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Research Article

Nutritional Intake and Lifestyle in Infertile Women with and without Polycystic Ovary Syndrome: A Case-control Study

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Abstract

Background: Polycystic ovary syndrome (PCOS), the most common endocrine pathology in females of reproductive age worldwide, is a multifactorial disorder. Although obesity, lifestyle, depression, and nutrition are considered possible contributing factors to PCOS pathogenesis, the association between nutrient intake, clinical indices, and adipokines in PCOS women is not comprehensively elucidated. Therefore, the current study aimed to reveal the contribution of nutritional intake and lifestyle to the pathogenesis of the disease.

Methods: 90 infertile women, 45 with PCOS as cases and 45 without PCOS as controls, aged 25–40 years were enrolled in the study. Different questionnaires including the antioxidant food frequency (using Nut4 software), international physical activity, fast food intake, depression, and internet addiction questionnaires were completed by participants. Moreover, demographic characteristics, weight, height, BMI, and the serum levels of hormones, fast blood glucose, malondialdehyde (MDA), chemerin, vaspin, and omentin-1 were measured.

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Results: No significant differences between the two groups were obtained regarding demographic characteristics, physical activity, depression, and fast food intake (p-value>0.05). Moreover, the intake of calories and macronutrients did not significantly differ between the two groups (p-value>0.05). However, androgens, AMH, LH, LH: FSH ratio, FBS, and MDA were significantly higher and estradiol was significantly lower in PCOS subjects compared to controls (p-value<0.001). Moreover, a significant correlation between nutritional parameters and PCOS indicators was observed (p-value<0.05).
Conclusion: The findings may suggest that nutrient intake crucially contributes to the pathogenesis of PCOS in infertile women through hyperandrogenism and weight gain.

Keywords: PCOS, Stress, Obesity, Hyperandrogenism, Diet

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine pathology in females of reproductive age worldwide [1]. Irregular menstruation, amenorrhea, hirsutism, acne, and enlarged polycystic ovaries are considered the main characteristics of PCOS [2]. Insulin resistance and pathological alterations in the secretion of androgen hormones, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) are contributing factors to PCOS establishment, all of which play significant roles in infertility [3, 4]. It is documented that the burden of infertility attributable to PCOS has grown more than twice all around the world during the last three decades and increased sharply in most regions and nations [5].

Lifestyle factors, including physical activity, internet addiction, fast food consumption, and mental health are possible contributors to PCOS development [6, 7]. Moreover, a plethora of evidence has suggested the interplay of lifestyle and nutritional factors as a pivotal contributor to female reproductive health [8]. There's an intricate connection between nutrients and endocrine status [9]. In fact, diet could impact the metabolism of sex steroids and LH secretion [10].

Visceral adiposity, a distinctive feature of PCOS, is considered to be associated with anovulation, hirsutism, and infertility. Hyperandrogenicity, a key endocrine symptom, correlates with localized fat accumulation in upper body regions, known as android fat distribution [11]. This pattern is associated with obesity and is considered an indicator of reduced female fecundity. Excess adipose tissue and the production of adipokines may contribute to ovulation disturbances as specific adipokines (e.g. vaspin, chemerin, and omentin-1) that are typically found in visceral fat deposits garnering attention in PCOS studies [12, 13]. The imbalance in adipokine secretion is believed to correlate with PCOS development by modulating the activity of the pituitary–ovary axis [14]. Increased oxidative stress and inflammation further complicate PCOS pathophysiology [15, 16] .

Despite the extensive research conducted during the recent two decades, the association between nutrient intake, clinical indices, and adipokines in PCOS women is not comprehensively elucidated. Hence, the current study aimed to address this issue by evaluating potential nutritional factors involved in the

development and pathophysiology of PCOS. In this regard, clinical and biochemical factors alongside nutrient intakes in infertile women, both with and without PCOS, were assessed.

2. Materials and Methods

2.1. Ethical Approvement and Consent Form

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved By the Institutional Review Board of the Infertility Center of the Maternal and Child Hospital, Shiraz University of Medical Sciences. Written informed consent was obtained from all subjects before the study.

