Serum free testosterone levels in polycystic ovarian syndrome patients and its correlation with clinical hyperandrogenism in Pakistan

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is the most frequent pathology among women of reproductive age characterized by menstrual irregularities, hyperandrogenism and polycystic ovaries on ultrasound. Evidence suggests that high androgen levels are the fundamental factor in the pathogenesis of PCOS. The objectives of the present study was to determine serum free testosterone levels in polycystic ovarian syndrome patients, and observe its correlation with clinical hyperandrogenism.

Patients and methods: This cross-sectional study was conducted at Jinnah Allama Iqbal Institute of Diabetes and Endocrinology Lahore, Pakistan from 15th May 2019 to 15th November 2019. The study included 140 patients of PCOS diagnosed as per Rotterdam criteria. Serum testosterone levels were determined in these patients by ELISA method. Ferriman-Gallwey (FG) score was used to assess severity of clinical hyperandrogenism in the form of hirsutism. Patients were categorized into three groups, mild (FG score 8-15), moderate (FG score 15-25) and severe (FG score >25). Correlation between clinical (hirsutism) and biochemical hyperandrogenism (serum free testosterone levels) was assessed using Fisher exact test. Data was analyzed using SPSS version 25.

Results: Biochemical hyperandrogenism in the form of raised free testosterone levels was present in 46 (32.9%) PCOS patients. Out of 12 patients having Ferriman Gallwey score >25, 10 (83.3%) had biochemical hyperandrogenism. Out of 70 patients having Ferriman Gallwey score 15-25, 22 (31.4%) had biochemical hyperandrogenism whereas out of 58 patients having Ferriman Gallwey score 8-15, only 14 (24.1%) patients had biochemical hyperandrogenism.

Conclusion: Prevalence of biochemical hyperandrogenism in PCOS patients in our studied population was significantly low when compared to the population studied worldwide making it less reliable as diagnostic tool in this part of the world. Also there was significant positive correlation between free testosterone levels and degree of hirsutism which means that diagnostic accuracy of free testosterone in PCOS patients is considerably high in those having clinical hyperandrogenism.

Keywords: Polycystic ovarian syndrome; Hyperandrogenism; Free testosterone

INTRODUCTION

Women in reproductive age group encounter a most frequent pathology known as polycystic ovarian syndrome (PCOs). The foremost characteristics of this condition comprise of anovulation or chronic oligo-ovulation, hyperandrogenism (clinical, biochemical), menstrual irregularity, infertility, and dermatological conditions as acne, alopecia. Various associated risk factors with this condition are obesity, insulin resistance, hyperinsulinemia and chronic diseases like type 2 diabetes mellitus, and cardiovascular diseases. PCOS and its manifestations can result in significant psychosocial, emotional morbidity and low quality of life. Prevalence of PCOS is dependent on age of the women, about 21.6% in women <35 years of age and about 7.9% in women aged >35 years. In a study conducted on Indian adolescents applying Rotterdam criteria to diagnose PCOs, about 9.13% subjects were found to have PCOS. Another data collected in Spain revealed 6.5% women to be affected with PCOs. Among Pakistani women, prevalence of PCOs is 10% which is lower when compared with the white population i.e. 20-25% in United Kingdom. Metabolic syndrome is more prevalent among women with PCOs when compared with the women in the general population.
population, and about half of the women with this condition are obese.9

In 2003, endocrinologists reached a consensus regarding the diagnostic criteria of polycystic ovarian syndrome termed as the Rotterdam criteria and is still widely used. According to Rotterdam criteria, presence of two out of the following three criteria (clinical or biochemical hyperandrogenemia, menstrual disturbance, polycystic ovaries on ultrasound) is consistent with the diagnosis of polycystic ovarian syndrome.10,11 In women with clinical hyperandrogenism (hirsutism, acne, or male-pattern hair loss on exam), we suggest measuring serum total testosterone.

There is accumulating evidence that high androgen levels i.e. serum total and free testosterone levels are the fundamental factor in the pathogenesis of PCOS.12 In a study on Greece population, the prevalence of biochemical hyperandrogenemia was 58.8% among PCOS patients.13 In another study from Germany, Elisabeth Lorchbaum et al found that 85.6% PCOS patients had evidence of biochemical hyperandrogenemia.14 Objective of the present study was to compare the prevalence of biochemical hyperandrogenism in PCOS patients in our studied population with the worldwide available literature and observe the correlation between clinical and biochemical hyperandrogenism.

