



## STUDY OF PREVALENCE AND PREVALENT PHENOTYPIC CHARACTERISTICS OF INFERTILE WOMEN WITH PCOS ATTENDING DEPARTMENT OF OBSTETRICS AND GYNECOLOGY / MOSUL GENERAL HOSPITAL IN IRAQ

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### ABSTRACT

Polycystic ovary syndrome (PCOS) is a major cause of anovulatory infertility worldwide. It is important to determine the prevalence and characteristic features of PCOS in different environments. This study aimed to determine the prevalence and the prevalent phenotypic characteristics of infertile patients with PCOS. This cross-sectional study was conducted on (87) women who attended the Department of Obstetrics and Gynecology / Mosul General hospital in Iraq between January and June 2019. Data collected from each patient included age, parity, height, weight, degree of hirsutism (using modified Ferriman-Gallway scoring), antral follicle count and ovarian volume. Other parameters included estimation of serum follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, progesterone and testosterone for each patient. Results showed that Polycystic ovarian syndrome (using Rotterdam criteria) occurred in 20.7% (18) of infertile patients. Hirsutism occurred in 61.1% (11) of infertile women with PCOS but in 13.3% (8) of infertile women with normal ovaries ( $P=0.005$ ). Oligomenorrhoea occurred in 27.7% (5) of infertile women with PCOS and in 3.3% (2) of infertile women with normal ovaries ( $P=0.03$ ). Significantly more infertile women PCOS had anovulation as the mean mid-luteal progesterone ( $5.21\pm 3.91$  ng/ml) was less than that for women with normal ovaries ( $18.12\pm 9.9$  ng/ml)  $P=0.005$  and higher mean testosterone level was also observed in infertile women with PCOS ( $0.99\pm 0.18$  IU/L) than in those with normal ovaries ( $0.41\pm 0.14$  IU/L)  $P < 0.005$ . It can be concluded from this study that the prevalence of PCOS in women with infertility was 20.7%. The infertile patients with PCOS had statistically higher occurrence of anovulatory cycle with oligomenorrhoea, hirsutism and serum testosterone levels compared to infertile women with normal ovaries.

**KEYWORDS:** Infertility; Polycystic Ovary Syndrome; Hyperandrogenaemia; Hirsutism; Oligomenorrea; Anovulatory infertility.

### INTRODUCTION

The vast majority of anovulatory infertility is caused by PCOS. PCOS has been documented as the commonest endocrine cause of anovulation and infertility.<sup>[1-4]</sup> Reports of classical appearance of polycystic ovaries (PCO) in normal healthy women without any endocrinopathy have been made, and so it is important to recognize a clear distinction between the normal women whose ovaries appear polycystic from women with clinical features that warrant the diagnosis of PCOS. Balen et al defined polycystic ovary as an ovary with at least 12 or more follicles measuring 2-9mm each in diameter in a single plain or an increased ovarian volume of more than  $10\text{cm}^3$  using transvaginal ultrasound scan.<sup>[5]</sup> The cysts in polycystic ovaries refer to antral follicles with arrested development. PCOS has been estimated to cause up to 75% of anovulatory infertility in some group of women.<sup>[6]</sup>

It is also estimated that nearly one out of every 4 women have polycystic ovaries (PCO) with a quarter of these women developing symptoms of PCOS.<sup>[2,7]</sup> The prevalence of PCOS varies widely across the globe and the population under study. This depends on ethnicity, race environment and the criteria used to make diagnosis of PCOS.<sup>[6,8]</sup> Globally, the prevalence of 5-10 % and 17-22%.<sup>[9-19]</sup> has been reported for PCOS and PCO respectively using the Rotterdam criteria.