2.2. Study Design and Subject's Characterization

A total of forty-five infertile women with PCOS (aged 25–40 years), and forty-five non-PCOS infertile women of a similar age (25–40 years) as controls were recruited from patients who visited the Infertility Center of the Maternal and Child Hospital, Shiraz University of Medical Sciences. The diagnosis of PCOS was based on revised 2003 Rotterdam criteria established by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine. The subjects with non-classic adrenal hyperplasia, hyperprolactinemia, hypothyroidism, androgen-secreting tumors, and those receiving hormonal therapy were excluded from the present study.

The medical history and menstrual status of included subjects were collected by the completion of a standard form. All participants were weighed barefoot on a verified electronic scale, and the scale was recalibrated prior to each weigh-in. A stadiometer was used to measure height and BMI was calculated from the following formula:

$$BMI = \frac{Weight\ (Kg)}{Height\ (m)^2}$$

An overnight fasting blood sample was obtained from the subjects between 08.00 and 10.00 hours during the first 3^{rd} of the menstrual cycle for hormone assays. Blood samples were stored at -80 °C until further analysis.

2.3. Laboratory Assays

Serum levels of hormones were assessed by commercial RIA kits (Diagnosis System Laboratories, Inc.). Blood glucose concentration was determined by the glucose oxidase method 30 min after blood was drawn. The level of malondialdehyde (MDA) was measured spectrophotometrically using the thiobarbituric acid reactive substances (TBARS) method [17].

Serum adipocytokine levels were measured by an enzyme-linked immunosorbent assay (ELISA, Instrument version 4.00.53, Thermo Scientific, Waltham, MA). The measurements of chemerin, vaspin, and omentin-1 were performed using available commercial material (Millipore, Billerica, MA), and according to the manufacturer's protocol.

2.4. Dietary and Daily Life Characteristics Assessment

The Antioxidant Food Frequency Questionnaire, which is a 98-item oral frequency questionnaire dedicated to the evaluation of antioxidants validated by Amani et al. was filled out by subjects. At the end of the study, the consumption of antioxidants and their exact numerical amount were determined by entering the questionnaire items in the Nut4 software (amount of vitamins and antioxidants). Four questionnaires including physical activity (International Physical Activity Questionnaire [IPAQ, standardized measure for estimation of daily practice of physical activities of populations from different countries with different cultures (Maddison, 2007 #40)] and MET scoring), addiction to the internet, depression, and fast food intake, which have been validated in previous studies [18–21], were also filled out by patients. Dietary intake was evaluated by three-day dietary recalls including 2 weekdays and 1 weekend day. Dietary intakes were analyzed using Nutritionist IV software (version 3.5.2; 1994, N-Squared Computing, San Bruno, CA, USA).

2.5. Statistics Analysis

Depending on the type of variable, Mean ± SD or percentage was used to represent the data. To check the normality of the data, the Kolmogorov-Smirnov test was employed. The qualitative and quantitative variables were compared between the two groups using appropriate statistical tests such as the Chi-square/Fisher's exact test or independent sample t-test/Mann-Whitney U-test. Moreover, the Pearson/Spearman tests were used to assess the correlation between variables. All analyses were conducted using SPSS version 24, and comparisons were considered statistically significant at the 5% level.

3. Results

3.1. Anthropometric Characteristics in the Studied Subjects

The measurement of anthropometric and hormonal levels was performed for all participants. PCOS subjects and controls were comparable for age and anthropometric parameters (Table **1**). The women with PCOS were ~ 3 years younger with a higher weight and BMI than controls (p-value<0.05). However, no significant differences between the two studied groups were found regarding the number of children,

number of abortions, occupation, level of education, type of delivery, history of medication, history of other diseases, and metformin usage (p-value>0.05).

Table 1: Demographic and anthropometric characteristics in the PCOS subject and controls.

