-0.95). In contrast, there was a positive association between history of 12-month infertility and adherence to a ketogenic diet (PR=1.31; 95% CI: 0.95-1.79). In contrast, vegan diets were followed as frequently among those with and without a history of 12-month infertility (PR=1.05; 95% CI: 0.60-1.82). Associations between history of 12-month infertility and diet adherence prevalence are shown in Table 2 and Figure 2.

Figure 2. Prevalence Ratios of Diets in Participants with an Infertility History or a Physician Visit



[a] Prevalence Ratios with 95% CI for participants with a history of infertility. Top panel evaluates Q1: history of infertility (yes vs. no).

[b] Prevalence Ratios with 95% CI for participants who visited a doctor for conception difficulties. Bottom panel evaluates Q2: visited a doctor (yes vs. no) from the participants who reported a history of infertility.

Physician Visit and Dietary Practices

Physician visits due to infertility difficulties demonstrated similar associations with vegetarian and ketogenic diets to what we found for history of 12-month infertility. For example, participants reporting physician visits for infertility were 20% less likely to adhere to a vegetarian diet (PR=0.80, 95% CI: 0.61-1.03), while they were 56% more likely to adhere to a ketogenic diet (PR=1.56; 95% CI: 1.17-2.09). The magnitude of association for adherence to a ketogenic diet was stronger among those who reported visiting a physician for an infertility work-up. In addition, participants who sought help from a physician for infertility were equally likely to follow Paleo and Weight Watchers® diets than those who did not seek help for infertility (PR=0.98; 95% CI:

0.54-1.78; PR=0.94; 95% CI: 0.62-1.43, respectively), but were 15-30% more likely to adhere to a vegan or Mediterranean diet (PR=1.15; 95% CI: 0.69-1.89; PR=1.28; 95% CI: 0.82-1.99, respectively).

Associations between history of physician visits due to infertility and dietary practices are shown in Table 2 and Figure 2.

Table 2. Infertility history and dietary practices, PRESTO (2017-2023)

	Vegetarian	Vegan	Mediterranean	Paleo	Weight Watchers	Ketogenic
	N=334	N=92	N=102	N=59	N=124	N=203
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
History of 12-month infertility Total (N=7,227) YES (N=1,862)						
Unadjusted	0.64 (0.49, 0.83)	0.87 (0.54, 1.40)	0.60 (0.36, 0.99)	0.44 (0.21, 0.92)	0.74 (0.48, 1.13)	1.65 (1.25, 2.17)
Adjusted	0.78 (0.60, 1.03)	1.05 (0.60, 1.82)	0.59 (0.37, 0.95)[+]	0.43 (0.19, 0.98)	0.55 (0.34, 0.91)	1.31 (0.95, 1.79)
NO (N=5,365)						
	Ref.	*Ref.*	*Ref*	*Ref*	*Ref*	*Ref*
Visited a doctor to seek help for infertility Total (N = 7,227) YES (N=2,184)						
Unadjusted	0.69 (0.53, 0.89)	0.99 (0.63, 1.57)	1.15 (0.76, 1.73)	0.98 (0.56, 1.70)	1.12 (0.77, 1.64)	1.87 (1.41, 2.48)
Adjusted Model	0.80 (0.61, 1.03)	1.15 (0.69, 1.89)	1.28 (0.82, 1.99)	0.98 (0.54, 1.78)	0.94 (0.62, 1.43)	1.56 (1.17, 2.09)
NO (N=4,491)						
	Ref.	*Ref.*	*Ref*	*Ref*	*Ref*	*Ref*

Table 2 cont.

