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# Reproductive and biochemical changes in obese and non obese polycystic ovary syndrome women



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## KEYWORDS

Body mass index;  
 Insulin resistance;  
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**Abstract** *Background:* Reproductive, clinical and laboratory implication varies in polycystic ovary syndrome (PCOS) according to body weight.

*Objective:* To compare reproductive, clinical and laboratory data between obese and non obese women with PCOS.

*Methods:* A cohort of 180 women with PCOS who attended outpatient clinic of Taibah University from January to September 2012 was included. Studied women were classified according to body mass index (BMI) into overweight/obese (BMI > 25 kg/m<sup>2</sup>) and normal weight women (BMI ≤ 25 kg/m<sup>2</sup>). Each participant answered a specially designed interviewing format and subjected to medical checkup for signs of hyperandrogenism. Fasting insulin and glucose, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E<sub>2</sub>), prolactin (PRL), progesterone and testosterone levels were estimated. Statistical analyses were performed as appropriate.

*Results:* Of the studied 180 PCOS women, there were 80 overweight obese women (44.4%) and 100 normal weight women (55.6%). Obese PCOS women were less highly educated, less working and reported low family history rate of PCOS. Compared to non obese PCOS women, obese PCOS women reported higher age of menarche, abortion and menstrual disturbance with statistically significant difference. Signs of hyperandrogenism and acanthosis nigricans were significantly more manifested in obese PCOS women. Mean levels of studied metabolic and sex hormones were significantly higher in obese PCOS women.

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**Conclusions:** Overweight and obese PCOS women had significantly higher age of menarche, abortion and menstrual disturbances. Also, signs of hyperandrogenism, acanthosis nigricans were more encountered among them with higher levels of fasting glucose, fasting insulin, FSH, LH and testosterone.

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## 1. Introduction

Polycystic ovary syndrome (PCOS) is a fairly common disorder of women in reproductive age. It is characterized by hyperandrogenism and chronic anovulation.<sup>1,2</sup> It has a prevalence of 5–10% based upon studies which found that; 20% of self-selected normal women had polycystic ovary morphology on ovarian ultrasound. Many of these studied women had endocrine abnormalities.<sup>3</sup> It was found that 75% of women with secondary amenorrhea fulfilled diagnostic criteria for PCOS.<sup>1,3–5</sup> PCOS was the cause of 82% of hirsutism among Saudi female population.<sup>6</sup> The recent theories of the pathogenesis of polycystic ovary syndrome (PCOS) have focused on the role of insulin resistance and hyperinsulinemia. Irrespective of the pathogenic mechanisms involved, many women with PCOS (between 38% and 88%) have been found to be overweight and obese, and the studies reported that obese PCOS women have more severe hyperandrogenism and related clinical features (such as hirsutism, menstrual abnormalities and anovulation) than normal weight PCOS women.<sup>7</sup> Even modest weight loss of 5% body weight has been shown to result in significant improvements in both symptoms of hyperandrogenism and ovulatory function in women with PCOS.<sup>8,9</sup> There is no doubt, therefore, 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.<sup>10</sup> Despite these reported data, there is still a shortage of studies, particularly in our region, that compare the reproductive, clinical and laboratory data in obese and non obese PCOS women. Therefore, this study was carried out to clarify if there is a difference in reproductive, clinical and laboratory parameters between obese and non obese patients with PCOS.

## 2. Subjects and methods

The study was carried out on a cohort of women with PCOS who attended the outpatient clinics at Taibah University, Female section from January to September 2012. All included women (180 cases) were previously diagnosed to have PCOS (depending on their ultrasound findings by presence of eight or more subcapsular follicular cysts  $\leq 10$  mm and increased ovarian stroma).<sup>2,3</sup> All studied women were not pregnant nor diabetic. The studied women were divided into two groups based upon their BMI: obese PCOS patients (80 cases) with BMI  $\geq 25$  kg/m<sup>2</sup> and non obese patients PCOS (100 cases) with BMI  $< 25$  kg/m<sup>2</sup> (100 cases).