Parameters	PCOS (n=45)	Control (n=45)	*p-value*
Age (years)	29.9±5.06	32.3±5.05	**0.02**
Weight (Kg)	73.9±15.1	69.6±18.5	**0.03**
BMI (Kg/m^2)	28.0±4.25	25.8±4.26	**0.04**
Number of children	0.15±0.56	0.20±0.40	0.66
Number of abortion	0.57±0.8	0.35±1.37	0.35
Occupation (%) *Housekeeper* *Employed*	 81.5 18.5	 83.4 16.6	0.5
Education (%) *Under diploma* *Diploma and upper* *Bachelor and upper*	 26.6 46.6 26.6	 26.6 35.5 37.7	0.46
Type of delivery (%) *Natural* *Caesarian* *No history*	 8.8 8.8 82.2	 0 6.6 91.1	0.06
History of other disease (%) *Hypothyroid* *Hypertension* *Total*	 6.6 4.4 88.8	 4.4 2.2 93.3	0.58
History of medication (%) *Hypothyroid* *Hypertension* *No history*	 6.6 4.4 88.8	 4.4 4.4 91.1	0.66
Metformin (%) *Yes* *No*	 13.3 86.7	 8.8 91.2	0.08

No significant difference was found in terms of demographic and anthropometric characteristics between the two groups, except for age, weight, and BMI (Body Mass Index). *p-value*<0.05 was considered significant.

3.2. Biochemical Analysis

Levels of fasting blood glucose and MDA as well as a variety of hormones were measured in all participants (Table **2**). The PCOS group had significantly elevated fasting blood glucose and MDA compared to the control group. Along with that, the PCOS subjects had a significantly higher level of total testosterone, AMH, LH, and LH: FSH (P<0·05) compared to the controls. However, the estradiol level in the PCOS subject was significantly lower when compared to controls. In addition, the obtained findings revealed no significant differences in the serum levels of omentin-1, chemerin, and vaspin between the two studied groups (p-value>0.05).

Table 2: Biochemical and hormonal factors in infertile women with PCOS and controls.

Variables	PCOS	Control	p-value
FBS (mg/dL)	96.8±18.31	83.2±8.06	<**0.0001**
MDA (μmol/L)	6.4±1.35	4.2±1.07	<**0.0001**
Chemerin (ng/mL)	296.2±97.77	281.9±50.92	0.264
Vaspin (ng/mL)	1.2±0.34	1.1±0.27	0.051
Omentin-1 (ng/mL)	275.5±53.82	284.4±31.66	0.342
AMH (ng/mL)	8.9±7.1	2.5±2.1	<**0.0001**
TSH (mIU/L)	2.6±2.66	3.3±2.46	0.238
Prolactin (ng/mL)	13.9±8.75	17.4±10.94	0.100
LH (IU/L)	8.6±3.61	7.3±2.59	**0.046**
FSH (IU/L)	6.1±2.01	6.9±2.32	0.084
LH: FSH ratio	1.5±0.90	1.1±0.55	<**0.05**
Estradiol (pg/mL)	53.3±22.23	63.1±19.71	**0.029**
Testosterone (nmol/L)	0.77±0.11	0.65±0.10	<**0.0001**

The two studied groups represented a significant difference when compared in terms of FBS, MDA, AMH, LH, Estradiol, Testosterone, and LH: FSH ratio. FBS: fast blood sugar; MDA: malondialdehyde; AMH: Anti-Müllerian hormone; TSH: thyroid-stimulating hormone; LH: luteinizing hormone; FSH: follicle-stimulating hormone. A p-value<0.05 was considered significant.

3.3. Dietary Intake and Physical Activity Assessment

An overall comparison of dietary intake for infertile women with/without PCOS revealed few differences (Table **3**). In this regard, there were no significant differences in energy or macronutrient intake (*P*>0.05). The percentage of energy intake derived from fat, protein, and carbohydrates also did not differ significantly between the two groups (p-value>0.05). After analyzing the dietary data with Nutritionist IV software, it was demonstrated that there was a high probability of insufficient intake of vitamin C and vitamin B6 in the infertile women with PCO compared to the control group (p-value≤0.05). Moreover, evaluation of the dietary intake indicated that infertile women with PCOS were at risk of insufficient intake of phosphorus (p-value≤0.0005). In addition, the overall comparison of self-reported physical activity revealed no differences between women with and without PCOS (p-value>0.05) as the two groups reported low activity.

