Differences in clinical and endocrine features between obese and non-obese women in polycystic ovarian syndrome

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Abstract

Background and objectives: The polycystic ovary syndrome is one of the commonest endocrine disturbance affecting 5-8% of reproductive age women. It is a heterogenous disorder that mainly presents with features of hyperandrogenism and anovulation. These clinical features are further affected by body mass index at presentation. This study aimed to estimate the impact of obesity on the clinical features of polycystic ovary syndrome and to compare hormonal and ultrasonography features between obese and non-obese polycystic ovary syndrome women. **Methods:** a cross-sectional comparative study carried on 230 infertile women with criteria of polycystic ovary syndrome attending Private Hawler Centre for Infertility and in vitro fertilization, Erbil, Iraq, in the period between the 1st of October 2015 and the 1st of April 2016. **Results:** Out of 230 polycystic ovarian syndrome women, the BMI was 25 kg/m^2 in 123 ladies (53.48%); 32 ladies 13.9% were overweight and 91 ladies 39.5% were obese. Obese polycystic ovary syndrome women had more sedentary life, more family history of polycystic ovary syndrome and associated with higher miscarriage rate. Amenorrhea and oligomenorrhoea were found more frequently in obese women 24.4% and 62.6% respectively than non-obese polycystic ovary syndrome women 21.5% and 53.3%. **Conclusions:** Obesity has a significant impact on the appearance of clinical features of polycystic ovary syndrome among infertile women, signs of hyperandrogenism, maximum ovarian volume and mean serum level of hormones including luteinizing hormone, progesterone and testosterone were significantly more reported in obese than non-obese polycystic ovary syndrome women.

Keywords: Amenorrhea; hirsutism; obesity; polycystic ovarian syndrome.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most commonly encountered endocrinological problems facing 5-8 % of reproductive age women[1]. PCOS is a heterogeneous syndrome that classically is characterized by features of anovulation (amenorrhoea, oligomenorrhoea, and irregular cycles) combined with symptoms of androgen excess (hirsutism, acne, alopecia)[2].This syndrome affects reproductive, metabolic, and cardiovascular components with health implications across the life span. The underlying Hyperinsulinaemia and insulin resistance is a major cause behind the development of metabolic disorders and type 2 diabetes, further more women with PCOS have multiple risk factors for diabetes including obesity and family history of type 2 diabetes. The most consistent biochemical abnormalities are elevation of serum androgen and luteinizing hormone (LH) concentrations, but with normal follicle-stimulating hormone (FSH) levels[3-4]. Two out of the three following criteria is required for the diagnosis of PCOS according to Rotterdam PCOS Consensus Workshop Group (1) oligo anovulation (O), (2) clinical and/or biochemical signs of hyperandrogenism (H) and (3) polycystic ovaries by ultrasound (P) and (4) the exclusion of other related disorders (congenital adrenal hyperplasia,androgen-secreting tumors, Cushing's syndrome). According to this workshop PCOS divided to four phenotypes (i) Phenotype A (O+H+P), (ii) Phenotype B (O+H), (iii) Phenotype C (H+P) and (iv) Phenotype D (O+P)5. The finding of 12 or more follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (10 mL) is consistent with polycystic ovarian morphology by ultrasound[5].

Although the exact pathophysiology of PCOS remains unclear, the underlying hormonal imbalance caused by a

combination of increased androgens and/or insulin, together with genetic and environmental factors may have a role. Other factors like obesity, ovarian dysfunction and hypothalamic pituitary abnormality also contributes to the etiology of PCOS[6-7]. Studies reported that between 38–88% of PCOS women have been found to be over-weight and obese, and that hyperandrogenism and related clinical features (such as hirsutism, menstrual abnormalities, and anovulation) are more sever in obese PCOS women than normal weight PCOS women[8], besides that loss of 5% body weight in women with PCOS have been associated with significant improvement in both symptoms of hyperandrogenism and ovulatory function[9-10]. This will raise the concept that adiposity plays a crucial role not only in the development but also in the maintenance of PCOS manifestations and strongly influences the severity of both its clinical and endocrine features in many women with the condition[11]. One of the supporting concepts that its phenotypes are a consequence of a polygenic mechanism is the presence of certain single-nucleotide polymorphisms associated with obesity contribute to elevated body mass index (BMI) in PCOS[12]. However, obesity is not taken into account for PCOS phenotypes.

Studies compared the prevalence of clinical manifestation and clinical health hazards in obese and lean PCOS women found that the menstrual irregularities and clinical hyperandrogenism were significantly higher in obese group among Indian population, but that study did not compare the endocrine features in infertile women[13]. This study aimed at estimate the impact of obesity on clinical manifestation of PCOS, and comparisons of the demographic characteristics, and hormonal and ultrasonographic features of PCOS of obese and non-obese infertile women visiting IVF center.

