

## Role of Body Fat Distribution, Tan of Skin, Type of Food Intake and Caffeine Intake in Infertility for Polycystic Ovarian Syndrome Women

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**Abstract:** This study aimed to calculate body fat of polycystic ovarian syndrome (PCOS) women according to different measurements. It investigated correlation between estradiol2 (E2) and testosterone (T) levels and type of obesity, correlation between skin tan and body mass index, correlation between E2 and T levels and food intake, and impact of high caffeine consumption on infertility. Thirty-two infertile PCOS women were included. Different body fat distribution measurements were calculated. On cycle day 2, E2 and T levels were measured. There were recognizable differences in number of obese PCOS women according to different body fat measurements. No significant increase was in E2 and T levels ( $p=0.41$ ,  $p=0.18$ , respectively) for android obese compared to gynoid obese. No significant association was between BMI and skin tan ( $p=0.57$ ). Notable increase was in number of brown-colored obese compared to white-colored obese. No significant increase was in E2 and T levels for mixed food consumers compared to vegetarian ( $p=0.82$ ,  $p=0.11$ , respectively). Type of infertility and caffeine intake were independent factors. Out of seven high caffeine consumption secondary infertile, five complained from spontaneous miscarriage. Obesity adversely affected fertility. Brown-colored was more susceptible to obesity. Inadequate food intake participated in infertility. High caffeine intake increased susceptibility to spontaneous miscarriage.

**Keywords:** obesity; estradiol 2; testosterone; tan of skin; food; caffeine; infertility

### INTRODUCTION

Infertility is defined as the inability to conceive with no contraception after one year of regular intercourse in women <35 years old and after 6 months in women >35 years old [1]. Polycystic ovary syndrome is an endocrine disorder affecting about 6-7 percent of women at reproductive ages. Polycystic ovary syndrome increases in line with expected increase in obesity recognized in this population [2].

Obesity is a disorder in systems regulating body weight characterized by accumulation of excess body fat [3]. Obese women are at increased risk for menstrual dysfunction, infertility, and complications during pregnancy and delivery [4].

It is difficult to measure the amount of body fat directly and thus it can be obtained from an indirect measure by calculating body mass index. The anatomic distribution of body fat whether android (apple-shaped) or gynoid (pear-shaped) has significant association with health risks [3]. Waist circumference correlates with body mass index and waist to hip ratio and is

considered an index of intra-abdominal fat mass and total body fat [5]. Type of food intake and caffeine consumption levels has been found to affect fertility of women [6].

### This study aimed to

- Distribute infertile women with polycystic ovary syndrome according to body mass index, waist circumference, and waist to hip ratio.
- Study the relationship between type of obesity (android or gynoid) and estradiol 2 and testosterone levels for these women.
- Study the impact of obesity on infertility for these women.
- Study the relationship between tan of skin (white or brown) and body mass index for these study cases.
- Study the effect of type of food intake on estradiol 2 and testosterone levels and the role of type of food intake in infertility for these cases.

- Study the role of caffeine intake in infertility and investigate the correlation between incidence of spontaneous miscarriage and caffeine intake for them.

## MATERIALS AND METHODS

### Study subjects

Thirty-two infertile women with polycystic ovary syndrome attending the consultant clinic in Higher Institute for Infertility Diagnosis and Assisted Reproductive Technologies at AL-Nahrain University in Baghdad/Iraq during January 2016 to March 2016 were enrolled in this study.

Information including age, type of food intake (vegetarian or mixed-food consumers), and caffeine consumption were obtained from all cases enrolled in the study. Information involved type and duration of infertility and history of incidence of abortion were obtained from their files in the consultant clinic. Tan of skin was recognized as either white or brown.

Diagnosis of polycystic ovary syndrome was done according to Rotterdam criteria (2003 ESHRE/ASRM consensus) [7]. 2003 European Society for Human Reproduction and Embryology and American Society for Reproductive Medicine (2003 ESHRE/ ASRM or Rotterdam) guidelines included that patient with polycystic ovary syndrome demonstrated two of the following three criteria: oligo-or chronic anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries. Other etiologies of androgen excess and anovulatory infertility were excluded before diagnosis of polycystic ovary syndrome. The excluded conditions comprised thyroid dysfunction, congenital adrenal hyperplasia, hyperprolactinaemia, androgen-secreting tumors, and Cushing's syndrome[2].

