Evaluation of PSA tumor marker in some Iraqi women with polycystic ovarian syndrome.

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Abstract:

Background:

Polycystic ovarian syndrome (PCOS) is the most common cause of hyperandrogenism anovulatory infertility; it affects 5- 10% female reproductive age.The present study aims to investigate the total prostate specific antigen levels, total serum testosterone, FSH and LH in women with PCOS and compare the results with control group of normal fertile females of corresponding age group on Iraqis PCOS patients.

Materials and Methods:

Seventy patients with PCOS diagnosed depending on three criteria: Menstrual history: Oligomenorrhea, Ultrasound reveals polycystic ovaries and Biomedical and/ or clinical hyperandrogenism.Twenty normal fertile females who serve as control group in this study. Blood samples were aspirated from all individuals from 24- day of menstrual cycle to measure total prostate specific antigen(PSA), total testosterone and FSH, LH .

Results:

Patients with PCOS and controls differed significantly in PSA, Total serum testosterone ($p<0.05$). Patients with PCOS and controls have highly significant difference in LH level, the mean was (7.88± 1.83 vs 3.90± 0.73) respectively ($p<0.001$)and, highly significant difference in LH/FSH ratio and BMI parameters. ($p<0.001$). No significant differences were found in FSH ($p>0.05$). Positive correlation between PSA and testosterone, PSA and BMI.

Conclusion:

Total serum prostate specific antigen levels are higher in patient with PCOS.Total testosterone levels are higher in patient with PCOS.Serum PSA measurement might be marker of hyperandrogenism in females suffering from PCOS.

Keywords: PCOS, PSA, Tumor marker

Introduction

Polycystic ovary syndrome(PCOS) is the most common endocrine problem in women of reproductive age1. PCOS affects 5–10 percent of all women of reproductive age and is associated with anovulation/ oligoovulation, hyperandrogenism, and polycystic ovaries (PCO)[1,2]. PCOS is associated with metabolic disturbances including obesity and insulin resistance with a high risk of developing type 2 diabetes, and cardiovascular disease1. In addition, women with PCOS display reduced health related quality of life as well as symptoms of anxiety and depression[3,4]. The National Institutes of Health (NIH) 1990 preliminary consensus definition has now been replaced by a more recent definition by the Rotterdam European Society for Human Reproduction and Ernbryology (ESHRE) and the American Society of Reproductive Medicine (ASRM) PCOS Consensus Workshop Group[5].This has suggested a broader definition for PCOS, with two of the three following criteria being diagnostic of the condition:
Polycystic ovaries (either 12 or more peripheral follicles or increased ovarian volume (greater than 10 cm[3].Oligo- or anovulation .Clinical and/or biochemical signs of hyperandrogenism.

Prostate Specific Antigen (PSA) was first discovered by Albin and Co-workers in prostatic tissue in 1970[6], and in seminal plasma in

1971 by Hara *et al*[7]. They called it gamma semino protein.Currently, PSA represents the best serum marker for prostate carcinoma, and it has the highest validity of any circulating marker for cancer today[8, 9]. PSA is a serine protease with trypsin like and a chymotrypsin –like activity[10]. It is produced almost exclusively in the cytoplasm of normal and neoplastic epithelial cells and secreted into the lumina of the prostatic duct during the formation of seminal plasma[11] .PSA is released from the normal prostate and appears at low serum concentrations in healthy men. High serum concentration can be detected in patients with advanced prostate cancer[12]. PSA is applied as a tumor marker for the clinical management of prostate cancer (PCA). PSA increased in patients with benign prostate hyperplasia (BPH), acute urinary retention and renal failure can also elevate the PSA level[13]. PSA was believed to be completely absent from all female tissues and fluids. PSA has been detected recently in some female tissues and body fluid[14]. The presence of PSA in these female tissues seems to be associated closely with steroid hormone regulation especially androgens, glucocorticoids and progestin>s[15]. Among women who have high levels of androgens, relatively high levels of serum PSA should be expected if PSA production in women is under the regulation of androgens[16].