Materials and Methods

This study is a cross-sectional comparative study. The subjects were women with criteria of PCOS attending Private Hawler Centre for Infertility and IVF, Erbil, Kurdistan region, Iraq, in six months duration, from the 1st of October 2015 till the 1st of April 2016. The Scientific and Ethical Committee at the College of Medicine, Hawler Medical University, approved this study. Written informed consent was obtained from all subjects after explanation of the study protocol. Rotterdam criteria was used for the diagnosis of PCOS, which is the presence of at least two out of three of the followings: oligomenorrheo/anovulation (delaying of the menstruations >35 days), clinical and/or biochemical hyperandrogenism (biochemical hyperandrogenism defined as serum total testosterone level above the 95th percentile (0.481 ng/ml), and polycystic ovary on ultrasonography (≥12 small follicles measuring 2-9 mm in at least one ovary and or ovarian volume > 10 cm^3). After taking the demographic characteristics, body mass index is measured by calculating (weight (kg)/height $(m)^2$). Height and weight are been measured with shoes taken off. Height is been measured against a wall a wall mounted tape measure. Weight is been measured with light clothing on using a platform scale.1.5 kg was subtracted from their weights to correct for clothing weight. PCOS women divided into two groups, obese and overweight ≥25 kg/m^2, and non-obese <25 kg/m^2. Waist circumference was measured in standing position at the level of umbilicus, while hip circumference was measured at the furthest circumference over undergarment. Then, waist to hip ratio (WHR) was calculated as waist circumference divided by hip circumference. WHR >0.85 is regarded as abnormal[14].

Menstrual history, history of infertility, hirsutism, acne, greasy skin and scalp hair loss were asked from all patients, followed by general, abdominal and pelvic examination. Hirsutism, which is the excess growth of terminal hair, is measured using modified Ferriman-Gallway method by scoring the presence of terminal hair over nine body regions (upper lip, chin, chest, upper and lower abdomen, upper and lower back, upper arms and thighs) from 0 to 4. A Ferriman-Gallway Score of ≥ 8 diagnosed as hirsutism[15]. A transvaginal ultrasound is performed in the second or third day of cycle by a specialist ultrasonographer measuring maximum ovarian volume and ovarian morphology. Blood samples were collected in the

Results

Total 230 PCOS women visited Hawler Infertility Centre during the study period, 123 women (53.48%) were overweight and obese and 107 women (46.52%) were non-obese (non-obese) as shown in Figure 1.

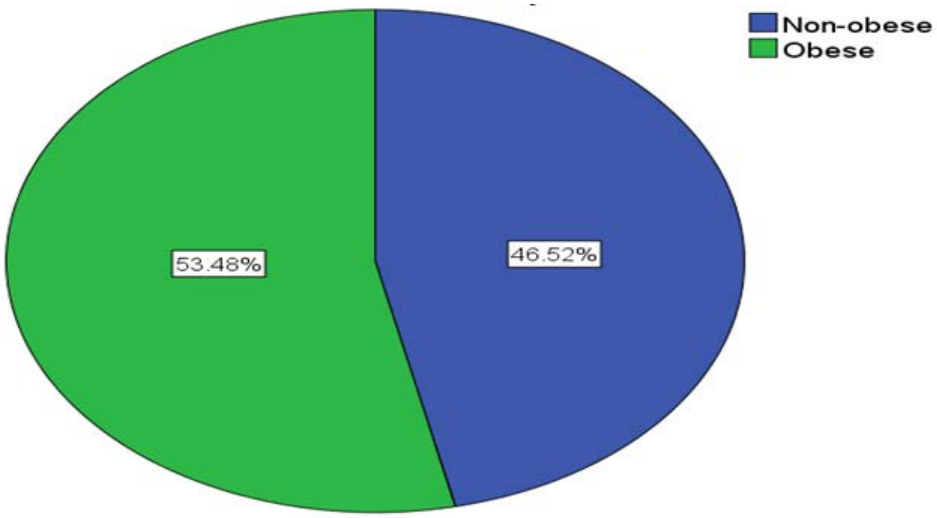

Figure (1): Distribution of obese and non-obese PCOS participants.

The data in Tables 1 & Table 2 show that demographic features of obese and non-obese PCOS women. The mean BMI in non-obese women was 23.4 kg/m^2, while it was 32.9 kg/m^2 in obese women, which was statistically significant and P-value was < 0.001. No statistical significant difference was present regarding mean age of presentation, parity, duration of infertility between the two groups. There was statistically significant correlation between study groups; occupation of participants, 41.1% of non-obese were employed (have jobs) while the employed ones in obese group was 17.9%, (P<0.001). Although family history of the presence of PCOS and secondary infertility were higher in obese than non-obese women, they were statistically insignificant. On the other hand the researcher observed that miscarriage rate was twice more common in obese 32.5% than non-obese women 15%, which was also statistically significant (P=0.002).