Table 3: Dietary intake of the participants in PCOS and control groups.

Variables	PCOS	Controls	p-value
Energy (kcal/day)	1726.03±1032.28	1517.91±875.06	0.305
Protein (g/day)	53.46±36.95	44.50±29.82	0.209
Carbohydrate (g/day)	266.96±179.93	220.53±159.82	0.199
Total Fat (g/day)	62.80±35.22	69.80±40.89	0.387
Cholesterol (g/day)	7.65±7.64	6.96±7.18	0.659
SFA (g/day)	8.32±4.64	7.89±4.05	0.637
MUFA (g/day)	20.45±10.5	20.59±8.93	0.944

Table 3: Continued.

Variables	PCOS	Controls	p-value
PUFA (g/day)	18.04±9,31	18.67±7.41	0.723
Oleic Acid (g/day)	20.73±9.63	20.72±9.45	0.997
Linoleic Acid (g/day)	17.18±9.02	17.66±8.65	0.797
Linolenic Acid (g/day)	0.70±0.54	0.72±0.52	0.859
Sodium (mg/day)	2101.00±2417.8	2292.85±2375.37	0.705
Potassium (mg/day)	4481.47±1536.71	4476.59±1641.75	0.988
Vitamin A (RAE)	478.23±295.37	377.00±282.24	0.100
β-carotene (µg/day)	5090.21±3349.7	3930.36±3149.53	0.094
α-carotene (µg/day)	894.85±512.71	807.65±527.22	0.429
Lutein (µg/day)	2893.52±1412.4	2763.03±2507.48	0.762
β-cryptoxanthin (µg/day)	341.56±262.7	239.30±248.38	0 061
Lycopene (µg/day)	6282.09±4156.5	6933.97±242.18	0.530
Vitamin C (µg/day)	273.52±158.05	174.96±146.36	**0.003**
Calcium (mg/day)	731.88±418.49	615.99±355.58	0.160
Iron (mg/day)	34.72±20.08	27.66±17.58	0.080
Vitamin D (µg/day)	0.04±0.12	0.02±0.08	0.345
Vitamin E (mg/day)	21.59±10.35	23.17±9.06	0.444
α-Tocopherol (mg/day)	14.82±6.70	15.80±5.84	0.462
Thiamin (mg/day)	1.32±1.38	1.02±1.23	0.284
Riboflavin (mg/day)	1.10±0.78	0.85±0.68	0.117
Niacin (mg/day)	15.31±13.72	12.34±11.78	0.273
Vitamin B6 (µg/day)	1.75±0.94	1.38±0.73	**0.045**
THF (µg/day)	525.68±257.90	461.11±193.43	0.183
Vitamin B12 (mg/day)	0.07±0.08	0.06±0.09	0.648
Biotin (µg/day)	34.06±23.35	27.94±21.45	0.199
Pantothenic Acid (mg/day)	3.79±2.47	3.03±2.23	0.128
Vitamin K (µg/day)	370.95±235.68	328.11±235.62	0.391
Phosphorus (mg/day)	1068.19±846.08	336.78±665.97	<**0.0001**
Magnesium (mg/day)	455.60±319.61	383.14±277.41	0.254
Zinc (mg/day)	9.47±7.05	7.89±6.28	0.265
Copper (mg/day)	1.95±1.23	1.62±0.98	0.163
Manganese (mg/day)	9.12±8.04	7.63±6.97	0.352
Selenium (mg/day)	89.59±125.22	68.63±109.42	0.400
Floride (µg/day)	1326.99±1101.26	1525.53±1031.53	0.380
Chromium (µg/day)	0.19±0.33	0.14±0.30	0.491
Total Fiber (mg/day)	50.12±30.21	41.54±22.96	0.133
Soluble Fiber (mg/day)	0.59±0.34	0.59±0.33	0.996
Insoluble Fiber (mg/day)	2.55±1.42	2.49±1.39	0.848
Total Sugar (g/day)	108.57±77.55	105.59±75.34	0.854
Caffeine (mg/day)	67.35±66.34	79.10±61.71	0.387

The two groups demonstrated no significant differences in terms of dietary intake, except for vitamin C, vitamin B6, and phosphorus. SFA: saturated fatty acid; MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid; RAE: retinol activity equivalents; THF: tetrahydrofolate. A p-value<0.05 was considered significant.