Every participant woman was interviewed and asked to answer a specially designed interviewing format including; socio-demographic data, menstrual, gynecological, obstetric, medical and family histories. Oligomenorrhea was considered

when menses flow every 6 weeks to 6 months.<sup>2,4,5</sup> She was also subjected to medical checkup for signs of hyperandrogenism and polycystic ovary. Anthropometric measurements including weight, height (to calculate BMI), waist and hip measurements (with calculation of waist to hip ratio (WHR)) were performed.

The following laboratory tests were recommended for each participant: fasting insulin level, fasting glucose level, follicle stimulating hormone (FSH), luteinizing hormone (LH), oestradiol (E<sub>2</sub>), progesterone, prolactin (PRL), and testosterone. All laboratory investigations were done in one of the reference labs in Medina. The collected reproductive, clinical and laboratory data were compared between the studied two groups.

Approval of Research Ethics committee for Medical College, Taibah University was considered and official permission was assured. Before inclusion of any participant in this study, an informed written signed consent was obtained after explanation of the objective and methodology of the research. Also, privacy and confidentiality of the participants were assured.

The data were analyzed by using SPSS package version 17. In order to compare the distribution of the studied factors in obese and non obese PCOS women,  $\chi^2$  tests for the categorical variables and *t* test for the continuous variables were used. The level of statistical significance was defined as  $p \leq 0.05$ .

## 3. Results

Of the studied 180 PCOS women, there were 80 (44.4%) overweight and obese women and 100 (55.6%) normal weight women. The mean age of the studied women was  $41.7 \pm 6.8$  years. Table 1 presents the general characteristics of the studied obese and non obese PCOS women. The mean age of obese PCOS women was higher than that of non obese patients with statistically significant difference ( $p = 0.002$ ). Obese women with highly educated level were significantly higher than highly educated non-obese women with PCOS (57.5% compared to 72.0% where  $p = 0.023$ ). The percent of ever married women, however, was significantly highly (67.5%) encountered among obese women compared with non obese patients (58.0%) ( $p = 0.030$ ). Also, positive family history of PCOS was significantly higher among first degree relatives of obese patients (67.5%) compared with non obese patients (52.0%) ( $p = 0.040$ ).

Table 2 shows the reproductive and clinical characteristics of obese and non obese women with PCOS. The mean age of menarche among obese women was significantly higher than that of non obese women ( $16.3 \pm 2.11$  and  $14.5 \pm 3.24$  respectively;  $p = 0.02$ ).

The mean number of reported abortion among non-obese women with PCOS was insignificantly lower than that among obese ones ( $0.9 \pm 0.62$  versus  $1.3 \pm 0.24$ ).

**Table 1** General characteristics of obese and non obese PCOS women.

	Obese PCOS (n = 80)		Non-Obese PCOS (n = 100)		P value
	n	%	n	%	
Basic education	41.7 ± 6.86		32.5 ± 8.94		0.002**
<i>Education level<sup>a</sup></i>					
Basic education	14	17.5	10	10.0	0.023**
Secondary education	20	25.0	18	18.0	
High education	46	57.5	72	72.0	
<i>Work status</i>					
House wife	46	57.5	38	38.0	0.001**
Working	34	42.5	62	62.0	
<i>Marital status</i>					
Never married	26	32.5	42	42.0	0.030**
Ever married	54	67.5	58	58.0	
<i>Family history of PCOS</i>					
Yes	54	67.5	52	52.0	0.040**
No	26	32.5	48	48.0	

<sup>a</sup> Basic education includes primary and preparatory level. High education includes University degree and more.

\*\* Significant.

**Table 2** Reproductive and clinical characteristics of obese and non obese PCOS women. The bold values are total and the italic below are subtotal.