Materials and method

Seventy women in their reproductive age (20- 40) years old, who had been diagnosed as PCOS, were recruited from infertility clinic population at the High Institute of Infertility Diagnosis and ART, Al-Nahrain University, between July 2011 and October 2011.The diagnosis of PCOS was based on the presence of polycystic ovaries on ultrasonography (10 or more follicles in each ovary, each follicle measuring 2–9 mm in diameter). One polycystic ovary is sufficient for the diagnosis with one or more of the following criteria(5):

1- Oligo-/anovulation; clinically diagnosed as oligo-/ amenorrhoea, i.e. menstrual cycles longer than 35 days, or fewer than 10 menstruations per year.

2- Hyperandrogenism; clinical or biochemical. Clinical manifestations of hyperandrogenism such as a hirsutism, acne and/or an elevated serum testosterone level. Twenty apparently healthy fertile women were served as control. Those who were matched for age and with regular menstrual cycle and normal ultrasound.

Exclusion criteria:-1- Diabetic patient.2- Patient taking medications (antiglycemic and contraceptive pill) for the previous 3 months that interfere with study results.

Blood samples were aspirated at 8:00- 12:00 am during 2nd – 4th day of menstrual cycle (early follicular phase) for those of normal cycle or progestin induced withdrawal bleeding . Blood samples were collected into plain tube and centrifuged within 30 min of collection. Serum was aspirated, and stored at -20 °c until time of assay. Serum FSH and LH level along with LH/FSH ratio testosterone and PSA were performed for those samples.Serum PSA was measured by using enzyme linked immune sorbent assay (ELISA). This kit for quantitative determination in human serum was supplied by Human Gesellschaft Biochemical. Germany.*(Normal value of PSA according to the kit is less than 4ng/ml.*

Statistical analysis:

Data were analyzed using SPSS version 16 and Microsoft Office Excel 2007. Numeric variables were expressed as mean ± standard deviation. Student T-test was used to compare independent two samples. Pearsons correlation coefficient was used to study correlation between two numeric variables. The differences between values were considered statistically significant at the level of ($p<0.05$) and highly significant at the level of ($p<0.001$).

Results:

The mean serum levels of total PSA in patients with PCOS was equal to (0.48± 0.38)ng/ml which was significantly elevated when compared with the normal controls group (0.25± 0.08) nag/ml. $P<0.05$(0.011) (table 1) . In the current study, the mean serum levels of total testosterone in patients with PCOS was equal to (0.33± 0.22) ng/dl which was significantly ($P<0.036$, table 1) elevated when compared with normal control group (0.22± 0.09) ng/dl. (table 1).There is positive correlation between PSA and BMI in PCO patients ($r=0.470$, $p<0.001$) (figure 1).There is positive correlation between total serum PSA and total serum testosterone ($r=0.668$, $p<0.001$, figure 2).

Table1: Comparison between control and PCOS patients

Parameter	Group 1 (control= 20) Mean±SD	Group2 (PCOS =70) Mean±SD	P value
Number	20	70	
Age	29.58±3.32	28.05±2.68	0.162 NS
PSA	0.25±0.08	0.48±0.38	0.011
FSH	5.34±0.65	5.65±1.47	0.372 NS
LH	3.90±0.73	7.88±1.83	<0.001
LH/FSH	0.73±0.12	1.43±0.36	<0.001
TESTO	0.22±0.09	0.33±0.22	0.036
BMI	24.33±1.35	27.62±1.96	<0.001

NS;not significant

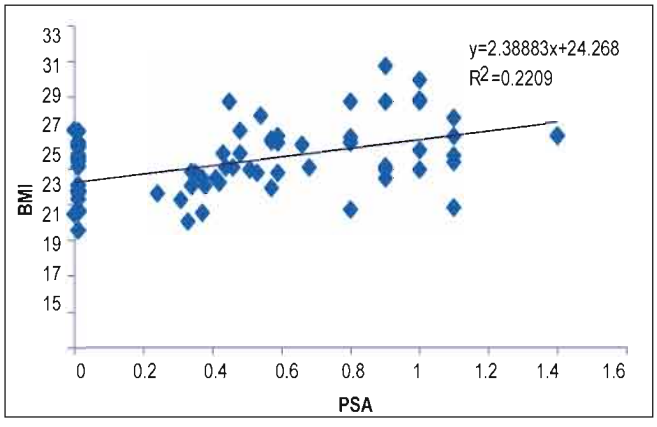

Figure (1): Persons correlation between PSA and BMI in PCOS patients ($r=0.470$,$p < 0.001$).