3.4. The Comparison of Internet Addiction and Fast Food Consumption Status

The current findings indicated that the majority of controls and PCOS subjects (95.6% vs 88.9%, respectively) were not addicted to the internet (p-value>0.05). In terms of fast food consumption, the results showed that the majority of participants in both groups were “never” fast food consumers. Moreover, the rest of the participants of both groups were classified into “once a week” (31.1% in controls vs 20.0% in PCOS), “once a month” (26.7% in controls vs 13.3% in PCOS), “every other day” (4.4% in controls vs 15.6% in PCOS), and “often” (2.2% in both groups) categories. Nevertheless, the present findings have not identified a significant difference between the two groups regarding fast food consumption (p-value>0.05).

3.5. Correlation Analysis between Selected Biochemical and Hormonal Parameters with Dietary Nutrients

The correlation between reproductive hormones and selected biochemical parameters and nutrients within the PCOS and control groups was analyzed. The findings revealed a significant negative correlation between vaspin and testosterone (p-value=0.037, r=-0.311) and omentin-1 and LH (p-value=0.044, r=-0.301) in the control group, while no significant correlation was obtained between hormonal and biochemical factors (p-value>0.05). In infertile women with PCOS, a significant positive correlation between chemerin and omentin-1 (p-value<0.0001, r=0.771), chemerin and testosterone (p-value=0.021, r=0.342), omentin-1 and testosterone (p-value=0.017, r=0.354), and AMH and MDA (p-value=0.012, r=0.375) was found, whereas LH and vaspin (p-value=0.014, r=-0.365) were negatively correlated.

3.6. Correlation Analysis between Hormonal and Biochemical Parameters with Dietary Nutrients

In women with PCOS, FBS showed a positive correlation with AMH (p-value= 0·004, r = -0.793) and MDA (p-value= 0·0001, r = 0.374). AMH revealed a positive correlation with MDA (p-value= 0.0001, r = 0.741) and lycopene intake (p-value= 0.023, r = 0.442). MDA showed a positive correlation with testosterone (p-value= 0.010, r = 0.670), LH: FSH (p-value= 0.025, r = 0.437), and chemerin (p-value= 0.031, r = 0.329), and negative correlation with vitamin E (p-value= 0.035, r = -0.224), beta-carotene (p-value= 0.020, r = -0.447), vitamin C (p-value= 0.003, r = -0.710), vitamin B6 (p-value= 0.013, r = -0.463). Testosterone represented a significant negative correlation with phosphorus (p-value= 0.004, r = -0.693) and a positive correlation with chemerin (p-value= 0.021, r = 0.341), and omentin-1 (p-value=0.017, r=0.454). Estradiol represented a positive correlation with omentin-1(p-value= 0.01, r=0.469) and a negative correlation with lycopene intake (p-value=0.02, r=-0.337). LH revealed a positive correlation with total Fat intake (p-value = 0.01, r=0.352), PUFA (p-value=0.04, r=0.216), lutein (p-value=0.01, r=0.348), vitamin E (p-value=0.04,

r=0.211) and a-tocopherol (p-value=0.04, r=0.209) and a negative correlation with vaspin (p-value=0.03; r=-0.525). In the control group, serum LH level revealed a negative correlation with BMI (p-value=0.042, r=-0.541). Serum testosterone level was negatively correlated with energy intake (p-value=0.017, r=-0.671). Serum FSH level was negatively associated with BMI (p-value=0.043, r=-.0512). Nutrients that showed no significant correlation have been omitted (Table **4**).