The diagnosis of PCOS, using Rotterdam criteria, is made when at least two of the three identifying features are present. The presence of clinical or laboratory evidence hyperandrogenism, oligo/anovulation and polycystic ovaries on transvaginal scan are seen in a woman.<sup>[20]</sup> It is now generally accepted that the broad Rotterdam criteria (2011) for the diagnosis of PCOS be maintained and specific patient phenotypes identified for

each patient with PCOS as this has implications for early and late complications of PCOS.<sup>[21]</sup> PCOS is a clinical syndrome with varying clinical and biochemical features. It presents as a spectrum of endocrine, reproductive and metabolic disorders which could be mild affectations in some patients but severe disturbances in others. The key features of hyperandrogenism and anovulatory cycle, recognized as the classic phenotype in PCOS, occur in varying proportions in different patients.<sup>[10,15,17,19,21]</sup> The disturbance in reproduction presents as oligomenorrhea, amenorrhea, or dysfunctional uterine bleeding which is associated with anovulation and results in infertility.<sup>[17-19]</sup> Serum levels of hormones in the Hypothalamo Pituitary Ovarian axis may become deranged in women with PCOS. This is responsible for some of other endocrine manifestation of PCOS such as elevation of serum LH resulting in an increased LH/FSH ratio in some patients.<sup>[8,22]</sup> It has also been identified that PCOS can affect response to ovulation induction agents and can also result in early pregnancy miscarriages in infertile women.<sup>[23-25]</sup> However, the appearance of polycystic ovaries alone has not been shown to have any significant impact on the fertility of women who conceive naturally when they have no features suggestive of PCOS.<sup>[22]</sup>

## METHODOLOGY

This prospective cross-sectional study involved infertile women attending the Department of Obstetrics and Gynecology / Mosul General hospital in Iraq from January to June 2019. The sample size of (87) was determined using the formula for determining sample size for descriptive studies with the average prevalence rate of PCOS at 13% and 1.95 as the proportion of normal distribution corresponding to the required of significance level of 5%.

The socio-demographic information, clinical and laboratory characteristics of each patient was collected with a questionnaire. The data collected included age, marital status, occupation, level of education, parity,

menstrual history (with regular menses as menstrual cycles recurring every 21- 35days), oligomenorrhoea defined as menstrual cycles longer than 35days or less than 10 menstrual cycles per year. Physical examination was done for each patient and the data generated are height(m), weight(kg), score for hirsutism using modified Ferriman-Gallway score and presence of acne vulgaris. A transvaginal ultrasound scan was conducted on each patient to determine the number of antral follicles and the volume of each ovary. Venous blood was collected and serum levels of FSH, LH, Prolactin and testosterone were all determined in the follicular phase of the menstrual cycle. Venous blood was also collected in the mid luteal phase for the determination of serum progesterone. All serum hormone analyses were conducted using enzyme linked immunosorbent assay.

## Statistical analysis

Data analysis was done with SPSS statistical package version 20.0 The means and proportions of characteristics of infertile women with PCOS were compared to that of infertile women without PCOS using the student t-test and chi square test respectively. The level for statistical significance was set at  $\alpha < 0.05$  at 95% confidence interval.

## RESULTS

The mean age of infertile women studied was  $35.67 \pm 5.15$  years with a range of 16-44 years. Majority of the women were  $< 35$ . The mean age of infertile women with polycystic ovaries (PCO) and those with normal ovaries were  $34.12 \pm 4.0$  and  $31.64 \pm 5.2$  years. In the 87 infertile patients studied, about 69% (60) had normal ovaries while polycystic ovaries and polycystic ovarian syndrome were identified in 10.3% (9) and 20.7% (18) of the infertile women respectively. Oligomenorrhoea was statistically more in those with PCOS 27.7% (5) compared to 3.3% (2) of the infertile women with normal ovaries ( $P=0.03$ ) as seen in table (1).