### Body mass index (BMI)

Body mass index (BMI) was calculated by dividing the body weight in kilograms (Kg) by the square of height in meters (m) [8]. The World Health Organization (WHO) classified body mass index as following: underweight ( $<18.5$ )kg/m<sup>2</sup>, normal weight (18.5-24.9) kg/m<sup>2</sup>, overweight (25-29.9)kg/m<sup>2</sup>, and obesity ( $\geq 30$ )kg/m<sup>2</sup>. Obesity was further divided to obese class I (30.0-34.9)kg/m<sup>2</sup>, obese class II (35.0-39.9)kg/m<sup>2</sup>, and obese class III ( $\geq 40$ )kg/m<sup>2</sup> [9].

### Waist circumference (WC)

Waist circumference was obtained by measuring narrowest portion between ribs and iliac crest [10]. Women with waist circumference (80-87.9)cm were considered overweight and women with

waist circumference  $\geq 88.0$ cm were considered obese [11].

### Waist-to-hip-ratio (WHR)

Waist-to-hip ratio was calculated by dividing waist circumference (narrowest portion between the ribs and iliac crest) in centimeters by hips circumference (at the level of the greatest protrusion of the buttocks) in centimeters [12]. The ideal range of waist-to-hip ratio for healthy premenopausal women was 0.67-0.80 [13-14]. For women and according to waist-to-hip ratio the World Health Organization considered normal weight  $<0.80$ , overweight (0.80-0.84), and obesity  $\geq 0.85$  [15].

For women, android obesity (apple-shaped or upper body obesity) was determined as a waist to hip ratio equal to or more than 0.80 and gynoid obesity (pear-shaped or lower body obesity) was determined as a waist-to-hip ratio of less than 0.80 [3].

### Caffeine intake

High caffeine intake levels were considered as  $>50$ mg per day, approximately  $>5$  cups per day [6].

### Blood sampling and serum estradiol 2 and testosterone levels measurements

Informed and signed consent was obtained at the time of blood sampling from all cases involved in this study. Peripheral venous blood samples were drawn on menstrual cycle day 2 (CD2). The samples were centrifuged at 2500rpm for 15 minutes.

For all cases serum estradiol 2 and serum testosterone levels were measured by using mini-Vidas kits for estradiol 2 and testosterone (Biomerieux/France).

### Statistical Analysis

Statistical analysis was performed using SAS (Statistical Analysis System-version 9.0). Unpaired t-test was used to compare difference between means. Proportions were compared by Chi-square.  $P<0.05$  was considered statistically significant [16].

## RESULTS

Thirty-two infertile women with polycystic ovary syndrome were included in this study. Their ages ranged from 20 years to 38 years old ( $27.56\pm 0.91$ ). Of them, 17 were primary infertile with duration of infertility ranged from 2 years to 13 years ( $5.23\pm 0.70$ ) and 15 were secondary infertile with duration of infertility ranged from 1 year to 8 years ( $3.80\pm 0.59$ ).

Results in table (1) revealed significant increase in the number of obese women distributed according to body mass index measurements.

**Table-1: Distribution of infertile women with polycystic ovary syndrome according to body mass index**

Number of patients & (%) BMI	BMI (Kg/m <sup>2</sup> ) (Mean±SE)	Number of patients & (%)
Normal weight	21.48±0.73	5 (15.62%)
Overweight	27.49±0.54	10 (31.25%)
Obesity	34.40±1.15	17 (53.13%)
Total number and (%)	-	32 (100%)
Chi-square test		5.99
Critical Chi-square test		33.80
P-value		0.01

BMI: body mass index, Kg/m<sup>2</sup>: kilogram/square meters, Mean±SE: Mean±standard error, (%): percentage, P: probability, P-value <0.05 was designated as significant.

Table (2) revealed significant difference in the number of obese polycystic ovarian syndrome women

according to different obesity classes and that most obese women were among class I obesity.

**Table-2: Distribution of obese infertile women with polycystic ovary syndrome according to obesity classes divided according to body mass index**

Number of patients & (%) Obesity classes	BMI (Kg/m <sup>2</sup> ) (Mean±SE)	Number of patients and (%)
Class I obesity	31.80±0.43	11 (64.71%)
Class II obesity	37.18±0.82	5 (29.41%)
Class III obesity	49.09	1(5.88%)
Total number and (%)	-	17 (100%)
Chi-square test		4.16
Critical value of Chi-square test		3.84
P-value		0.04

(%): percentage, BMI: body mass index, Kg/m<sup>2</sup>: kilogram/square meters, P: probability, P-value <0.05 was designated as significant.