Cause of infertility identified by doctor Total (N=1,860)						
Cervical YES (N=82)						
Unadjusted	0.50 (0.13, 1.97)	1.00 (0.14, 7.08)	1.75 (0.44, 6.96)	1.42 (0.20, 10.10)	2.15 (0.70, 6.59)	2.23 (0.85, 5.83)
Adjusted	0.55 (0.14, 2.13)	1.13 (0.16, 7.93)	1.70 (0.42, 6.92)	1.35 (0.19, 9.67)	1.90 (0.65, 5.59)	1.91 (0.74, 4.95)
Tubal YES (N=132)						
Unadjusted	0.61 (0.23, 1.60)	1.22 (0.30, 4.91)	0.55 (0.08, 3.92)	1.73 (0.42, 7.02)	1.77 (0.66, 4.73)	2.68 (1.35, 5.34)
Adjusted	0.67 (0.25, 1.75)	1.28 (0.31, 5.32)	0.61 (0.09, 4.29)	1.82 (0.48, 6.94)	1.54 (0.57, 4.16)	2.22 (1.09, 4.49)
Ovulatory YES (N=709)						
Unadjusted	0.65 (0.42, 1.01)	1.49 (0.81, 2.75)	1.22 (0.65, 2.29)	1.07 (0.46, 2.51)	1.81 (1.12, 2.93)	2.61 (1.82, 3.75)
Adjusted	0.84 (0.53, 1.32)	2.07 (1.07, 3.99)	1.42 (0.71, 2.81)	1.22 (0.46, 2.73)	1.28 (0.76 2.15)	2.01 (1.38, 2.94)
Unidentified YES (N=995)						
Unadjusted	0.63 (0.44, 0.91)	0.66 (0.32, 1.37)	1.16 (0.68, 1.99)	0.93 (0.44, 1.98)	0.73 (0.40, 1.34)	1.32 (0.87, 1.99)
Adjusted	0.70 (0.48, 1.03)	0.75 (0.36, 1.58)	1.23 (0.70, 2.17)	0.89 (0.41, 1.95)	0.62 (0.34, 1.14)	1.10 (0.71, 1.69)
NO (N=4,491)						
	Ref.	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*

PR = prevalence ratio. CI = confidence interval.
Adjusted = overall-adjusted prevalence ratios for age, BMI, and income
[+]Adjusted for age and BMI

Unadjusted = unadjusted prevalence ratios

Infertility Factor Diagnosis and Dietary Prevalence

Participants diagnosed with any factor infertility were more likely to adhere to Weight Watchers® and ketogenic diets when compared with participants without infertility. Across all types of infertility factors, except for unidentified infertility, the ketogenic diet was at least twice as prevalent. Specifically, diagnosis with tubal or ovulatory factor infertility was associated with increased adherence to the ketogenic diet (PR=2.22; 95% CI: 1.09-4.49; PR=2.01; 95% CI: 1.38-2.94, respectively). Similarly, adherence to a Weight Watchers® diet was 1.5-2 times more prevalent among participants with any type of identified infertility compared to participants without infertility. Adherence to a vegan diet was also more common among all types of identified infertility, but the strongest association was among participants with ovulatory infertility, for whom the prevalence of adhering to a vegan diet was twice that of participants without infertility (PR=2.07; 95% CI: 1.07-3.99). In contrast, adherence to a vegetarian diet was 30-45% less common among participants with any cause of infertility.

While the Mediterranean diet was 1.3-1.7 times more prevalent across most infertility diagnosis groups, it demonstrated a 40% decreased prevalence among participants with tubal infertility (PR=0.61; 95% CI: 0.09-4.29), albeit this association was very imprecise. Participants diagnosed with ovulatory infertility were 1.5-2.5 times more likely to adhere to any one of these diets over no diet when compared to participants without infertility. Participants with unidentified causes of infertility were unlikely to adhere to any particular diet (Table 2).

DISCUSSION

In this preconception cohort study of North American female pregnancy planners, a history of infertility—whether defined as 12-month clinical infertility, a physician visit for an infertility work-up, or a diagnosed cause of infertility—was associated with greater adherence to a ketogenic diet and reduced adherence to a vegetarian diet. A history of 12-month infertility was also associated with lower adherence to Weight Watchers®, Paleo, and Mediterranean diets, while visiting a physician for an infertility work-up was associated with increased adherence to vegan and Mediterranean diets. A diagnosis of ovulatory factor infertility was most often associated with greater adherence to specific diets (e.g., vegan, Weight Watchers®, and ketogenic) than a diagnosis with other types of infertility.

Our findings suggest that participants experiencing infertility might be motivated to change their dietary behaviors to improve their fertility outcomes. For example, there is a large body of literature supporting the use of ketogenic and Mediterranean diets to enhance fertility among individuals with obesity or PCOS.[17] Studies show that these diets help promote or sustain weight loss, improve metabolic profiles, and subsequently improve fertility outcomes.[18-19] Accordingly, our study found an increase in adherence to the ketogenic diet among those with a history of 12-month infertility or visiting a physician due to conception difficulties. These findings indicate that pregnancy planners are aware of or are educated adequately by their physicians about this literature which supports the ketogenic diet as a method for improving fertility. Also, participants with ovulatory infertility, which includes PCOS, were most likely to follow a ketogenic diet.