	Obese PCOS (n = 80)		Non-obese PCOS (n = 100)		P value
	n	%	n	%	
Age of menarche (mean ± SD)	16.3 ± 2.11	14.5 ± 3.24	0.02**		
<i>Obstetric history<sup>a</sup></i>					
Age at first marriage	19.4 ± 3.62	21.8 ± 2.95	0.02**		
Gravidity	2.3 ± 0.65	1.5 ± 0.34	0.060		
Abortion	1.3 ± 0.24	0.9 ± 0.62	0.240		
Parity	1.1 ± 0.21	0.8 ± 0.31	0.310		
<i>Menstrual disturbances</i>					
No disturbance	<b>12</b>	<b>15.0</b>	<b>24</b>	<b>24.0</b>	0.006**
With disturbance	<b>86</b>	<b>85.0</b>	<b>76</b>	<b>76.0</b>	
<i>Oligomenorrhea</i>	46	67.7	42	55.3	
<i>Amenorrhea</i>	18	26.5	22	28.9	
<i>Dysfunctional bleeding</i>	4	5.8	12	15.8	
<i>Acromegalic features</i>					
Yes	22	27.5	26	26.0	0.080
No	58	72.5	74	74.0	
<i>Signs of hyperandrogenism</i>					
Yes	38	47.5	36	36.0	0.020**
No	42	52.5	64	64.0	
<i>Acanthosis nigricans</i>					
Yes	34	42.5	28	28.0	0.040**
No	46	57.5	72	72.0	

<sup>a</sup> Analyses included 112 ever married women.

\*\* Significant.

Menstrual disturbances were significantly highly encountered among whole studied women with PCOS (162 out of 180 representing 90%). When considering obesity, menstrual disturbances were significantly highly encountered in obese women with PCOS (85%) particularly oligomenorrhea (67.7%). Omit  $p = 0.006$ . Also, the signs of hyperandrogenism and acanthosis nigricans were more significantly observed among obese PCOS women compared with non obese patients ( $p = 0.020$  and  $0.040$  respectively).

Table 3 displays the biochemical data in the studied obese and non-obese PCOS women. The mean values for most of the studied biochemical parameters were significantly higher in obese PCOS patients than that for non-obese ones.

#### 4. Discussion

Polycystic ovary syndrome is a common disorder of premenopausal women characterized by hyperandrogenism and

**Table 3** Biochemical data in obese and non obese PCOS women.

	Obese PCOS (n = 80)	Non obese PCOS (n = 100)	P value
Fasting glucose level (mg/ml)	121.5 ± 5.9	114.8 ± 2.98	0.035**
Fasting insulin level (pmol/ml)	61.5 ± 4.45	53.29 ± 75	0.041**
FSH level (mIU/ml)	5.4 ± 0.12	6.4 ± 1.22	0.048**
LH level (IU/ml)	6.7 ± 2.67	4.32 ± 1.93	0.036**
Progesterone level (ng/ml)	1.9 ± 0.76	1.7 ± 0.98	0.079
E <sub>2</sub> (Pg/ml)	49.9 ± 5.85	48.5 ± 4.86	0.362
PRL (µg/ml)	24.9 ± 2.37	21.6 ± 5.65	0.069
Testosterone level (ng/dL)	110.7 ± 5.56	90.6 ± 8.65	0.009**

\*\* Significant.

chronic anovulation.<sup>1,2</sup> PCOS women are characterized by being obese in 16–80% of cases.<sup>11–14</sup> It is reported that PCOS is accompanied by menstrual irregularity ranging from oligomenorrhea, amenorrhea, or dysfunctional uterine bleeding.<sup>2,4,5</sup> The results of the present study appeared consistent with these reports where menstrual irregularities were a complaint among 90% of studied PCOS women. Studying menstrual and obstetric features showed a statistical significant difference between obese and non-obese women regarding the obstetric and menstrual histories. Delayed age at menarche, oligomenorrhea and abortion was manifested in obese women. It is well known that obesity is associated with anovulation, pregnancy loss and late pregnancy complications (pre-eclampsia, gestational diabetes).<sup>8</sup> Obesity in PCOS is also linked to failure or delayed response to the various treatments including clomiphene citrate, gonadotropins and laparoscopic ovarian diathermy. It has been reported that, after losing as little as 5% of initial body weight obese women with PCOS improved spontaneous ovulation rates and spontaneous pregnancy.<sup>8,9</sup>

