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Polycystic Ovarian Syndrome: Clinical Correlation with Biochemical Status

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ABSTRACT

Objective: To find out the correlation between various biochemical and clinical features of polycystic ovarian syndrome and to determine the best hormonal marker for the same. **Material and Methods:** The study included 100 patients of polycystic ovary syndrome (50 married & 50 unmarried) and a control group comprising of 50 women (25 married & 25 unmarried) in the age group of 18 - 30 years. The pregnant females and those having hyperandrogenism due to any other endocrine disorders were excluded. **Results:** Mean age was 27.66 years in the married study group and 25.46 years in the unmarried study group. About 71% of patients had oligomenorrhea. It significantly correlated with raised LH:FSH ratio and raised total testosterone levels. Body mass index was raised (>25 kg/m^2) in 66.7% married and 72.66% unmarried patients in study group and in 22% in control group. 95% of the patients in the study group and 4% in the control group were detected to have polycystic ovaries on ultrasonography. 62% of the patients had raised LH levels; total testosterone was elevated in 57.7%. The LH:FSH ratio was raised in 41% in study group patients more in the unmarried group 56% than in married group 26%. 20% of patients in the control group had an elevated LH:FSH ratio. Total testosterone level was elevated in 60% of our patients. None of the patient in the control group had elevated testosterone levels. About 31% of the patients in study group were hirsute. **Conclusion:** Hormonal values correlate well with polycystic ovarian syndrome and serum total testosterone served as the best hormonal marker for such patients.

Keywords: Polycystic Ovarian Syndrome; Hormonal Analysis; Clinical Correlation; Best Marker

1. Introduction

Polycystic ovary syndrome (PCOS) is a common heterogeneous endocrinological disorder that occurs in 5% to 10% women in reproductive age group. It is the most prevalent endocrinopathy and common cause of infertility [1]. Polycystic ovary syndrome consist of Chronic anovulation, menstrual disturbance, hyperandrogenism, polycystic ovaries, metabolic syndrome [2-4]. The current definition of PCOS is based on Rotterdam consensus meeting in 2003. It defines the syndrome as presence of any two of the following three criteria.

1) Menstrual disturbance; oligomenorrhoea/anovulation.

2) Clinical and/or biochemical signs of hyperandrogenism like acne, hirsutism etc., after other causes of hyperandrogenism have been ruled out.

3) Ultrasound appearance of polycystic ovary as polycystic adnexae [5,6].

The etiology of this disorder is still uncertain, although it has been recognized in a familial pattern suggesting genetic etiology. The rate of PCOS in first degree relative is 33% [7]. PCOS is associated with various endocrine abnormalities such as increased serum LH levels, increased ratio of LH:FSH, increased serum testosterone. Estimation of these hormones aids in the diagnosis. In PCOS ovary is enlarged >9 ml in volume, is smooth, sclerotic, has thickened capsular & subcapsular follicular cysts with atresia and hyperplastic theca and stroma [8]. Polycystic ovary contain 2-3 fold the normal number of follicles [8]. A classical ultrasound features of polycystic ovary syndrome described by (Adam *et al.* 1985) which included enlarged ovary with presence of 10 or more cysts 2-8 mm in diameter arranged either peripherally "string of pearls "around dense core of stroma or scattered throughout an increased amount of stroma. Hyperandrogenism is the second common defining characteristic features of PCOS. The increased androgen levels are principally ovarian in origin, clinically commonly manifested by hirsutism, and acne. 70% of patients with PCOS present with hirsutism [6]. Most of the late complications of PCOS are related to insulin resistance. In mild Insulin resistances, patients will have slightly elevated fasting serum insulin levels whereas in severe forms it may manifest with acanthosis nigricans [9]. Although all women with PCOS have evidence of insulin resistance it is more pronounced

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in those with chronic anovulation [8]. 50% of patients with PCOS are obese [8,9]. Patients with PCOS have central obesity, increased deposition of fat around waist (an apple shaped instead of pear shaped). The obesity is android in type with increased waist to hip ratio & fat in anterior abdominal wall & mesentry [9]. Another risk of insulin resistance is the development of type 2 diabetes. More than 40% of women with PCOS demonstrate impaired glucose tolerance test, 10% have type 2 diabetes [1,9]. PCOS patients are at increased risk of cardiovascular disorders such as myocardial dysfunction, stroke and hypertension [9,10]. PCOS patients are at increased risk of developing endometrial carcinoma, due to increased circulating estrogen mainly estrone and unopposed action of progesterone [10]. These women also have increased chance of developing ovarian carcinoma, breast cancer and also carcinoma colon [9-11]. Our primary aim to conduct this study was to find out the correlation between various biochemical and clinical features of polycystic ovarian syndrome and to determine the best hormonal marker for the same.