Table (3) demonstrated significant difference in the number of women distributed according to different waist circumference classes and that nineteen (59.38%) of polycystic ovarian syndrome women were

with waist circumference equal to or greater than 88centimeters which indicated that they were suffering from central obesity.

**Table-3: Distribution of infertile women with polycystic ovary syndrome according to waist circumference**

Number of patients & (%) Waist circumference(cm)	Waist circumference (cm) (Mean±SE)	Number of patients and (%)
WC<80 cm	73.71±2.28	7 (21.87%)
(80-87.9) cm	82.50±0.62	6 (18.75%)
WC≥88 cm	95.73±2.32	19 (59.38%)
Total number and (%)	-	32 (100%)
Chi-square test		28.30
Critical value of Chi-square test		5.99
P-value		<0.00001

(%): percentage, WC: waist circumference, cm: centimeter, Mean±SE: mean±standard error.

Results in table (4) showed significant variation in body fat distribution according to waist to hip ratio for thirty-two polycystic ovarian syndrome

women and that seven (21.87%) were with ideal waist to hip ratio, fourteen (43.75%) were overweight and that eleven (34.38%) were complaining from obesity.

**Table-4: Distribution of infertile women with polycystic ovary syndrome according to waist to hip ratio**

Number of patients and (%) WHR	WHR (Mean±SE)	Number of patients and (%)
WHR<0.80	0.75±0.01	7 (21.87%)
WHR(0.80-0.84)	0.82±0.00	14 (43.75%)
WHR≥0.85	0.88±0.01	11(34.38%)
Total Number and (%)	-	32 (100%)
Chi-square test		9.28
Critical value of Chi-square test		5.99
P-value		0.01

(%): percentage, WHR: waist to hip ratio, Mean±SE: mean±standard error, P: probability, P-value<0.05 was designated as significant.

Table (5) showed that there were recognizable differences in the number of obese polycystic ovarian syndrome women according to different body fat distribution measurements. Out of thirty-two polycystic ovarian syndrome women, and according to body mass

index as a measure of total body fat seventeen women (53.13%) were obese, while according to waist circumference as indicator of central obesity (visceral obesity) nineteen (59.38%) were obese, and according to waist to hip ratio eleven (34.38%) were obese.

**Table-5: Number of obese polycystic ovarian syndrome women according to different body fat distribution measurements**

No. of obese patients Type of body fat distribution	Number of obese patients
Body mass index (Kg/m <sup>2</sup> )	17 (53.13%)
Waist circumference (cm)	19 (59.38%)
Waist-to-hip ratio	11(34.38%)

Kg/m<sup>2</sup>: kilogram/square meters, cm: centimeter.

Table (6) exhibited highly significant difference in the type of body fat accumulation, apple-shaped (android) or pear-shaped (gynoid), and that out of thirty-two polycystic ovarian syndrome women, twenty-five (78.13%) were complaining from harmful

type of body fat accumulation (apple-shaped or android obesity) which meant suffering from visceral adiposity while seven (21.87%) were with benign type of body fat accumulation (gynoid or pear-shaped obesity).

**Table-6: Distribution of infertile women with polycystic ovary syndrome according to type of obesity**

Number of patients and (%) Type of obesity	WHR (Mean±SE)	Number of patients and (%)
Android	0.85±0.00	25 (78.13%)
Gynoid	0.75±0.01	7 (21.87%)
Total number and (%)	-	32 (100%)
Chi-square test		46.28
Critical value of Chi-square test		3.84
P-value		<0.00001

(%): percentage, WHR: waist to hip ratio, Mean±SE: mean±standard error, P: probability, P-value<0.05 was designated as significant.

Results in table (7) showed no significant increase in the mean levels of estradiol<sup>2</sup> of polycystic

ovarian syndrome women with android type of body fat distribution compared to gynoid type.