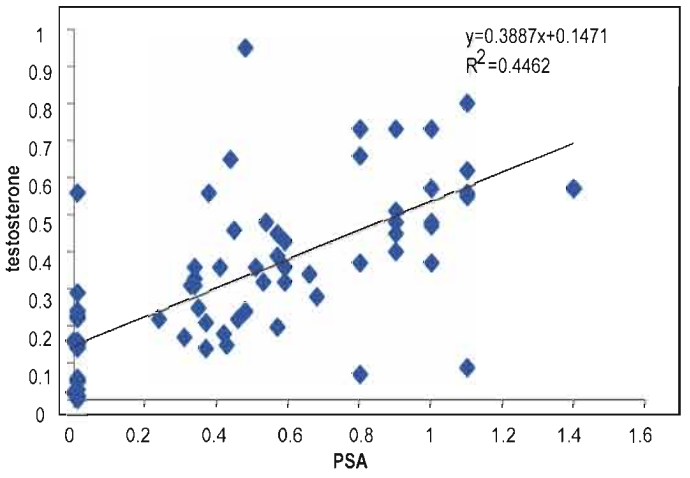

Figure (2): Persons correlation between PSA and testosterone in PCOS patients (r=0.668,p < 0.001).

Discussion

Polycystic ovary syndrome is a heterogeneous disorder, characterized by hirsute, abdominal obesity, hyperandrogenism, polycystic ovaries and insulin resistance.The syndrome is often accompanied by infertility because of anovulation[17]. PCOS develops when the ovaries are stimulated to produce excessive amounts of male hormones (androgens), particularly testosterone, either through the release of excessive LH by the anterior pituitary gland or through high levels of insulin in the blood (hyperinsulinaemia) in women whose ovaries are sensitive to this stim ulus[18]Hyperandrogenism is a key feature of PCOS with elevations of ovarian androgens, testosterone and androstenedione[19] PCOS ovaries have lower activity of aromatase enzyme[20] Aromatase is responsible for the aromatization of androgens into estrogens. It catalyzes the last steps of estrogen biosynthesis from androgens (specifically, it transforms androstenedione to estrone and testosterone to estradiol)[21,22] and this fact contribute to hyperandrogenic state in PCOS.

Until few years ago PSA was believed to be produced only in men and only in the prostate. However using high sensitive PSA assay, new concepts for the clinical use of PSA has been established[23] Determination of PSA in female tissues had become available. The expression of PSA gene is under androgenic regulation. Therefore hyperandrogenemic states, such as PCOS are expected to be presented with the higher levels of PSA[24] Different studies have already demonstrated that females with hyperandrogenism usually have elevated serum total and free PSA[24],. Also other studies have indicated that women treated with testosterone over prolonged period of time had significantly increased serum total PSA[25] .Administration of androgens or progestin>s to patients cause significant elevations of PSA in urine, serum and tissues[23,25,26] The result of the present study shows that the mean serum levels of total PSA in patients with PCOS was equal to (0.48± 0.38) ng/ml which was significantly elevated when compared with the normal controls group (0.250.08+) ng/ml. P<0.05(0.011).This finding is in agreement with Obiezu *et al* (2001)[28] who found that urinary PSA and possibly urinary Human kallikrein 2 (hk2) promising marker of hyperandrogenism in female suffering from PCOS. Rifat *et al* (2003)[24]found that serum PSA could be used as a marker for hyperandrogenemic, hirsutism or PCOS because both total and free PSA levels were found to be significantly higher in patient with PCOS than in healthy subject.Ansam A *et al* (2004) [29] found that serum total PSA can be a promising marker in patient with PCOS and hirsute in detectable level by using ELFA.Kocak (2005)[30] found that serum PSA levels in hirsute women were higher than in non-hirsute women. We conclude that total serum prostate specific antigen levels are higher in patient with PCOS,total testosterone levels are higher in patient with PCOS and serum PSA measurement might be marker of hyperandrogenism in females suffering from PCOS.

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