2. Material and Methods

This prospective study included 100 patients of polycystic ovary syndrome (50 married & 50 unmarried) and a control group comprising of 50 (25 married & 25 unmarried) women in the age group of 18 - 30 years. The Exclusion criteria were pregnancy and hyperandrogenism due to any other endocrine disorders. Patients were evaluated on outpatient basis and complete history was taken especially menstrual and obstetric. Obstetric history included fertility status of the patient classified as fertile (had previous pregnancy with no subsequent infertility), infertile (primary or secondary infertility of at least 1year duration), unproven (pregnancy not attempted). Clinical examination focused on anthropometry; height in cm, weight in kg. BMI > 25 kg/m^2 was taken significant. Waist: hip ratio was calculated and a value of >0.88 was taken significant. Hirsutism was graded on the bases of Ferriman Galleway score. A Score > 8 was taken significant. Each patient underwent an ultrasound examination with a probe of 3.5 MHz. Cysts > 5 - 9 mm in diameter and >5 in single ovary was taken significant. For hormonal assessment blood sample was taken either in morning or after 10 - 12 hrs fasting and analyzed for LH, FSH, and total testosterone. Samples were taken in early follicular phase (day 2/3 of cycle) in a women with normal menstrual rhythm and at random in women with oligomenorrhea. For FSH normal values were taken as 3 - 4.3 mIU/ml. For LH normal values were taken as 4.2 - 6.3 mIU/ml. LH:FSH ratio 2:1 was taken significant.

3. Results and Analysis

1) Age: The age in our study was 19 - 30 years. Mean age was 27.66 years in the married Study group and 25.46 years in unmarried study group.

2) BMI was raised >25 kg/m^2 in 66.7% married and 72.66% unmarried patients in study group and 22% in control group.

3) Infertility: Prevalence of infertility in our study group was 74%.

4) 71% of patients had oligomenorrhea. It was most common symptom in unmarried study group and second common complaint in married group. It was found to be significantly correlated with raised LH:FSH ratio and raised total testosterone levels. There was statistically significance of raised LH with oligomenorrhea.

5) In our study weight gain was found in 16% of patients in married group and 22% of the unmarried group it was the second commonest complaint seen in unmarried group.

6) 31% patients were hirsute.

7) 95% study group & 4% control group were detected to have polycystic ovaries on ultrasound (USG) examination. The sensitivity of USG in our study was 95%.and specificity 96%. 5% of our patients had normal ovaries on USG and 4% of normal females had PCO on USG.

8) 63% patients in the study group had raised LH while as total testosterone was elevated in 57.7%. Hormone analysis was done on day 2 - 3 of the menstrual cycle. There was significant difference in hormone profile of the study and control group. Total Testosterone level was elevated in 60% of our patients. None of the patient in the control group had elevated testosterone levels. In our study positive predictive value of total testosterone was 93.3% in patients with USG documented PCO. In our study LH was raised in 63% patients and 32% controls. The LH:FSH ratio was raised in 41% in study group patients more in the unmarried group 56%. In married group 26% patients had raised LH:FSH ratio. 20% of patients in the control group had an elevated LH:FSH ratio.

4. Discussion

The study group included 100 women and a control group of 50 women. The two were similar in their demographic profiles. The age in our study was 19 - 30 years. Mean age was 27.66 years in the married study group and 25.46 years in unmarried study group. Most of the previous studies focused on the similar age groups. Ahmed Abdul Nasr (2004) conducted a study on oligomenorrheic infertile women, & included patients with age group of 21 - 35 years [12]. Sharquie *et al.* 2007 included patients in the age group of 15 - 39 (mean 26.12 +/– 6.36) in their study [13]. Prevalence of PCOS in our study was 19.7%. Fouzia Nazir *et al.* (1999) conducted a retrospective study on 52 women having polycystic ovary syndrome with fertility deprivation [14]. The prevalence of PCOS in their study was found 20.7% which is almost

similar to our study. Ahemad Aboul Nasr *et al.* (2004) conducted a prospective study on 50 patients to assess the morphological findings of the ovary based on transvaginal ultrasound in infertile oligomenorrheic women and their predictivity for endocrine sign of polycystic ovary syndrome. They found prevalence of PCOS in their study was 22%. R. Hart *et al.* (2004) concluded that PCOS perplexing endocrine disorder of women in their reproductive years with prevalence up to 10%. Abdul Ahad Zargar *et al.* (2005) conducted a study on 105 patients < 45 yrs. They found prevalence of PCOS in their study was 5% - 10% [1]. Prevalence of infertility in our study was 74%. Fouzia Nazir *et al.* (1999) found primary infertility in 75% of patients [14]. Fouzia Haq *et al.*; (2007) evaluated a total of 508 patients for epidemiological features of PCOS. Frequency of PCOS in infertileity clinic was 17.6% [15]. In our study 71% of patients had oligomenorrhea. It was most common symptom in unmarried study group and second common complaint in married group. Fouzia Nazir *et al.* (1999) found 75% patients had oligomenorrhea in their study. Fouzia Adil *et al.* (2005) conducted a study on polycystic ovary syndrome found oligomenorrhea in 79% [16]. H. Hassa *et al.* (2006) conducted a retrospective study to determine the hormonal and clinical profiles of polycystic ovarian syndrome. 46% patients in their study had oligomenorrhea [17]. On correlating oligomenorrhea with hormone levels we found that it significantly correlated with raised LH:FSH ratio and raised total testosterone levels. There was statistical significance of raised LH with oligomenorrhea. Abdul Razak *et al.* (2007) [18] concluded that oligomenorrhea correlated with raised LH:FSH ratio [17]. 95% study group & 4% control group were detected to have polycystic ovaries on USG. Sensitivity of USG in our study was 95% and specificity 96%. Sharquie *et al.* (2007) conducted a study to evaluate hormonal changes and pelvic sonography in patients of PCOS USG findings was positive in 80% of patients. Battacharya Dipankar *et al.* (2005) found USG to be sensitive but not specific. 5% of our patients had normal ovaries on USG and 4% of normal females had PCO on USG. Ahmed Aboul Nasr *et al.* (2004) conducted a study on 50 infertile oligomenorrhric patients in the age group of 21 - 35 yrs. This study includes patients with infertility and oligomenorrhea only whereas our study include other parameters like weight gain, hirsutism as well. Polycystic ovaries was observed in 20% of normal control patients in this study. We analyzed patients who had PCO on USG with there hormonal pattern. 63% had raised LH, total testosterone was elevated in 57.7%. Ahemad Aboul Nasr *et al.* (2004) conducted a prospective study to assess the morphological findings of the ovary based on transvaginal ultrasound in infertile oligomenorrheic women and their predictivity for endocrine sign of polycystic ovary syn-

