

ORIGINAL STUDY

# Clinical and Hormonal Profile of Polycystic Ovary Syndrome

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## Abstract

**Objectives:** The objectives of the study were to find out the clinical features, biochemical and hormonal profile of patients with polycystic ovary syndrome (PCOS) in Bangladesh.

**Material and Methods:** A case control and cross-sectional study was undertaken among 78 PCOS patients attending infertility clinic and 33 controls at BIRDEM Hospital, Dhaka. Inclusion criteria for cases were oligo/amenorrhea, transvaginal sonography suggesting PCO and/or features of hyperandrogenemia with exclusion of other causes. Controls were women with regular menstrual cycle.

**Results:** Age and height of cases and controls were similar. BMI >25 was 67% among cases and 19% among controls ( $P<0.001$ ); waist hip ratio >0.8 was 64% among cases and 29% among controls ( $P<0.001$ ). Mean BMI of cases was  $28.2 \pm 4.5$  and that of controls was  $21.05 \pm 4.1$ ; mean fasting glucose among cases was  $5.93 \pm 1.08$  and among controls was  $4.4 \pm 1.11$  mmol/L ( $P<0.01$ ); mean fasting serum insulin level was  $32.15 \pm 12.13$  among cases and  $11.32 \pm 10.02$   $\mu$ U/ml among controls ( $P<0.001$ ); insulin resistance (fasting HOMA-IR >6.8) was 42.32% in cases and 12% in control ( $P<0.001$ ). Patients with PCOS had following clinical and biochemical parameters: oligomenorrhea-74%, amenorrhea-26%, mean Ferriman-Galaway score  $-19.89 \pm 5.06$ . At day 3 of menstrual cycle mean serum LH was  $12.79 \pm 7.1$   $\mu$ /ml, serum FSH was  $5.23 \pm 2.5$  mIU/ml and serum prolactin was  $415.15 \pm 180.5$   $\mu$ iu/ml; 30% had biochemical hyperandrogenemia.

**Conclusions:** PCOS patient in Bangladesh are usually overweight, hirsute (grade I and II), hyperandrogenemic, insulin resistant and have altered LH to FSH ratio.

**Keywords:** PCOS, polycystic ovary syndrome, PCO, insulin resistance, hyperandrogenemia.

## INTRODUCTION

The polycystic ovary syndrome (PCOS) is considered the most common gynecological endocrinopathy characterized by hyperandrogenism.<sup>1</sup> Stein and Leventhal described for the first time in 1935 the association of bilateral polycystic ovaries (PCO)

and amenorrhea, oligomenorrhea, hirsutism and obesity.<sup>2</sup> The term "PCOS" came into use in the 1960s with the recognition of the clinical and histological diversity of this syndrome.<sup>3</sup> In the USA, at the National Institute of Health (NIH) Conference on PCOS in 1990, three minimal criteria for the diagnosis of PCOS were proposed: (1) menstrual irregularity, (2) evidence of hyperandrogenism, either clinical (hirsutism, acne, or male pattern balding) or biochemical (elevated androgen levels), and (3) the exclusion of other diseases (hyperprolactinemia, thyroid disorders and nonclassical adrenal hyperplasia).<sup>4</sup>

The 2003 Rotterdam consensus workshop concluded that PCOS is a syndrome of ovarian dysfunction along with the cardinal features hyperandrogenism and polycystic ovary (PCO) morphology.<sup>5</sup> PCOS remains a syndrome, and as such no single diagnostic criterion (such as hyperandrogenism or PCO) is sufficient for clinical diagnosis.<sup>5</sup> The presentation of the patients of PCOS are variously described in different literature.<sup>6-8</sup> Its clinical manifestations may include menstrual irregularities, signs of androgen excess, and obesity. Insulin resistance and elevated serum LH levels are also common features in PCOS. PCOS is associated with an increased risk of type 2 diabetes and cardiovascular events.<sup>5</sup> In a recent study conducted in the USA, in which the NIH "consensus" definition was used, the prevalence of PCOS was 4.6% (range 3.5 to 11.2%).<sup>4</sup> The prevalence of PCO only has varied between 20 and 25% in previous studies.<sup>9</sup> In Bangladesh 28.8% infertile women were diagnosed as cases of PCOS in a teaching hospital (Polycystic ovary as a cause of infertility).<sup>10</sup> The objectives of the study were to find out the clinical features, biochemical and hormonal profile of patients with polycystic ovary syndrome (PCOS) in Bangladesh.