**Table (1): Social and physical characteristics of the studied groups.**

Variables	Women with Normal Ovaries (N=60)	Women with Polycystic Ovaries Alone (N=9)	Women with Polycystic Ovary Syndrome (N=18)	P Value
Age				
< 35years	56(93.3%)	7(77.8%)	15(83.3%)	0.22
$\geq 35$ years	4(6.7%)	2(22.2%)	3(16.7%)	
Parity				
0	48(80.0%)	7(77.8%)	14(77.8%)	0.946
1	9(15.0%)	2(22.2%)	3(16.8%)	
>1	3(5.0%)	0(0.00%)	1(5.6%)	
Duration of Menstrual Flow (Days)				
<2 days	3(5.0%)	0(0.0%)	1(5.6%)	0.017
2 - 7days	56(93.3%)	9(100%)	13(72.2%)	
>7 days	1(1.7%)	0(0.0%)	4(22.2%)	
Menstrual Cycle Length (Days)				
<21	0 (0%)	0(0%)	1(5.6%)	0.03

21-35	58(96.7)	8(88.9%)	12(66.7%)	
>35	2(3.3%)	1(11.1%)	5(27.7%)	
Body Mass Index (Bmi)				
18.5–24.9 (normal)	17(28.3%)	1(11.1%)	2(11.1%)	0.169
25–29.9(pre-obesity)	26(43.3%)	5(55.6%)	12(66.6%)	
30.0- 34.9(class1)	16(26.7%)	2(22.2%)	2(11.1%)	
35.0 -39.9(class2)	1(1.7%)	1(11.1%)	1(5.6%)	
>40 (class 3)	0(0.0%)	0(0.0%)	1(5.6%)	
Hirsutism (F-G) Score Score				
0 – 8	52(86.7%)	8(88.9%)	7(38.9%)	0.005
8 –15	8(13.3%)	1(11.1%)	11(61.1%)	
>15	0	0	0	
Acne				
Present	19(31.7%)	7(77.8%)	7(38.9%)	0.029
Absent	41(68.3%)	2(22.2%)	11(61.1%)	

A total of 19 out of the 87 infertile patients had elevated testosterone levels, (14) (77.8%) out of 18 of those with PCOS had elevated testosterone, 16 (88.9%) of infertile women with PCOS had at least one polycystic ovary and 11 (61.1%) of those with PCOS had anovulation. Obesity occurred more often in the infertile women with normal ovaries compared to women with PCOS (28.4% versus 22.3%) but hirsutism and acne are significantly associated with the women with PCOS than those with normal ovaries (61.1% versus 13.3%) and (38.9% versus 31.7%).

There was significantly higher mean testosterone level in infertile patients with PCOS than those with normal ovaries ( $0.99 \pm 0.18$  IU/L versus  $0.41 \pm 0.14$  IU/L;  $P=0.005$ ). There was significantly lower mean mid luteal phase progesterone level in infertile women with PCOS

and those with normal ovaries ( $5.21 \pm 3.91$  ng/ml versus  $18.12 \pm 9.9$  ng/ml;  $P=0.005$ ). There was no significant difference in the mean luteinizing hormone level in the infertile patients with PCOS and those with normal ovaries ( $10.01 \pm 8.15$  IU/L versus  $6.71 \pm 6.04$  IU/L;  $P=0.157$ ). The mean follicle stimulating hormone level was higher in the infertile patients with PCOS than in those with normal ovaries ( $8.9 \pm 5.78$  IU/L versus  $5.82 \pm 4.99$  IU/L;  $P=0.088$ ). The mean prolactin level in infertile women with PCOS was not statistically different from those with normal ovaries ( $35.16 \pm 4.21$  IU/L versus  $30.69 \pm 7.92$  IU/L;  $P=0.077$ ). There was also no significant difference in the mean oestradiol level in the infertile patients with PCOS and those with normal ovaries ( $54.17 \pm 20.5$  versus  $51.68 \pm 15.01$ s;  $P=0.868$ ) as shown in table (2).