Table 4: Correlation of biochemical and hormonal markers with dietary nutrients in PCOS women and control.

Variables	Prolactin	Estradiol	LH	Testosterone	AMH	Chemerin	Vaspin	Omentin-1	MDA
Energy	.055	-.045	.182	.071	.074	.038	-.007	.064	-.078
Protein	.052	.037	.142	.061	.129	.101	.072	.095	-.155
Carbohydrate	.021	-.046	.121	.047	.151	.047	.084	.083	-.167
Total Fat	.010	-.036	.252*	.163	.065	.162	-.085	.094	.181
Cholesterol	.063	-.081	-.023	.077	-.075	.215*	.031	.062	.026
SFA	-.001	.015	.107	.129	.091	.173	.094	.088	-.015
MUFA	-.042	-.009	.138	.121	.133	.154	.110	.076	.020
PUFA	-.009	.073	.216*	.130	.139	.224*	.017	.109	.057
Oleic Acid	-.055	-.109	-.128	.012	-.025	-.020	.063	.034	.011
Linoleic Acid	-.084	-.046	-.066	.031	.044	.036	-.030	.031	.061
Linolenic Acid	-.096	-.017	-.047	.049	.060	-.033	-.004	-.046	-.009
Sodium	.005	-.065	.183	.128	.096	.051	-.043	.057	.073
Pottasium	.097	-.012	.031	-.061	.081	-.091	.018	-.089	.058
Vitamin A	.104	-.067	.166	-.045	-.090	.151	-.056	.197	-.224*
β-carotene	.090	-.048	.158	-.055	-.096	.146	-.064	.206	-.222*
Lutein	.126	-.109	.248*	.081	.009	.141	-.059	.166	-.030
β-cryptoxanthin	.137	-.029	.204	-.026	.125	-.026	-.049	-.008	-.173
Lycopene	.027	-.237*	.191	.102	.242*	.180	-.080	.161	.037
Vitamin C	.044	-.031	.071	-.136	-.036	.021	-.037	.178	-.310**
Calcium	.154	-.040	.141	.041	.049	.178	-.007	.179	-.119
Iron	87	90	90	90	88	90	90	90	89
Vitamin D	-.058	.180	-.007	-.003	.033	.088	-.011	.108	-.088
Vitamin E	-.060	-.026	.211*	.152	.189	.153	-.010	.122	.094
α-Tocopherol	-.018	-.049	.209*	.145	.152	.174	-.034	.142	.087
Thiamin	.008	-.008	.083	.054	.153	-.020	.085	.028	-.157
Riboflavin	.011	-.017	.109	.025	.115	.100	.040	.146	-.166
Niacin	.014	-.034	.101	.064	.159	.024	.067	.070	-.161
Vitamin B6	.047	-.020	.134	.023	.052	.085	.019	.155	-.263*
THF	.135	.023	.187	.064	.034	.125	.054	.139	-.187
DHF	.049	-.013	-.069	-.044	.048	-.047	.038	-.002	.077
Vitamin B12	.019	-.008	-.024	.101	-.018	.198	-.011	.098	.034
Biotin	.035	-.045	.140	.075	.156	.052	.034	.108	-.203
Pantothenic Acid	.046	-.036	.162	.058	.150	.027	.035	.088	-.216*

Table 4: Continued.