## PATIENTS AND METHOD

The study was carried out between January 2002 to December 2003 in Bangladesh Institute of Research and Rehabilitation in

Diabetes, Endocrine and Metabolic Disorder (BIRDEM), Dhaka, Bangladesh, a tertiary hospital and the only WHO collaborating Center for prevention and control of diabetes in south east Asia region. It was a cross-sectional and case control study. Seventy eight patients of PCOS and 33 controls were studied according to inclusion and exclusion criteria. The study group were women presenting with oligo/amenorrhea, nonpregnant, between 15 to 35 years of age, hyperandrogenemic (Clinical and/or biochemical) and diagnosed as polycystic ovary syndrome (PCOS); not taking medication like oral contraceptive pill (OCP), antidiabetic or antihypertensive medicine for last six months and had altered LH and FSH ratio. Exclusion criteria of the study group were pregnancy; systemic disease (liver, kidney, heart or any other systemic diseases); age >35 years and <15 years; patient taking any of the above mentioned medications and associated other endocrine disorder, e.g. hypothyroidism, hyperprolactinemia and congenital adrenal hyperplasia. The control group were healthy female subjects selected from among the staffs of BIRDEM or their relatives. After fulfilling the selection criteria, informed written consent was obtained.

A detailed history was obtained. All findings were recorded in a preformed data collection instrument. Height in cm (bare foot, standing erect against wall), weight in kg (in a weighting scale, bare foot, light clothing), waist circumference in cm (minimum circumference at the waist level); hip circumference in cm (maximum circumference below the level of umbilicus) was measured by the principal investigator. Hormone profile was done on day three of menstrual cycle. For amenorrhatic patients blood was drawn any day of the cycle. Fasting venous blood was drawn with a 21G intravenous cannula for fasting blood sugar, insulin, FSH, LH, TSH, Prolactin, DHEAS, total testosterone. Patient was allowed to drink 75G Glucose solution and blood was again drawn after two hours. Hormone assay was done in the endocrine laboratory of BIRDEM by AXSYM Antianalyzer by MEIA method (Microparticle Enzyme Immuno Assay) and blood glucose was estimated by glucose-oxidase method by SIMENS autoanalyzer. Insulin was measured by AXSYM system of assay. Ferriman-Galaway score(FGS) was used to categorize hirsutism. Insulin resistance (IR) was measured by HOMA-IR (Homeostatic Model Assessment of Insulin Resistant) was calculated by the formula:  $IR = \text{Fasting insulin } \mu\text{u/ml} \times \text{fasting glucose (mmol)}/22.5$ . Cut of level for IR was taken as 6.8. SPSS program was used for data analysis. Pre and Postintervention quantitative data was analyzed through t-test and proportion analysis through Z test.

**RESULTS**

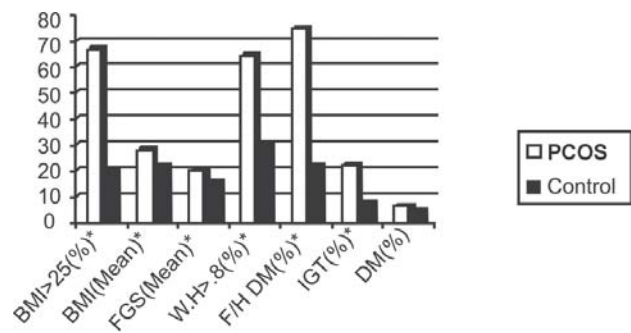
The background characteristics of the study and controls were similar (Table 1). Figure 1 shows the clinical profile of study control group body mass index (BMI) of study and control group differ significantly( $28.2 \pm 4.5$  vs.  $21.05 \pm 4.1$ ;  $P < 0.001$ );