PATIENTS AND METHODS
This cross sectional study was conducted at Jinnah Allama Iqbal Institute of Diabetes and Endocrinology (JAIDE) Lahore Pakistan over a period of 6 months from 15th May 2019 till 15th November 2019. Sample selection was done with the help of non-probability purposive sampling technique.

Patients were selected with the help of predefined sample selection criteria. All patients with diagnosed PCOS aged between 15 to 40 years were included in the study. Rotterdam criterion was used for the confirming the diagnosis of PCOS. According to this criteria, 2 out of the 3 (Oligo- and/or anovulation, hyperandrogenism either Clinical and/or biochemical, polycystic ovarian morphology on Ultrasound) are required to confirm the diagnosis of PCOS.10,11

Patients with Hypothyroidism, Hyperprolactinemia, Non-classic CAH (congenital adrenal hyperplasia), Cushing’s syndrome, women using oral contraceptive pills or anabolic steroids, other endocrine disorder, associated co-morbid conditions and patients with age <15 years and >40 years were excluded from the study. Patients fulfilling inclusion criteria were asked to participate in the study. Only those patients were taken into study who were agree to participate and sign informed consent. Demographic information e.g. name, age, height, weight, gender, was recorded. Patients were asked questions about their menstrual cycle, excessive growth of terminal hair in a male pattern, areas of excess hair growth to determine the “Ferriman Galloway Score.” Recent changes in weight, and family history of such complaints. Blood samples were taken and sent to laboratory to determine serum free testosterone value. Abbot’s Latest second generation kit and reagent were used to analyze free testosterone value via ELISA method. Correlation between clinical and biochemical hyperandrogenism was assessed. Data was analyzed using SPSS version 25. Frequencies and percentages were used to describe qualitative data. Mean±SD was used to present quantitative data. Association was observed between clinical and biochemical Parameter. Fisher exact test was applied to see association between hirsutism and biochemical hyperandrogenism. A p-value of <0.05 was taken as statistically significant.

RESULTS
Total 140 patients of PCOSs diagnosed on the basis of Rotterdam criteria were selected from JAIDE (Jinnah Allama Iqbal Institute of diabetes and endocrinology). Mean age was 24.9 ± 3.7 years. Insulin resistance in the form of acanthosis nigricans and skin tags was noted in 30.0% patients, followed by dyslipidemia (17.9%), hypertension (12.9%), obstructive sleep apnea (10.7%), thromboembolic (5.7%) events and diabetes mellitus (3.5%). Details regarding frequency of these variables are given in Table 1. Out of 140 patients, 56 (40.0%) were pre-diabetic and 5 (3.6%) were diabetic. There were 58 (41.4%) patients having Ferrimman Galloway score 8-15, 70 (50.0%) patients having Ferrimman Galloway score 15-25 and 12 (8.6%) patients having Ferrimman Galloway score >25. Biochemical hyperandrogenism were present in 46 (32.9%) patients. Fisher’s exact test was used to determine the association between hirsutism and biochemical hyperandrogenism. Results revealed that there was significant association between hirsutism and biochemical hyperandrogenism (p-value<0.001). Out of 12 patients having Ferriman Galloway score >25, 10 (83.3%) had biochemical hyperandrogenism. Out of 70 patients having Ferriman Galloway score 15-25, 22 (31.4%) patients had biochemical hyperandrogenism whereas out of 58 patients having Ferriman Galloway score 8-15, only 14 (24.1%) patients had hyperandrogenism. (Table 2)
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androgens and aging. 22,23 A recent study showed that androgen excess in polycystic ovarian syndrome patients also contributes to insulin resistance and obesity like metabolic complications. 24 Clinical evidence of hyperandrogenism is not always present, especially in patients of Asian descent, and biochemical hyperandrogenemia may be present in the absence of clinical evidence. 25

CONCLUSION

Prevalence of biochemical hyperandrogenism in PCOS patients in our studied population was significantly low when compared to the population studied worldwide making it less reliable as diagnostic tool in this part of the world. Also there was significant positive correlation between free testosterone levels and degree of hirsutism which means that diagnostic accuracy of free testosterone in PCOS patients is considerably high in those having clinical hyperandrogenism.

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