Original Article

Relationship of Serum Prostate Specific Antigen with Hirsutism in Women Having Polycystic Ovary Syndrome Belonging to the Province of Khyber Pakhtunkhwa, Pakistan

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ABSTRACT

OBJECTIVE: To find the relationship of serum PSA with Hirsutism in PCOS females of Khyber Pakhtunkhwa.

METHODOLOGY: It was a cross-sectional/comparative study. This study was conducted in Khyber Teaching Hospital, Lady Reading Hospital, and Hayatabad Medical Complex from June to December 2021. A total of 172 study subjects were involved in this study. Serum PSA, testosterone and DHEAS levels of 86 newly diagnosed cases of PCOS (Group A) were compared with 86 healthy age-matched controls (Group B). These parameters were estimated using the ELISA method. Distribution of Hirsutism of the study subjects was also established with FGS. SPSS version 21 was used to analyze the data.

RESULTS: The results showed that serum PSA significantly increased (0.325±0.243 Vs 0.119±0.209, P <0.0001) in females with PCOS. Serum total testosterone (1.639±0.773 vs 0.739±0.965, P<0.0001) and DHEAS (3.397±1.243 Vs 2.035±1.203, P <0.0001) levels were also raised. A highly significant positive relationship was seen between PSA with Hirsutism through FGS (r 0-609, P 0.000), testosterone (r 0.352, P 0.000) and DHEAS levels (r 0.432, P 0.000)

CONCLUSION: This study observed significantly high PSA correlating positively with Hirsutism in females with PCOS.

KEYWORDS: Prostate Specific Antigen, Hirsutism, Polycystic Ovary Syndrome

INTRODUCTION

PCOS is a hormonal problem of childbearing age in females; roughly 5-6% of females are affected globally. The exact cause of PCOS is unknown; however, multiple factors can lead to this condition, such as family history, obesity, and insulin resistance[1]. According to the Rotterdam Consensus (2003-2004), PCOS is determined by the presence of at least two of the following features: i) Hyperandrogenism, clinical/ biochemical, ii) polycystic ovaries on ultrasound and iii) menstrual dysfunction including anovulation (no menses for more than three months) and oligomenorrhea (infrequent menses >35 days)[2]. Other causes of androgen excess, including Cushing's syndrome, androgen-secreting tumors, hyperprolactinemia and congenital adrenal hyperplasia, should be excluded. PCOS diagnosis is somewhat complicated for several reasons, such as menstrual irregularities in females, anovulatory cycles, especially in young girls, intricacy in explaining clinical features and biochemical indices of hyperandrogenic status and ambiguity concerning the importance of the ovarian cysts morphology[3, 4].

A prostate-specific antigen is a 33KD glycoprotein initially thought to be only secreted by a male prostate gland. Later studies showed that PSA is also produced in the female body by several different tissues like breast tissue, endometrial tissue, periurethral glands like skene glands and parotid glands[5]. PSA in normal females is <0.1ng/ml, which is markedly raised if there is a state of Hyperandrogenism like PCOS[6]. In this condition, androgen levels, such as testosterone, are high in females. Ovaries and adrenal glands produce androgens in PCOS due to faulty LH and FSH discharge because of defective gonadotropin-releasing hormone (GnRH) secretion[7]. LH causes theca cells of ovaries to produce more than normal androgens. Several studies show ovarian androgen synthesis in PCOS is more than in adrenal androgens. Hirsutism, acne, voice changes, hyperpigmentation and androgenic alopecia, characterize Hyperandrogenism. Hirsutism is the most disturbing psychosocial problem among females[8]. Hirsutism is the appearance of thick, course hair on unwanted body areas, in a pattern more common in males. Androgens have inconsistently diverse outcomes on hair follicles, varying according to body site[9].

Hirsutism is graded using the gold standard Ferriman Gallwey Scoring method[10]. The modified system

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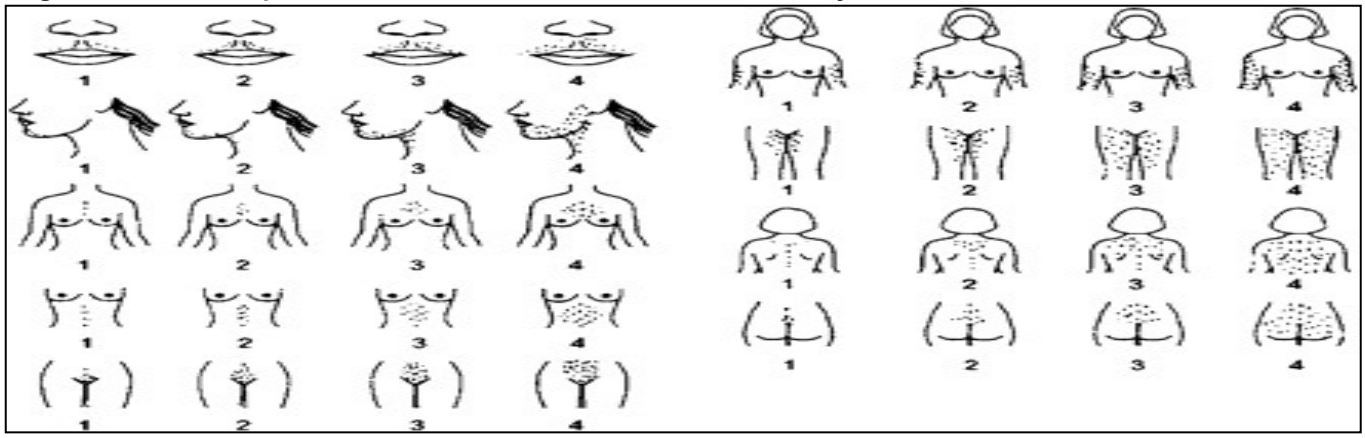
Figure I: Detailed representation of the modified Ferriman Gallwey Score