Table (1): Demographic features of obese and non-obese women.

Variables	Categories	Study groups		P-value
		Non-obese	Obese	
Occupation	Housewife	63 (58.9%)	101(82.1%)	< 0.001
	Working	44 (41.1%)	22 (17.9%)	
Family history of PCOS	No	59 (55.1%)	52 (42.3%)	0.051
	Yes	48 (44.9%)	71 (57.7%)	
Type of infertility	Primary	64 (59.8%)	65 (52.8%)	0.28
	Secondary	43 (40.2%)	58 (47.2%)	
Miscarriage	No	91 (85.0%)	83 (67.5%)	0.002
	Yes	16 (15.0%)	40 (32.5%)	

Table (2): Age, parity, infertility and BMI of study groups

Variables	Obesity	Mean	S.D	P-value
Age	Non-obese	28.8	4.85	0.33
	Obese	29.5	5.92	
Parity	Non-obese	0.57	0.94	0.66
	Obese	0.63	1.01	
Duration of infertility	Non-obese	5.28	3.51	0.13
	Obese	6.07	4.24	
BMI	Non-obese	23.4	1.31	< 0.001
	Obese	32.9	4.32	

Table 3 shows that W/H ratio > 0.85 is more common in obese women (93.5%) than non-obese women (77.6%) with statistical significant difference between them. Although oligomenorrhoea, amenorrhoea, and scalp hair loss were more common in obese women but they were statistically not significant. Other features of hyperandrogenism including hirsutism, acne and greasy skin were more common in obese than non-obese women with statistically significant difference observed between them.

Table (3): Clinical features of obese and non-obese PCOS patients.

Variables	Categories	Study groups		P-value
		Non-obese	Obese	
Waist hip ratio	≤ 0.85	24 (22.4%)	8 (6.5%)	0.001
	> 0.85	83 (77.6%)	115 (93.5%)	
Hirsutism	No	47 (43.9%)	23 (18.7%)	0.001
	Yes	60 (56.1%)	100 (81.3%)	
Acne	No	83 (77.6%)	54 (43.9%)	0.001
	Yes	24 (22.4%)	69 (56.1%)	
Greasy skin	No	78 (72.9%)	44 (35.8%)	0.001
	Yes	29 (27.1%)	79 (64.2%)	
Scalp hair loss	No	51 (47.7%)	44 (35.8%)	0.06
	Yes	56 (52.3%)	79 (64.2%)	
Menstrual cycle	Regular	27 (25.2%)	16 (13%)	0.06
	Oligomenorrhea	57 (53.3%)	77 (62.6%)	
	Amenorrhea	23 (21.5%)	30 (24.4%)	
Total	**No. (%)**	**107 (100%)**	**123 (100%)**	

Table 4 shows that hormonal level including LH, LH/FSH ratio, total and free testosterone, serum prolactin and serum progesterone were all higher in obese than non-obese PCOS, with statistically significant difference between them, while no difference observed in FSH and serum TSH levels between the two groups.

Table (4): Hormonal profile of obese and non-obese PCOS participants.

Variables	Obesity	N	Mean	S.D	P-value
LH IU/ml	Non-obese	107	8.448	3.10	0.001
	Obese	123	10.23	3.44	
FSH IU/ml	Non-obese	107	5.597	1.73	0.99
	Obese	123	5.597	1.75	
LH / FSH ratio	Non-obese	107	1.567	0.55	0.001
	Obese	123	1.933	0.70	
Total testosterone ng/dl	Non-obese	107	90.52	48.1	0.001
	Obese	123	109.4	52.6	
Free testosterone Pg/ml	Non-obese	107	5.659	2.74	0.001
	Obese	123	7.735	2.88	
Prolactin level ng/ml	Non-obese	107	16.90	7.54	0.001
	Obese	123	22.86	10.0	
Progesterone level ng/ml	Non-obese	107	1.075	0.53	0.001
	Obese	123	1.663	0.50	
TSH IU/ml	Non-obese	107	2.630	1.37	0.29
	Obese	123	2.868	1.92	

The findings of Tables 5 and 6 indicate that there were no statistical significant correlations between PCOS morphology and study groups. In both obese and non-obese patients the majority of them showed PCOS morphology using US examination. PCOS morphology was observed in 88.6% of obese PCOS women versus 93.5 % of non-obese PCOS women. Meanwhile the maximum ovarian volume in obese women was 11.6 cm^3 versus 11.1 cm^3 in non-obese women and this difference in mean volume was statistically significant using T-test (P value 0.03).

Table (5): Relationship between PCOS morphology and study groups (P: 0.20).