67% of the PCOS patient and 19% of controls had BMI >25, ( $P,0.001$ ); 64% of the PCOS patients and 29% of the controls had waist to hip ratio >0.8, ( $p < 0.001$ ); 75% of PCOS patients and 19% of the controls had history of the diabetes mellitus among close relatives, ( $p < 0.0001$ ); 22% of PCOS patients and 7.5% controls had impaired glucose tolerance(IGT); and 6% of PCOS patients and 4% of controls had diabetes mellitus (NS).

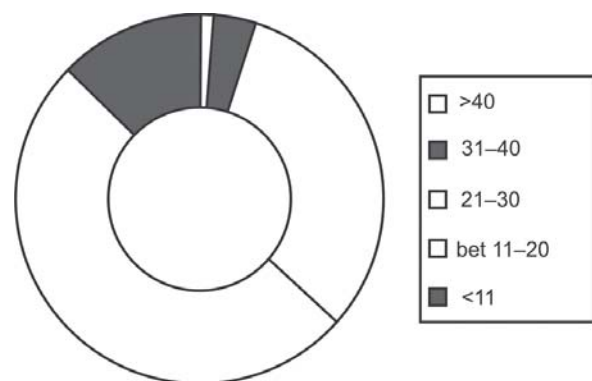
**Table 1:** Background characteristics of study and control group

Particulars	Study group (mean range)	Control group	P value
Age (years)	22.67 (18–35)	21.50 (20–35)	NS
Height(cm)	155.25 (140–169)	158.25 (141–170)	NS

Hirsutism was categorized by Ferriman-Galaway score (FGS). Score 11-20 Grade-I; 21-30 Grade-II, 31-40: Grade-III and >40 Grade-IV and score <11 was considered normal. Among the PCOS patient mean FGS was 19.7%. FGS of the control group was 13.5% ( $p < .05$ ) (Fig. 1). Among PCOS patients 1.5% had FG score >40; 3.1% had FG score 31-40; 32% had FGS 21-30; 51% had FG score 11-20 (Fig. 2). Among the PCOS patients 74% presented with oligomenorrhea and 26% with amenorrhea (Fig. 3).



**Fig. 1:** Clinical profile of PCOS and controls (Statistically significant)



**Fig. 2:** Ferriman-Galaway score(Hirsutism)



**Fig. 3:** Menstrual irregularities among PCOS patients

Table 2 shows the hormone profile of PCOS patients and controls. Mean LH of PCOS group was  $12.79\% \pm 7.1$  mIU/ml and that of control group was  $4.67 \pm 3.1$  ( $P < .05$ ). Mean FSH of study group was  $5.23 \pm 2.5$  mIU/ml and that of controls was  $3.25 \pm 2.3$  mIU/ml ( $P < .05$ ). Mean prolactin level was  $415.15 \pm 780.5$   $\mu$ IU/ml in study group and  $389.21 \pm 121.3$   $\mu$ IU/ml in controls, (NS). Reference range for LH is taken as 1.2-12.5 mIU/ml and that of FSH as 3.2-10 mIU/ml for adult female. LH: FSH was  $>2$  in 51%; between 1 and 2 in 34% and upto 1 in 15% of PCOS patient.