**Table-7: Estradiol 2 means levels of infertile women with polycystic ovary syndrome according to type of obesity**

E2 mean levels Type of obesity	E2 mean levels (pg/ml) (Mean±SE)	Total number of patients & (%)
Android	52.62±5.65	25 (78.13%)
Gynoid	43.68±1.61	7 (21.87%)
Total number & (%)	-	32 (100%)
t-test		0.82
P-value		0.41

E2: estradiol 2, pg/ml: pictogram/millileters, Mean±SE: Mean±Standard Error, (%): percentage, P: probability, (P<0.05) was designated as significant.

Results in table (8) exhibited no significant increase in the mean levels of testosterone of polycystic

ovarian syndrome women with android type of body fat distribution compared to gynoid type.

**Table-8: Testosterone mean levels of infertile women with polycystic ovary syndrome according to type of obesity**

Testosterone Mean Levels Type of obesity	Testosterone (ng/ml) (Mean±SE)	Total number of patients & (%)
Android	0.65±0.04	25 (78.13%)
Gynoid	0.52±0.05	7 (21.87%)
Total number & (%)	-	32 (100%)
t-test		1.35
P-value		0.18

Mean±SE: Mean±Standard Error, ng/ml: nanogram/millileters, (%): percentage, P: probability, (P<0.05) was designated as significant.

Table (9) revealed no significant association between skin tan (white-colored or brown-colored) and obesity according to body mass index measurements. However, our findings showed that out of seventeen obese polycystic ovarian syndrome women, eleven

were brown colored which might indicate that brown-colored polycystic ovarian syndrome women were more susceptible to complain from obesity than white-colored obese polycystic ovarian syndrome women.

**Table-9: Distribution of infertile women with polycystic ovary syndrome according to body mass index and tan of skin**

Tan of skin Number & (%) BMI	Brown colored Number & (%)	White colored Number & (%)	Total number Number & (%)
Normal weight	4 (12.50%)	1 (3.12%)	5 (15.62%)
Overweight	4 (12.50%)	6 (18.75%)	10 (31.25%)
Obesity	11(34.38%)	6 (18.75%)	17 (53.13%)
Total number & (%)	19 (59.38%)	13 (40.62%)	32 (100%)
Chi-square test		0.31	
Critical value of Chi-square test		3.84	
P-value		0.57	

BMI: body mass index, (%): percentage, P: probability, (P<0.05) was designated as significant.

Results in table (10) revealed no significant increase in the mean levels of estradiol2 for mixed food consumers compared to mean levels of estradiol2 of

vegetarian group among polycystic ovarian syndrome women.

**Table-10: Estradiol 2 mean levels of infertile women with polycystic ovary syndrome according to type of food intake**

E2 Mean Levels Type of food intake	E2 mean levels (pg/ml) (Mean±SE)	Total number & (%)
Vegetarian	48.56±8.45	6 (18.75%)
Mixed food	51.15±5.20	26 (81.25%)
Total number & (%)	-	32 (100%)
t-test		0.22
P-value		0.82

E2: estradiol 2, pg/ml: pictogram/millileters, Mean±SE: Mean±standard error, (%): percentage, P: probability, (P<0.05) was designated as significant.

Table (11) showed no significant increase in the mean levels of testosterone for mixed food consumers in comparison with vegetarian group of polycystic ovarian syndrome women.

**Table-11: Testosterone means levels of infertile women with polycystic ovary syndrome according to type of food intake**

Testosterone Mean Levels Type of food intake	Testosterone (ng/ml) (Mean±SE)	Total number & (%)
Vegetarian	0.49±0.08	6 (18.75%)
Mixed food	0.65±0.04	26 (81.25%)
Total number & (%)	-	32 (100%)
t-test		1.64
P-value		0.11

Mean±SE: Mean±standard error, ng/ml: nanogram/millileters, (%): percentage, P: probability, (P<0.05) was designated as significant.

Table (12) showed that type of infertility and caffeine consumption were recognized as independent factors. Out of thirty-two infertile women with polycystic ovary syndrome, sixteen were high caffeine

consumers. This study revealed that out of seven secondary infertile high caffeine consumers' women, five suffered from spontaneous miscarriage.

**Table-12: Distribution of infertile women with polycystic ovary syndrome according to caffeine intake and type of infertility**

Caffeine Intake (Number & %) Type of infertility	Normal caffeine intake (Numbr & %)	High caffeine intake (Number&%)	Total number & (%)
Primary infertility	8 (25%)	9 (28.13%)	17 (53.13%)
Secondary infertility	8 (25%)	7 (21.87%)	15 (46.87%)
Total number & (%)	16 (50%)	16 (50%)	32 (100%)

(%): percentage.