PCO morphology	Study groups		Total
	Non-obese	Obese	
No	7 (6.5%)	14 (11.4%)	21 (9.1%)
Yes	100 (93.5%)	109 (88.6%)	209 (90.9%)
Total	**107 (100%)**	**123 (100%)**	**230 (100%)**

Table (6): Maximum ovarian volume of obese and non-obese patients.

Measure	Obesity	N	Mean	S.D	P-value
Maximum ovarian volume	Non-obese	107	11.1	1.38	0.03
	Obese	123	11.6	1.82	

Discussion

Polycystic ovary syndrome is one of the commonest reason for failure of conception that women visits infertility center seeking assisted reproduction, during 6 month period 230 women with PCOS visited Private Hawler Centre for Infertility and IVF, Erbil, Iraq, of which 123 women (53.48%) have BMI ≥25 which is overweight and obese, 39.56 % were obese BMI ≥ 30. In other studies 16-80% of PCOS women were reported to have obesity[16]. The Abha Majumdar et al study, found 37.5% prevalence of obesity in PCOS women in his study[13], which is in consistent to this study. Being on a diet high in carbohydrate and fat, low in protein, and low exercise rate of the subjects may be the reason behind the high rate of obesity in this study. Furthermore, central obesity was also found to be high in obese PCOS women, WHR (>0.85) were observed

more in obese women 119 (96.7%) versus 94 women in non-obese PCOS (87.85%). This finding was close to Thathapudi et al study which was 94% versus 90% respectively[17].

In this study obesity was more common among house wife women with only 17.9% of obese women had a job, while 44.1% of non-obese women were employed. In addition, the employed ones indulge in more activity; this may be attributed to their higher educational levels that make them more aware of hazards of obesity on health. This finding was also reported in Mahmoud et al[18] who reported 62% of non-obese women and 42.5% of obese women had active working status. Family history of PCOS was higher in obese versus non-obese PCOS women, 57.7% and 44.8% respectively; this was parallel to Mahmoud et al. study which was 67.5% and 52% respectively[18].

Studies found that the risk of miscarriage increases with increasing BMI, in overweight women the risk was 29%; in obese, 71%; in BMI over 35, 119%[19]. In addition, obese PCOS women have nine times higher rate of miscarriage than non-obese PCOS women[20]. Furthermore, spontaneous ovulation and pregnancy rate found to be improved after 5% loss of body weight in obese women with PCOS[9-10].This study also found higher miscarriage rate in obese PCOS women, which was statistically significant.

PCOS is associated with a wide range of menstrual irregularities ranging from oligomenorrhoea, amenorrhoea, and dysfunctional uterine bleeding[3]. In this study oligomenorrhoea and amenorrhoea were more common in obese PCOS women than non-obese women, similar to Mahmoud et al[18] study who also found higher menstrual irregularities in obese than non-obese PCOS women. Studies showed that higher rate of menstrual irregularities like amenorrhoea and oligomenorrhoea may be attributed to high level of total and free testosterone levels and depressed SHBG in obese women with PCOS[21- 22]. In this study, we also observed higher hormonal profiles including serum LH, LH/FSH ratio, serum progesterone, serum prolactin, total and free testosterone levels in obese versus non-obese women, but no difference in serum FSH and TSH found between them, this was parallel to Mahmoud et al. study[18]. Thathapudi et al study[17] also found higher LH and LH/FSH levels in the obese rather than non-obese PCOS women. On the other hand, our findings disagree with Silfen et al[23] study, who found lower LH and total testosterone level but higher free testosterone level in obese versus non obese PCOS women, regarding the fact that his study was done on adolescent PCOS, with lower sample size, and not infertile women like that in this study. Studies showed that obesity may have an important role in appearance of features of hyperandrogenism, not only in PCOS women but also in women with normal ovaries[24]. Similarly this study found that clinical features of hyperandrogenism including hirsutism, acne, greasy skin, and scalp hair loss were more observed in obese than non-obese PCOS women. This was also consistent to Mahmoud et al[18] study who found higher rate of signs of hyperandrogenism in obese than non-obese women. This finding may be attributed to increased level of total and free testosterone level in obese PCOS women. Sonographic features in obese women showed no statistical significance difference in polycystic appearance between obese and non-obese PCOS women, which was compatible to Silfen et al study except in our study we observed higher ovarian volume in obese PCOS women, which disagrees with Silfen et al[23] who found no difference in the mean ovarian volume between the two groups. This difference again may be attributed to his lower sample size and different age target of his study subjects which was the adolescence.

Conclusions

Body mass index has an effective impact on the relative appearance of clinical, sonographic and endocrine features of PCOS in infertile women. Obese women have more menstrual abnormalities, features of hyperandrogenism, and hormonal disturbance than non-obese PCOS women, therefore it is important to advice these women to reduce weight as the first line of management, which may increase the chance of spontaneous pregnancy, success of assisted reproductive technology, and decline

of miscarriage rate .

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