drome. The hormonal characteristics in the form of high LH, and high total testosterone showed statistically significant difference between study and control group (P < 0.05). About 31% patients were hirsute. Pache TD *et al.* (1993) conducted a study on 95 patients and found hirsutism in 63% patients. Fouzia Nazir (1999) conducted a study on diagnosis and management in fertility deprivation in patients of PCOS found the hirsutism in 84.6% of patients. Abdul Razzak *et al.* (2007) found 64.49% patients hirsute. The weight gain was found in 16% of patients in married group and 22% of the unmarried group it was the second commonest complaint seen in unmarried group .Fouzia Adil *et al.* (2005) found 50% of patients were obese. Fouzia haq *et al.* (2007) found obesity in 68.5% of patients. It was the commonest complaint seen in their study. Abdul Razzak *et al.* (2007) conducted a study and found 63.55% patients were obese. Sharquie *et al.* (2007) found obesity in 80% of patients. BMI was raised >25 kg/m^2 in 66.7 % married and 72.66% unmarried patients in study group and 22% in control group. Fouzia Nazir *et al.* (1999) had 86.5% of patients with BMI > 25 kg/m^2. Battacharya Dipankar *et al.* (2005) study had mean BMI of 28.98 kg/m^2 (mean 25 - 39). Abdul Razzak *et al.* (2007) had 63.55% of patients with weight > 25kg/m^2 in his study. The result of their study is almost similar to our study. Total Testosterone level was elevated in 60% of our patients. None of the patient in the control group had elevated testosterone levels. In our study positive predictive value of total testosterone was 93.3% in patients with USG documented PCO. K. Michelmore *et al.* (1999) found elevated total testosterone level in patients with PCOS. Analysis of their biochemical data showed that women with polycystic ovaries had higher total testosterone levels than in women with normal ovaries (P = 0.03 Sharquie *et al.* (2007) found that total Testosterone levels were seen elevated in 60% of patients in the study the results are in agreement with results obtained in our study. S. Robinbson *et al.* (1992) conducted a study to assess frequency of abnormal values for hormone measurement used in biochemical diagnosis of PCOS They concluded that the total testosterone hormone level was raised in 70% of patients They concluded total testosterone as best hormonal marker for the condition and was the single most diagnostic test. Total testosterone was the best hormonal marker in our study as well. LH was raised in 63% patients and 32% controls. Ahmed Aboul Nasr *et al.* (2004) concluded that LH elevated in 86.7% of patients. Robinsons *et al.* 1992 found LH abnormality in 35% of patients in our study raised LH correlated significantly with oligomenorrhea. J. Holte *et al.* (1994) study found mean concentration of LH to be elevated in patients with PCOS. LH:FSH ratio was raised in 41% in study group patients more in the unmarried group 56%. In married group 26%

patients had raised LH:FSH ratio. 20% of patients in the control group had an elevated LH:FSH ratio. Fouzia Nazir *et al.* (1999) found high LH:FSH ratio in 75% of patients. Fouzia Aadil *et al.* (2005). 67.42% patients were having elevated ratio LH:FSH in their study. Ratio was significant and abnormally raised in 41% - 44% of patients in study of Robinson Set *et al.* (1992). The results are similar to the results derived from our study. Battacharya Dipankar *et al.* (2005) found LH:FSH ratio increased in 55.55% of patients. Sharquie *et al.* (2007), 60% of patients were having raised LH:FSH ratio.

5. Conclusions

From the present study we can draw the following conclusions for our population: Raised LH has statistically significant correlation with oligomenorrhea. It also correlated significantly with raised LH:FSH ratio and increased testosterone levels. Total Testosterone which was elevated in 60% of patients in PCOS proved to be the best hormonal marker for patients of PCOS.

However a larger study is required to exactly find the prevalence of disease as well as the correlation of different parameters commonly found in this disease.

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