## DISCUSSION

Obesity is associated with increased accumulation of intracellular lipids in some tissues [17]. There is considerable increase in the number of adipose cells in obese persons. A body mass index measure overall adiposity, waist circumference is an indicator of central adiposity, and waist to hip ratio reflects type of body fat distribution [18]. It was demonstrated that body mass index did not show the variation in body fat distribution and that individuals with the same body mass index might significantly vary in their abdominal fat mass [19]. Excess body fat accumulated in the central abdominal area of the body is called android "apple-shaped" obesity and excess body fat distributed in the lower extremities around the hips or gluteal region is called gynoid "pear-shaped" obesity [3]. Waist to hip ratio was clinically considered a method of identifying patients with excess abdominal fat accumulation. Waist circumference was considered as good simple measure of both intra-abdominal fat mass and total body fat [19]. Some studies showed that waist circumference was strongly correlated with the level of abdominal visceral adipose tissue than was waist to hip ratio [20-22]. Our study showed variation in the number of obese polycystic ovary syndrome women distributed according to body mass index, waist circumference, and waist to hip ratio measurements and this variation in the number was attributed to the differences in sites of body fat accumulation. In addition, as most obese women in our study were in class 1 obesity according to body mass index obesity classes this meant that changing life style and loss of weight might overcome infertility complains and could lead to significant reduction in polycystic ovary syndrome symptoms and manifestations.

The anatomic distribution of body fat strongly affects body health. Android "apple-shaped" obesity is associated with a greater risk for hypertension, insulin resistance, diabetes, dyslipidemia, and coronary heart disease [3]. Human body fat distribution is regulated by steroid hormones. Testosterone stimulates fat deposition in the abdominal region and inhibits fat deposition in the gluteofemoral region producing android obesity. Estrogen stimulates fat deposition in the gluteofemoral region and inhibits fat deposition in the abdominal area producing gynoid obesity [10]. To explain our findings that android type of body fat distribution for polycystic ovarian syndrome women showed no significant increase in both estradiol<sub>2</sub> and testosterone mean levels compared to gynoid type of body fat distribution for these women was that these women principally were suffering from endocrine disorders and that they were with high testosterone mean levels and thus these high testosterone mean levels overcame the impact of increased estradiol<sub>2</sub> mean levels and consequently accumulated more adipocytes in the abdominal region rather than gluteofemoral region.

Abdominal adipocytes are notably larger and have a higher rate of fat turnover than lower body adipocytes. The abdominal adipocytes respond to hormones more than adipocytes in the legs and buttocks. Substances released from abdominal fat cells are absorbed via the portal vein and consequently have direct access to the liver. Fatty acids taken up by the liver may cause insulin resistance and increased synthesis of triacylglycerols which are released as very-low-density lipoprotein (VLDL). Free fatty acids released from gluteal adipocytes enter the general circulation, and have notable action on hepatic metabolism [3]. As mentioned above, there was significant association between obesity, especially abdominal obesity, and dyslipidemia. Dyslipidemia is characterized by reduced high-density lipoprotein (HDL) and increased triglycerides. This mechanism is mainly due to insulin resistance. It is known that VLDL clearance in plasma is dependent on the rate of hepatic synthesis and catabolism by lipoprotein lipase, the enzyme which also participates in the synthesis of HDL [23]. Insulin resistance is correlated with increased synthesis of VLDL and impaired lipoprotein lipase [24-25]. Android obesity causes more metabolic disruption than gynoid obesity and, thus, patients with metabolic syndrome and infertility have increased waist to hip ratio [5]. Dyslipidemia negatively affect steroid hormones synthesis and consequently negatively impact fertility. Waist to hip ratio is a considerable indicator of reproductive ability of women at reproductive ages. It was demonstrated that women with gynoid obesity had fewer irregular menstrual cycles, optimal sex hormone profile, ovulated more frequently, and had lower endocervical pH which favored sperm penetration [12]. A study showed that women with android obesity were associated with menstrual and ovulatory problems and had considerable difficulty in becoming pregnant and had their first live birth at a later age [10].