**Table (2): Serum hormone levels of the studied women.**

Variables	Women with Normal Ovaries (N=60)	Women with Polycystic Ovaries Alone (N=9)	Women with polycystic Ovary Syndrome N=18)	P Value
Mean Testosterone	$0.41 \pm 0.14$ IU/L	$0.45 \pm 0.31$ IU/L	$0.99 \pm 0.18$ IU/L	0.005
Mean LH	$6.71 \pm 6.04$ IU/L	$6.92 \pm 3.92$ IU/L	$10.01 \pm 8.15$ IU/L	0.157
Mean FSH	$5.82 \pm 4.99$ IU/L	$6.1 \pm 4.89$ IU/L	$8.9 \pm 5.78$ IU/L	0.088
Mean Prolactin	$30.69 \pm 7.92$ IU/L	$31.15 \pm 7.31$ IU/L	$35.16 \pm 4.21$ IU/L	0.077
Mean progesterone	$18.12 \pm 9.9$ ng/ml	$9.91 \pm 4.4$ ng/ml	$5.21 \pm 3.91$ ng/ml	0.005
Mean estradiol	$51.68 \pm 15.01$ IU/L	$52.68 \pm 26.1$ IU/L	$54.17 \pm 20.5$ IU/L	0.868

## DISCUSSION

This study showed that the prevalence of PCO and PCOS among infertile women were 10.3% and 20.7% respectively. This is comparable to the prevalence of PCOS of 18.1% in infertile women in a study in Nigeria, but lower than that found in some centres around the world such as Tanzania (32%), Iraq (74.6%), Iran (69.7%) and Denmark (68%).<sup>[23,26-31]</sup> Most of these reports reflecting the PCOS prevalence in general population and not just in women with infertility. This variation with several other studies may be due to racial or ethnic differences. It may also be due to the average age of the population studied, as wide variations exist in

population prevalence studies even when studies were based on the same Rotterdam criteria for the diagnosis of PCOS. Studies have also shown that typical polycystic ovarian morphology appeared to diminish with increasing age, so also the improvement with the menstrual cycle in the women with PCOS.<sup>[7,20,31,32]</sup>

This study showed that infertile women with polycystic ovarian syndrome significantly have anovulation with menstrual cycle affectation such as oligomenorrhoea in few of them and majority having normal duration of menstrual flow. This is similar to reports in some previous studies around the globe.<sup>[13,20,22]</sup> The only difference is that the percentage of infertile women with

polycystic ovaries that have oligomenorrhoea in this study was less than the percentage with oligomenorrhoea in these other studies.<sup>[19,2,30]</sup>

In a similar study to this study, it was shown that 90.7% of the non-PCOS group versus 7.5% of the PCOS group showed ovulatory cycles and another study also showed a low progesterone level (confirming anovulation) in patients with PCOS.<sup>[25,26]</sup>

The data showed that over 80% of those with PCOS had elevated testosterone levels and over 77.8% had at least one polycystic ovary. Anovulation tend to be frequent with a low mid-luteal phase progesterone despite fairly regular menstrual cycle in the majority of these infertile women with PCOS. The predominant phenotype for this group of infertile women with PCOS appears to be that of hyperandrogenaemia, polycystic ovary morphology.

Association of PCOS with obesity had been noted in infertile women in some regions of the world but absent in women in other regions.<sup>[23,30-35]</sup> It is difficult to associate the obesity in this study with PCOS, however obesity is known to exacerbate symptoms of PCOS and to cause poor response to ovulation induction agents in patients with PCOS.<sup>[36]</sup>

In this study, the mean serum LH and FSH levels in those with PCOS were more than in those with normal ovaries. This is similar to the finding of many authors.<sup>[23,30,34]</sup> However, there are inconsistencies in the levels of LH and FSH in women with PCOS in different reports by different authors reportedly make the levels of these hormones inappropriate for use as diagnostic criteria for PCOS.

This study revealed that there was no significant difference in mean prolactin level between infertile women with PCOS and those without PCOS as previously observed.<sup>[26,35]</sup> Hyperprolactinemia produces similar symptoms to PCOS and need to be excluded in patients suspected to have PCOS.<sup>[34]</sup> Prolactin levels have however been shown to be unaffected in patients with PCOS.<sup>[32]</sup>

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