suggests examining nine body parts for hair growth. These include; i. upper lip, ii. chin iii. chest iv. upper abdomen v. lower abdomen vi. upper back vii. lower back viii. forearm and ix. Thigh[11]. Every part is given a maximum of 4 points and a minimum of zero. So, the maximum score is 36, and the minimum is zero. A score of 0-8 is considered normal, mild Hirsutism is 9 to 15, 16 to 25 is moderate Hirsutism, and severe Hirsutism is when the score is above 25[12].

However, Hirsutism may vary by ethnicity, and all other causes of Hirsutism, like hypertrichosis and idiopathic Hirsutism, should be excluded.

The study aims to evaluate the relationship between serum PSA levels with hirsutism status in PCOS females of Khyber Pakhtunkhwa.

METHODOLOGY

This cross-sectional, comparative study was conducted in the outpatient department (OPD) of Khyber Teaching Hospital, Lady Reading Hospital and Hayatabad Medical Complex, Peshawar, the three tertiary-level hospitals of Khyber Pakhtunkhwa from June 2021 to December 2021. One hundred seventy-two participants were involved in this study, separated into two groups; 86 cases (Group A) and 86 controls (Group B).

The cases group included newly diagnosed patients of PCOS, and the control group included healthy age-matched females with no major/chronic illnesses like diabetes mellitus, thyroid disease, and hypertension. Consent of all participants was taken. Data were taken and maintained on a well-designed questionnaire, including name, age, marital history, menstrual history, and obstetrical history. Clinical signs of Hyperandrogenism, including acne, pigmentation and Hirsutism, were checked. Hirsutism was scored according to the Ferriman Gallwey scoring system. Pelvic ultrasounds of all the study subjects were done. 5ml of blood was taken, and serum was collected by centrifuging at 3500 rounds per minute for 5 to 10 minutes in Eppendorf tubes, properly labelled and stored for later use at -20°C.

Biochemical analysis

The blood serum was tested for total PSA, testosterone and DHEAS levels. PSA was determined using the principle of sandwich enzyme-linked immunosorbent assay using a Calbiotech ELISA kit. Total testosterone was defined using Calbiotech ELISA kit no.TES5663 is based on the principle of solid phase competitive ELISA. The level of DHEAS was determined using Demeditec kit no.DEH3366, based on the principle of competitive ELISA.

Statistical analysis

We analyzed all data using SPSS and expressed the results as Means and Standard Deviation. The quantitative variables between the study groups were compared with the independent students' t-test. The relationship between PSA and other parameters was established with Pearson's correlation coefficient r.

RESULTS

Cases presented with a mean age of 25.24±4.395 years and mean BMI of 32.82±2.04 are shown in **Table I**. It can be seen that there was a significant difference in the mean BMI of cases and control with a p-value <0.0001.

Table I shows a statistically raised serum total PSA level in cases than in controls (0.325±0.243 Vs 0.119±0.209) with a p-value of 0.0001. Significantly higher levels of total testosterone (1.639±0.773 vs 0.739±0.965, p-value <0.0001) and DHEAS (3.397±1.243 Vs 2.035±1.203, p-value <0.0001) were observed in cases than controls. FGS shows that Hirsutism is statistically higher in cases than in control (p-value <0.0001).

Table II shows the relationship of serum PSA levels with other parameters. The association was established using Pearson's correlation coefficient r, and a P-value less than 0.05 was considered significant. A highly significant positive relationship is seen between PSA with testosterone (r 0.352, P 0.000) and DHEAS levels (r 0.432, P 0.000). A statistically significant and positive relationship was observed between PSA levels and FGS (Hirsutism) with r 0.609 and p 0.000.

Out of 86 cases, 70 subjects were obese, having BMI >30; 8 cases had borderline obesity with a BMI

between 25 & 30, and 8 cases were non-obese, having a BMI <25. While in the control group, 69 participants were non-obese, and 17 had borderline obesity.

Figure II shows the status of Hirsutism in the study groups. Out of 86 cases, 34 females had got mild Hirsutism (FG between 9 and 15), 33 females had moderate Hirsutism (FG between 16 and 25), 11 females had got severe Hirsutism (FG >25), and 8 cases did not have Hirsutism.