In overweight and obese women, notable hypoxia occurs among adipocyte cells and this leads to the release of proteins named adipokines [26]. Leptin which is secreted by adipocytes is of these proteins [18]. Leptin production is usually proportional to the adipose mass [3]. Leptin secretion increases in high weight individuals [26]. Leptin was found to be elevated in the follicular fluid of obese women revealing that systemic alterations associated with obesity could affect ovarian follicular environment [17]. Leptin acts through the receptors on the theca and granulosa cells of ovarian follicles [27]. Increased follicular fluid levels of leptin inhibit ovarian functions through adverse alteration of steroids production as it is seen in polycystic ovary syndrome women [18]. Abdominal obesity are associated with glucose intolerance and insulin resistance which can lead to increased production of insulin in a way by the body to maintain blood glucose levels [3]. High body weight is associated with a decrease in serum adiponectin levels [27]. Lower serum adiponectin levels are correlated

with increase in circulating insulin levels and mediate insulin resistance which can lead to hyperandrogenaemia partly by inhibiting production of hepatic sex hormone binding globulin (SHBG) [27, 3]. Follicular fluid insulin levels are increased markedly in elevated weight women compared to normal weight women [17]. Insulin acts via insulin like growth factor 1 (IGF1) enhances luteinizing hormone function in steroidogenesis in the theca cells and hence leads to considerable increase in ovarian androgens [27]. Hyperandrogenaemia results in anovulation as seen in polycystic ovarian syndrome women [18]. Hyperandrogenaemia causes granulosa cell apoptosis, while peripheral conversion of androgens to estrogen in adipose tissue inhibits gonadotrophin secretion [28]. So, as most polycystic ovarian syndrome women are obese, obese women are seen to have significant hormonal and metabolic dysfunction and consequently infertility sufferings [27]. The dramatic alterations in the follicular environment of obese women are associated with increased reactive oxygen species and oxidative stress leading to heightened inflammation that adversely affect oocyte quality and development [17]. Obese women are predisposing to recognizable risks of menstrual disturbances, involving long menstrual cycle length, usually more than thirty-five days, and anovulation. These complaints can be clearly found in high weight polycystic ovarian syndrome women [18].

A study found that obesity was more prevalent in Black Americans than in White Americans and mentioned that fatness in Black Americans was associated with a positive serotype [10]. Although results in our study showed no significant relationship between body mass index and tan of skin, eleven out of seventeen obese polycystic ovary syndrome women according to body mass index measurements were brown colored and this could be explained that dark women were more prone to obesity than white women due to genetic factors and genes were important in determining person's susceptibility to weight gain [5].

It was suggested that oxidative stress could affect female fertility [6]. Oxidative stress is characterized by increased production of reactive oxygen species and free radicals followed by decreased serum total antioxidant levels [29]. Oxidative stress negatively affects oocyte maturation [6]. Increased oxidative stress in oocyte microenvironment might impair their development [30]. A cohort study indicated that decreased ovulatory disorders were among women consumed multivitamins compared with not utilizing multivitamins [31]. It was demonstrated that adult women consuming fruits and vegetables rich with antioxidants negatively affected oxidative stress [32]. Antioxidants circulating vitamins C and E (ascorbic acid and  $\alpha$ -tocopherol, respectively) and antioxidant cofactors as selenium, zinc, and copper have the ability to dispose, scavenge, or suppress the formation of reactive oxygen species [6]. Vural *et al.* revealed that

plasma levels of vitamin C and vitamin E were significantly lower among women with recurrent spontaneous abortion [33]. All the amino acids that appear in the finished protein must be present at the time of protein synthesis. Nonessential amino acids can be synthesized in sufficient amounts from the intermediates of metabolism or, as in case of cysteine and tyrosine, from essential amino acids. In contrast, the essential amino acids cannot be synthesized or produced in sufficient amounts by the body, and, therefore, must be obtained from the diet in order for normal protein synthesis to occur. If the diet does not contain an essential amino acid, translation stops at the codon specifying that amino acid. This demonstrates the importance of having all the essential amino acids in sufficient quantities in the diet to ensure continued protein synthesis [3]. Animal sources are complete protein sources but most plant foods are not [33]. The essential amino acids missed from most plant foods comprise lysine (which converts fatty acid to energy), tryptophan (a neurotransmitter), methionine (a powerful antioxidant), and phenylalanine (synthesis of brain chemicals dopamine and norepinephrine and thyroid hormones synthesis) [34]. If a woman has MTHFR gene as many polycystic ovarian syndrome women have, this leads to too much homocysteine which causes increase in polycystic ovary syndrome symptoms. High meat consumption is often coupled with decreasing carbohydrates and this is a serious issue for polycystic ovarian syndrome women sufferings. Polycystic ovary syndrome women are with poor thyroid gland functions and thyroid gland needs glucose, so high meat consumption among polycystic ovary syndrome sufferers adversely affect thyroid functions. Moreover, glucose is essential for pituitary gland functions and little glucose intake negatively affects hormonal balance and consequently negatively affect fertility [35]. Vegetarian polycystic ovary syndrome women cannot get from their diet essential amino acid phenylalanine which is essential for thyroid functions [34]. All these explanations illustrate role of type of food consumption in regulating body hormones and consequently reproductive hormones. So additional factor participated in increasing infertility complaining among polycystic ovarian syndrome women enrolled in this study was their inadequate type of food intake as vegetarian polycystic ovarian syndrome women their diet lack essential amino acids and mixed food eating polycystic ovarian syndrome women their diet depended on meat consumption and thus lack sufficient antioxidants and glucose needs.