Variables	Prolactin	Estradiol	LH	Testosterone	AMH	Chemerin	Vaspin	Omentin-1	MDA
Vitamin K	.214*	-.091	.108	.024	-.058	.223*	-.062	.224*	-.050
Phosphorus	.069	.153	-.041	-.271**	-.151	-.038	-.150	.111	-.228*
Zinc	.026	.016	.132	.061	.141	.077	.041	.085	-.155
Copper	.051	-.013	.146	.059	.129	.081	.074	.109	-.202
Manganese	.037	-.020	.067	.069	.138	.024	.079	.055	-.130
Selenium	-.005	-.012	.066	.062	.164	-.016	.091	.020	-.122
Fluoride	-.140	-.012	-.137	.229*	.045	-.005	-.157	.075	.253*
Chromium	-.020	-.021	.054	.064	.173	-.038	.091	.002	-.111
Total Fiber	.085	-.014	.161	.052	.091	.096	.059	.123	-.186
Soluble Fiber	.056	.016	.051	-.057	-.011	-.162	.004	-.235*	-.051
Insoluble Fiber	.097	.024	.055	-.058	-.024	-.160	.036	-.236*	-.079
Glucose	.195	-.045	.057	-.110	.068	-.110	.043	-.134	-.008
Galactose	.022	-.062	.192	-.014	.090	-.109	-.041	-.151	-.091
Fructose	.222*	-.025	.040	-.112	.057	-.093	.065	-.118	-.010
Sucrose	-.023	-.026	.122	-.063	.063	-.146	-.012	-.226*	-.063
Lactose	.256*	-.177	.054	-.114	.049	-.139	-.082	-.130	-.055
Maltose	.252*	-.073	-.048	-.053	.003	-.039	.060	.022	.002
Caffeine	-.142	-.022	-.144	.244*	.040	.007	-.154	.090	.243*

The table describes the correlation between hormonal and biochemical indices with dietary nutrients in studied individuals. The values of r are mentioned in the table and marked values with * represent the significant correlation. LH: luteinizing hormone; AMH: antimullerian hormone; MDA: malondialdehyde; SFA: saturated fatty acid; MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid; THF: tetrahydrofolate; DHF: dihydrofolate. A p-value<0.05 was considered significant.

4. Discussion

A population-based prevention strategy is critical to combating PCOS in infertile women. The role of nutrition has been particularly controversial in such strategies [22]. The present study examined the dietary intake and physical activities of infertile women with PCOS. Moreover, the correlation between hormonal and metabolic status and dietary intake in infertile women with and without PCOS was assessed. The results of this study could bring new insight into the important role of nutrition in the development of hormonal disorders such as PCOS in infertile women.

The current study found that the BMI of infertile women with PCOS was higher than that of the control subjects. Concordantly, it is documented that obesity is more common in 30-70% of women with PCOS [23]. The present data also showed that 60% of infertile women with PCOS had a BMI of 29 kg/m^2. Previous studies have shown that women with PCOS have more visceral fat than normal women [24, 25]. Clinical measurements in the present study showed that the PCOS group had higher serum levels of AMH, LH, LH: FSH ratio, and free testosterone, but lower estradiol compared to the control group. Fasting blood glucose and MDA levels were also higher in infertile women with PCOS. These

results indicated a significant positive correlation between BMI and hyperandrogenism in women with PCOS. Evidence has shown that serum testosterone levels are significantly higher in obese women with PCOS compared to non-obese PCOS women [26, 27]. Thereby, overweight and obesity in women with PCOS exacerbate hyperandrogenism and disrupt metabolic profiles [28]. Studies have shown that sex steroid-binding globulin (SSBG) is negatively related to body weight and suggest that obesity affects SSBG levels, which are independent of hormonal status. When SSBG levels fall, it can increase the serum level of free testosterone [29]. It is, therefore, reasonable to assume that obesity can lead to hyperandrogenism in this group of infertile women. In general, obese infertile women are more likely than normal-weight women to have oligomenorrhea and anovulation [30]. It is documented that obesity negatively impacts infertility treatment [31] as the rate and outcome of pregnancy are strongly influenced by obesity [32]. Obesity and weight gain also have a direct inhibitory effect on estradiol production in the follicular phase. Overweight women suffer from menstrual dysfunction, ovulation, and infertility more than other women and represent complex problems with gonadotropin secretion [33, 34]. It has been suggested that a weight loss program should be an essential component of infertility management [35]. However, an investigation of the level of physical activity between infertile women with/without PCOS showed that there was no significant difference in physical activity between the two groups and all subjects reported a low physical activity.