Table III shows the relationship of serum PSA with Hirsutism in cases according to the mild, moderate and severe groups. The PSA levels are significantly higher among the groups according to the severity of Hirsutism, further strengthening the positive association of PSA with Hirsutism in females with PCOS.

Table I: Comparison of clinical and biochemical characteristics between Group A and Group B

Variables	Group A (Cases) Mean ± SD	Group B (Control) Mean ± SD	P value
Age	25.24±4.395	25.860±4.229	NS
BMI	32.82±2.04	24.60±4.35	<0.0001
PSA	0.325±0.243	0.119±0.209	<0.0001
Testosterone	1.639±0.773	0.739±0.965	<0.0001
DHEAS	3.397±1.243	2.035±1.203	<0.0001
FGS	18.9±4.9	4.1±2.1	<0.0001

**P-value significant <0.05, NS not significant, PSA ng/mL, Testosterone ng/mL, DHEAS µg/mL*

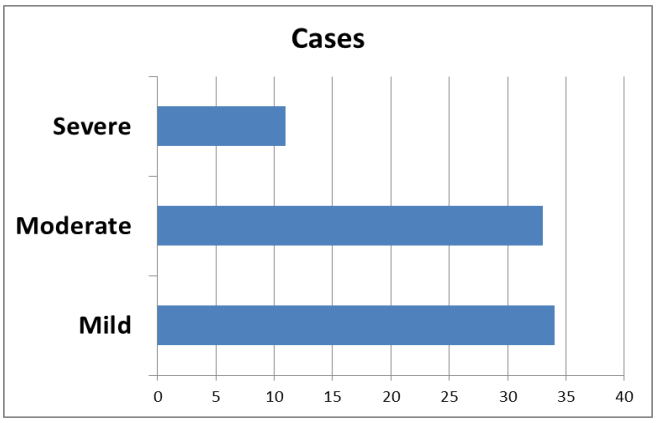
Table II: Correlation of PSA with Different Parameters in Study Groups

Parameters	r	p
Age	-0.093	0.143
Testosterone	0.352	0.000**
DHEAS	0.432	0.000**
FGS	0.609	0.000**

Table III: Relationship of serum PSA with a degree of Hirsutism in cases

PSA in Mild Hirsutism	PSA in Moderate Hirsutism	P-value
.104±.05	.203±.14	<0.0001
PSA in Moderate Hirsutism	PSA in Severe Hir-sutism	
.203±.14	.281±.17	<0.003

Figure II: Description of Hirsutism in Cases



DISCUSSION

PCOS is associated with Hyperandrogenism causing Hirsutism, acne, obesity and menstrual irregularities[13]. The hyperandrogenic state in PCOS is associated with augmented production of luteinizing hormone by theca cells which causes increased DHEAS and testosterone levels in the body. Various studies have reported increased expression of the PSA gene in hyperandrogenic states (like PCOS), leading to increased serum PSA levels[14-16]. Female sources of circulating PSA are unclear; however, it may act as a reliable biomarker of the biological action of androgen in females[6,17]. Some studies have suggested the diagnostic role of PSA level in female colorectal and breast cancer[18,19]. Due to the lack of sufficient relevant research, the mechanism of PSA in the pathophysiology of PCOS remains to be elucidated to date.

Vural B 2007[20] reported significantly raised serum PSA, testosterone and dehydroepiandrostenedione in PCOS cases. In a study conducted by Ibrahim WW 2016[21], a positive relationship between PSA with Hirsutism and DHEAS was observed. Similar results were observed in the present study. The results of Uknic K 2009[22], Rudnicka E 2016[23], and Tokmark A 2018[24] are consistent with the current research. Uknic K 2009[22] has recommended the diagnostic use of PSA in PCOS with high specificity, sensitivity and accuracy based on their outcomes. Similar results have been reported by Nagaraj S 2019[25] and Bhat K 2019[26].

The present study compared serum concentrations of PSA, testosterone and DHEAS and clinical evidence of Hirsutism in PCOS cases with healthy age-matched controls. This is a novel study in people of this area, which may show PSA as a more logical and sole biomarker of hyperandrogenic activity in PCOS females, reducing the health system's financial burden.

CONCLUSION

It is concluded that in PCOS, the level of androgens like DHEAS and total testosterone is raised, which in turn may cause the PSA levels to be increased than normal. Furthermore, Hyperandrogenism and raised PSA levels are also related to Hirsutism status in PCOS. Limitations of the study include its relatively small sample size. Thus, future large-group studies are recommended to investigate PSA's potential diagnostic and prognostic role in PCOS cases.

Ethical Permission: Khyber Medical College Peshawar, ERC letter No. 762/DME/KMC.

Conflict of Interest: No conflicts of interest.

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Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publically.

AUTHOR CONTRIBUTIONS

Khattak N: Design, acquisition, analysis, and interpretation of data
Durrani S: Design, acquisition, analysis, and interpretation of data
Ali S: Design, acquisition, analysis, and interpretation of data
Tariq K: Design, acquisition, analysis, and interpretation of data
Ur Rahman U: Design, acquisition, analysis, interpretation of data
Khan MA: Design, acquisition, analysis, interpretation of data

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