Nutrition influences female reproductive system through affecting hormone-emanating from fat cells (leptin) and insulin secreted from pancreas, which changes the availability of estradiol<sup>2</sup> and testosterone by affecting the production of sex-hormone-binding globulin (SHBG) from the liver [18]. A diet rich in animal proteins causes decrease in sex-hormone-binding globulin which polycystic ovarian syndrome

patients need to decrease their high testosterone levels. Many polycystic ovarian syndrome women have MTHFR gene that creates too much homocysteine which causes increase in polycystic ovary syndrome symptoms [35]. Animal-derived foods contain endogenous estrogens or estrogen metabolites and their consumption can directly lead to altered circulating steroid hormones concentrations. Additionally, consumption of animal foods might affect endogenous steroid hormones production indirectly through their nutrient components. Cholesterol is a major substrate for steroid hormones synthesis and animal products are rich sources of cholesterol, saturated fats, and protein [36]. A study showed that changing from a diet rich in animal fat to one that was rich in vegetable fat and protein reduced circulating estrogen levels by more than 40% [37]. A diet high in fat is usually associated with high protein consumption [36]. It was demonstrated that large differences in fat intake were required to cause a significant change to circulating hormones levels [38]. Small epidemiological studies done in the 1980s showed higher circulating concentrations of 17- $\beta$  estradiol, androstenedione, and testosterone for postmenopausal mixed food consumers compared to postmenopausal fruits and vegetables consumers [38-39]. The none significant increase in both estradiol<sub>2</sub> and testosterone mean levels among mixed food consumers compared to vegetarian among all cases enrolled in our study were attributed to that there should be high and even upping meat intake in order to cause significant changes.

It was indicated that high caffeine intake increased the time needed to conceive and an important predisposing factor for subfertility [6]. European Study of Infertility and Subfecundity demonstrated that high caffeine intake resulted in 45% increased risk of subfecundity ( $\geq 9.5$  months to conception) [40]. These agreed with our results which demonstrated that high caffeine intake played a recognizable role in infertility but not correlated with the type of infertility. A 2008 study recorded an increased risk of miscarriage among high caffeine consumers [41]. This almost agreed with our finding.

## CONCLUSIONS

There was notable difference in the number of obese polycystic ovarian syndrome women distributed according to body mass index, waist circumference, and waist to hip ratio measurements which was related to differences in the sites of body fat accumulation. None significant increase in both serum estradiol<sub>2</sub> and testosterone mean levels among android type compared to gynoid type of body fat accumulation were attributed to that most of these polycystic ovarian syndrome women were with high levels of testosterone which overcame the effects of high estradiol<sub>2</sub> levels preferring intraabdominal fat accumulation. Brown-colored polycystic ovarian syndrome women were more susceptible to obesity than white-colored polycystic

ovarian syndrome women indicating the role of genetic inheritance in obesity. Inadequate type of food intake participated in increasing the signs of infertility among polycystic ovarian syndrome women. The none significant increase in both estradiol<sub>2</sub> and testosterone mean levels among mixed food consumers compared to vegetarian polycystic ovarian syndrome women were related to that there should be upping in meat intake to yield significant increases. Type of infertility and high caffeine intake among polycystic ovarian syndrome women were independent factors but it was noticed that high caffeine intake might participated in incidence of spontaneous miscarriages among polycystic ovarian syndrome women.

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