Fasting blood sugar (FBS) was  $5.93 \pm 1.08$  mmol/L among PCOS and  $4.4 \pm 1.11$  mmol/L among controls ( $P < 0.01$ ). Fasting Insulin level was  $30.15 \pm 12.13$  among PCOS patients and  $11.32 \pm 10.02$   $\mu$ U/ml among controls. Mean fasting HOMA-IR was  $5.72 \pm 1.6$  among PCOS and  $4.42 \pm 0.47$  among controls ( $< 0.05$ ); 42% of PCOS patients and 12% of controls had fasting HOMA-IR  $> 6.8$  ( $p < 0.001$ ) Reference value to serum testosterone (total) in adult female is 0.2-0.9 mg/ml: 30% of PCOS patients had serum testosterone level above 0.9 mg/ml. Total testosterone level (mean) was  $0.85 \pm .41$  and  $.49 \pm 0.21$  among PCOS and controls respectively ( $< 0.05$ ).

## DISCUSSION

Women with PCOS are on an average more obese than their non-PCOS counterparts; with 50% having a BMI over 30 kg/ml;<sup>11,12</sup> 61% of PCOS patients were found to be obese.<sup>13</sup> Among PCOS patient 47% had oligomenorrhea and 19.2% had amenorrhea<sup>6</sup>. Oligomenorrhea and amenorrhea was found in

52% and 26% by Franks ( $n = 300$ )<sup>1</sup> and 29% and 51% by Goldzieher ( $n = 1079$ ).<sup>14</sup> Hirsutism was found by 66%<sup>6</sup>, 64%<sup>1</sup> and 69%<sup>14</sup> among PCOS patients. Mean FGS was found to be  $20.1 \pm 6.08$  among PCOS patients.<sup>13</sup>

The prevalence of hyperandrogenism within different group and ages for women with PCOS has not been determined. It appears that age has a major effect with younger women more likely to experience acne and hirsutism and androgenic alopecia. In a large multicentric trial on an insulin sensitizing agents in PCOS, only 50% of the randomized subjects had evidence of hirsutism.<sup>15</sup> There is racial differences with hirsutism being significantly less prevalent in hyperandrogenic women of Eastern Asian origin and more so, in those from southern Asia.<sup>16</sup> Serum LH concentrations are significantly elevated in PCOS women as compared to controls.<sup>17-19</sup> This is due to an increased amplitude and frequency of LH pulses.<sup>20</sup> Elevated LH Concentrations (above 95th percentile of normal) can be observed in approximately 40-60% of PCOS women.<sup>6,7,21</sup> Changes in pulsatility of GnRH are thought to alter the ratio of secretion of two pituitary gonadotrophins throughout the menstrual cycle. When GnRH pulsatility is slow, FSH secretion predominates and when rapid, LH secretion predominates. There have been a large number of studies demonstrating increased insulin resistance in both obese and nonobese women while others failed to demonstrate IR in nonobese women.<sup>22-24</sup>

From the findings of the study following conclusions can be drawn about PCOS patients of Bangladesh: they are usually overweight; menstrual irregularities ranges from oligomenorrhea to amenorrhea; they are androgenemic either clinically and/or biochemically; they usually present with grade I and grade II hirsutism; LH : FSH  $< 2$  was found significantly higher among PCOS patients; most of the PCOS patients are insulin resistance and majority of the patient had family history of diabetes mellitus.

**Table 2:** Hormone profile of study and control group

Variable	Study group (mean range)	Control group	P value
LH (mIU/ml)	$12.79 \pm 7.1$	$4.67 \pm 3.1$	$< .05$
FSH (mIU/ml)	$5.23 \pm 2.5$	$3.25 \pm 2.3$	$< .05$
Prolactin ( $\mu$ IU/ml)	$415.15 \pm 180.5$	$389.21 \pm 121.3$	NS
Fasting blood sugar (mmol/L)	$5.93 \pm 1.08$	$4.4 \pm 1.11$	$< .05$
Fasting Insulin ( $\mu$ U/ml)	$30.15 \pm 12.13$	$11.32 \pm 10.02$	$< .001$
Fasting HOMA-IR. $>6.8$	42%	12%	$< .001$
Total testosterone $>.9$ mg/ml	30%	0%	
Total testosterone (mean)	$.85 \pm .41$	$.49 \pm .21$	$< .05$

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