Correlation analyses have shown that MDA levels positively correlated with increased levels of AMH, fast blood glucose, and free testosterone. Increased oxidative stress, indicated by higher levels of MDA is associated with increased inflammation [36–38]. Inflammation can cause the production of inflammatory cytokines and directly stimulates the overproduction of androgen in the ovaries [39]. Elevated free testosterone levels may initiate the sequence of events seen in PCOS by inhibiting follicular excretion [40]. Factors such as rising fast blood glucose levels can also exacerbate this condition. Previous studies have suggested that the antioxidants improve the prognosis of PCOS [28, 41].

There is a general idea that improving diet can reduce the incidence and symptoms of PCOS [42]. Antioxidants, including those derived from plants and natural sources, have demonstrated beneficial effects in alleviating infertility-related conditions by reducing oxidative stress and inflammation, thereby enhancing reproductive health and improving the overall chances of conception [43, 44]. These natural compounds not only support cellular health but also promote a more balanced hormonal environment, ultimately contributing to improved fertility outcomes. Therefore, it was a necessity to quantitatively measure dietary intakes in infertile women with/without PCOS.

Our quantitative dietary intake study revealed that infertile women with PCOS had a lower intake of vitamin C and vitamin B6. It is established that vitamin C plays a crucial role in controlling oxidative balance and insufficient intake of vitamin C can disturb this balance [45]. It has also shown that low intake and low concentrations of vitamin B6 are associated with inflammation and increased oxidative stress in adults [46]. In addition, the present study found a significant correlation between dietary intake of

vitamin C and vitamin B6 with MDA levels. A plethora of evidence has suggested the role of vitamin B6 in reducing the symptoms of PCOS, which is attributed to the contribution of homocysteine (Hcy) to PCOS pathoeyiology [47–49]. Hcy is an essential amino acid derived from dietary methionine, and an increase in total plasma Hcy levels increases the risk of infertility in PCOS. Hcy is also involved in many of the metabolic pathways required for cell and tissue growth. Vitamin B6 along with folic acid and vitamin B12 play an important role in regulating Hcy levels. There is also a link between obesity and increased Hcy levels in PCOS patients. Women with PCOS need more daily intake of vitamin B6, folic acid, and vitamin B12, which have important roles in the decrease of Hcy levels [47, 50, 51]. Regular exercise has also been suggested to reduce plasma Hcy concentration in the pathophysiology of PCOS. According to a study by Randeva et al., Regular exercise for six months significantly reduces plasma Hcy levels in obese and overweight young women with PCOS [52]. Daily administration of folic acid and B vitamins can be effective in reducing high Hcy levels in women with PCOS [47]. No significant relationship was observed between reduced vitamin B6 intake and androgen levels in infertile women with PCOS. Previous studies have also reported that supplementation with B-group vitamins has no effect on androgen levels in the pathophysiology of PCOS [47, 53]. Concordantly, the significant role of vitamin B6 in reproductive health has been documented which is through a variety of mechanisms such as maintaining and balancing the estrogen and progesterone hormones, increasing uterine mucosa, and strengthening the luteal phase [53, 54]. The findings of the current study represented that the level of phosphorus intake in infertile women with PCOS was much lower than in the control group. Additionally, a negative correlation between phosphorus intake and free testosterone levels was observed. The inverse correlation between free testosterone and serum phosphorus levels has been reported previously, however, the underlying mechanism is not elucidated [55].

Therefore understanding nutritional intake and lifestyle factors in infertile women with polycystic ovary syndrome (PCOS) is crucial. Many women may be unaware that poor dietary choices, sedentary lifestyles, and specific health conditions like PCOS can significantly impact reproductive health and fertility. Overall, increased awareness about infertility risk factors can lead to proactive measures that promote better reproductive health and appropriate medical consultations, ultimately helping to reduce infertility rates and improve reproductive outcomes [56, 57].

Taken together, the findings of the present study may suggest that diet and nutrient intake crucially contribute to the pathogenesis of PCOS in infertile women through hyperandrogenism and weight gain. Therefore, an appropriate diet can be considered a management strategy for the prevention and/or treatment of PCOS in the infertile women.

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