The present work showed a higher mean level of fasting blood sugar and fasting insulin level among obese PCOS women. The same finding was also obtained from a recent hospital-based Saudi study where obesity in Saudi women was associated with hyperinsulinaemia and insulin resistance.<sup>6</sup> Since the report by Solomon Thomas et al.<sup>14</sup> in 1980 that PCOS was associated with hyperinsulinemia, it has become clear that the syndrome has major metabolic as well as reproductive morbidities.<sup>14</sup> Insulin resistance, hyperinsulinemia, and beta-cell dysfunction are very common in PCOS, but are not required for diagnosis. It is an important defect in the pathogenesis of noninsulin-dependent diabetes mellitus (NIDDM).<sup>15</sup> It was proved that hyperinsulinemia in PCOS occurred independent to the presence of obesity.<sup>16,17</sup> Nevertheless, obese PCOS had significantly increased blood glucose levels in 20% of cases than control.<sup>17</sup> The majority of affected women are in their third and fourth decade of life<sup>19,20</sup> which was concomitant with the results of the present study where the mean age of the recruited women was 41.7 ± 6.8 years. These findings, together with the evidence obtained from previous reports that a huge number of PCOS women show a condition of insulin resistance and hyperinsulinemia, suggested that insulin may play the basic role in the promotion and/or the maintenance of PCOS, particularly on obese women.

In the current study, acanthosis nigricans was detected in 42.5% of studied obese women compared to only 28% detected

in non obese one. Similar to these findings, mild to moderate acanthosis nigricans has been reported to occur more in obese PCOS women.<sup>15,18</sup> Also, hyperandrogenism was found in 47.5% of studied obese cases. Obesity may also contribute to features of hyperandrogenism even in women with normal ovaries.<sup>19</sup> It plays a pivotal role in the promotion or the maintenance of PCOS. Moreover, obesity seems to amplify the degree of hyperandrogenism in PCOS. Previous studies have shown that obese PCOS women have total and free testosterone levels higher with respect to non-obese PCOS. Abdominal obesity may also further worsen the hyperandrogenic state in PCOS women.<sup>19,20</sup> In the current study a higher mean testosterone level (110.7 ± 5.56) was detected in obese PCOS women.

As reported in a previous study that PCOS women may occasionally have acromegaloid features,<sup>21</sup> this study have found about one-fourth of the studied women to have had acromegalic features with no statistically significant difference between obese (27.5%) and non obese (26%.0%) PCOS women.

Endocrinal changes have been compared in the present study between obese and non obese PCOS women. FSH level was low in the studied obese women, meanwhile prolactin was high. Insignificant differences in the values of both estradiol and progesterone between obese and non obese PCOS were also detected. Increase of body weight and fat tissue in women was associated with several abnormalities of sex hormone balance,<sup>22</sup> and obesity per se represents a condition of functional hormonal imbalance. FSH plays a central role in the control of oogenesis, follicle development and gametogenesis.<sup>23,24</sup> Diminished secretion of FSH in PCOS can result in failure of gonadal function (hypogonadism).<sup>23</sup> This can also result from high prolactin levels; which tends to suppress the ovulatory cycle by inhibiting the secretion of FSH.<sup>25</sup>

As this study was performed in the outpatient clinics at Taibah University, Female section, the generalization of its results is difficult. It is also important to realize that results which come from one center may simply not be similar for other centers as differences in the socio-demographic characteristics of patients attending such centers. However, and according to our knowledge, this study is the first in our region to compare reproductive, clinical and laboratory data between obese and non obese PCOS women.

In summary, obesity appeared to further increase the reproductive, clinical and laboratory changes known to be associated with PCOS. Consequently, obese PCOS women tend to be at more risk of menstrual irregularities and obstetric complications. Also, signs of hyperandrogenism, acanthosis nigricans with endocrinal and hormonal disturbances tend to be more in obese than normal weight PCOS women. From these points of view, weight reduction should be included as an adjunct tool in the management plan for obese PCOS.

#### Conflict of interest

There is no conflict of interest to declare.

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