Studies indicate that the Mediterranean diet may improve outcomes during the IVF cycle and during pregnancy among normal weight females.[20-21] This favorable effect among normal weight females was attributed to the high antioxidant, food variety, and anti-inflammatory content that the Mediterranean diet provides.[13,21] In our study, there was a lower prevalence of the Mediterranean diet among participants with a history of 12-month infertility, but there was a higher prevalence among participants who visited a physician for infertility work-up. It is unclear to what extent those who received an infertility work-up received nutritional counseling from their clinicians; however, these data could indicate that counseling by a physician guided dietary choices among participants with infertility.

Previous studies have evaluated vegan diets as effective short-term methods of weight loss in patients experiencing infertility due to PCOS.[22] Most behavioral treatment prescribed around treating infertility due to PCOS focuses on following a diet with a low glycemic index while promoting weight loss.[22-23] The lower prevalence of adherence to a vegetarian diet among those with a history of infertility in PRESTO diverges from studies that promote plant-based diets for fertility.[10] However, our findings of greater ketogenic and vegan adherence among participants with ovulatory infertility align with studies evaluating the benefits of these diets for patients with PCOS.

To our knowledge, this is the first study to evaluate the association between history of infertility and dietary practices during the preconception period among a cohort of females attempting spontaneous pregnancy. This is also the first study to evaluate several definitions of infertility as correlates of dietary practices. Previous studies have demonstrated that varied infertility definitions can make a difference in the interpretation of results in epidemiologic investigations.[24-25]

The most important limitation of our study is the cross-sectional design and our inability to distinguish the temporality of the observed associations (i.e., the extent to which infertility history preceded adherence to a particular

diet or vice versa). Thus, the observed associations may not be causal, and we cannot determine whether infertility caused dietary modifications or vice versa. Our reliance on self-reported data is another limitation, which could have potentially introduced misclassification of infertility causes because it relies on the participant's ability to understand the medical diagnosis given by their doctor. Twenty percent of participants opted to write the identified cause for their infertility in an open text box for "other" instead of selecting an infertility factor from the list provided. This option allowed us to manually group participants by their reported diagnosis and the criteria we followed for each infertility factor. There was also likely some misclassification of 12-month infertility, as some participants may have had different understandings of what it meant to be "trying" for pregnancy. Previous studies have demonstrated that demographic characteristics, such as age, ethnicity, and marital status influence pregnancy planning and intensity of trying to conceive.[26-27] Misclassification of dietary adherence was also likely, and we did not query participants on all possible diets that they may have followed. Given the cross-sectional nature of the analysis, misclassification of exposure and outcome could have been differential, which could have biased our results in an unpredictable direction. Finally, the generalizability of our results may be limited given that our study population comprised pregnancy planners who were not using fertility treatments, and who were more likely to be non-Hispanic White and of higher socioeconomic status than the general population. In addition, the overall proportion of study participants adhering to any particular diet was low. However, our unselected study population with respect to fertility treatment and the large geographic diversity of the cohort (representing all 50 U.S. states and 10 Canadian provinces) are strengths.

CONCLUSION

In this preconception cohort study of North American pregnancy planners, a history of infertility was associated with dietary practices, specifically greater adherence to a ketogenic diet and lower adherence to a vegetarian, Paleo, Weight Watchers®, and Mediterranean diet. The diets followed by females with a history of infertility are generally consistent with what would be expected based on the literature regarding the effects of diet on infertility. These results suggest that individuals who experience infertility may seek out information about behavioral modifications, whether it be via the scientific literature, other affected individuals (e.g., communications via infertility community forums), or physician recommendations, which could potentially guide dietary practices. Thus, ensuring that infertility patients have access to the most accurate, high-quality research on diet and infertility is of high clinical importance.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, or publication of this article.

DISCLOSURE STATEMENT

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AUTHOR CONTRIBUTIONS

All authors have contributed substantially to, reviewed, and approved the final manuscript. Andriana Velmahos contributed to conceptualization, formal analysis, visualization, and the original draft of writing. Lauren Wise contributed to conceptualization, supervision, writing—review and editing, and project administration. Tanran Wang contributed to formal analysis and writing—review and editing. Wendy Kuohung contributed to writing—review and editing.

DATA AVAILABILITY STATEMENT

Data can be available through a data sharing agreement consistent with participant informed consent.

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