

Serum Prostate Specific Antigen level in Women with Polycystic Ovary Syndrome

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Abstract:

Background: Polycystic ovary syndrome (PCOS) is a common disorder in women in the reproductive age associated with disturbance of reproductive, endocrine and metabolic functions. The pathophysiology of PCOS appears to be multifactorial and polygenic.

Objective: To measure the level of prostate –specific antigen (PSA) and to evaluate the value of prostatic specific antigen as a marker of hyperandrogenism in women with PCOS.

Patients and Methods: One hundred women were enrolled in this study, 50 women were PCOS group and the remainder was healthy women served as control group. Hormonal profile (serum testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH) levels were measured. Ferriman-Gallway Score (FGS) was assessed. Serum prostate specific antigen level was measured in both groups. Correlation between PSA level and (LH/FSH, testosterone and FGS) were evaluated.

Result: Mean serum PSA level was significantly higher in PCOS women compared to control women (0.15 ± 0.09 , 0.016 ± 0.003) respectively with P value < 0.05 . Serum PSA level in women with PCOS had significant positive correlation with FGS, LH/FSH ratio and serum testosterone with r values: 0.964, 0.988, 0.922 respectively. There was a strong correlation between serum PSA levels with the degree of hirsutism as evaluated by Ferriman –Gallwayscore. Serum PSA level in the 1st group (4-8) was 0.07 ± 0.009 , in the 2 nd group (FGS9-12) was 0.1 ± 0.06 and in the 3 rd group (FGS 13-16) was 0.3 ± 0.03 .

Conclusion: Prostate – specific antigen level is significantly higher in women with PCOS and correlate positively with LH/FSH, testosterone and Ferriman-Gallway score. It is also concluded that the higher score of hirsutism correlate with the higher serum PSA level.

Key words: Polycystic ovary syndrome, Prostate specific antigen ,Ferriman –Gallway score .

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Introduction:

Polycystic ovarian syndrome is one of the most common endocrine disorders in women of reproductive age (1). It often complicated by chronic an ovulatory infertility and hyper androgenism with the clinical manifestation s of oligomenorrhoea ,hirsutism and acne (2). Many women with this conditions are obese and have a higher prevalence of impaired glucose tolerance , type 2 diabetes and sleep apnea than is observed in the general population.(3)

The prevalence of this syndrome varies widely ranging from 2.2% to as high 26%.(4)Hyperandrogenism is a key feature of PCOS , approximately three-quarters of patients with PCOS have evidence of hyperandrogenism. The hypersecretion of androgens by stromal theca cells of polycystic ovary leads to the cardinal clinical manifestation of the hyperandrogenism (hirsutism , acne, and/ or androgenic alopecia features of PCOS).(5,6)

Clinical evidence of hirsutism is based on Ferriman – Gallweyhirsutism scoring system which involved the scoring of 9 body areas

used to grade hirsutism are upper lip , chin, chest , upper abdomen, lower abdomen , upper arm, thigh , upper back and lower back. Each individual area is usually scored on a scale of 0 - 4. A patient' s score may range from a minimum score of 0 to a maximum score of 36. A score of 8 or higher is regarded as indicative of hirsutism.(7,8)

Prostatic specific antigen (PSA), also known as gamma- seminoprotein or Kallikrein -3 (KLK3) encoded in humans by the KLK3 gene.(9,10)It is available tumor marker used for diagnosis and management of prostate cancer.(10,11) Recently PSA has been found in several female tissues and fluids in very low concentration and its level varies during menstruation. The normal range of female serum PSA (0.01- 0.53) ng/ ml.(11,12)It appears to be up- regulated by androgen and progestins .(12,13)

Subjects and methods:

One hundred women in their reproductive age were included in this study, they were attended to the Obstetric and Gynaecology outpatient clinic in Baghdad Teaching Hospital during the period from January – September 2014. Subjects were divided into two groups: group A: Fifty (50) women with PCOS and group B: fifty women without signs of PCOS as control group. PCOS can be diagnosed when two of three following criteria are present

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(Oligoovulation and /or anovulation , clinical and /or biochemical hyperandrogenism and polycystic ovaries defined by ultrasonography).Clinical evidence of hirsutism was based on Ferriman-Gallewey Score (FGS) .

Exclusion criteria were included idiopathic hirsutism , Cushing syndrome ,Thyroid dysfunction,Hyperprolactinemia, Androgen secreting ovarian or adrenal tumor , Congenital adrenal hyperplasia (CAH) , medications : contraceptive pills , anti-obesity drugs and drugs used for treatment of hirsutism that may interfere with the normal hypothalamic – pituitary gonadal function.

Blood samples (5cc) were collected in early follicular phase of menstrual cycle (day 2-6) in eumenorrheic , oligo – menorrheic women for measurement of serum testosterone , FSH , LH and Prostate- specific antigen levels. LH, FSH and testosterone measured using standard radio-immuno assay . Serum PSA was measured by using enzyme linked immune sorbent assay(ELISA) .

In addition body mass index was calculated as weight (kg) per height (m2) .women were considered as normal weight at BMI (18.5 -24.9 kg/m2), overweight women (25- 29.9 kg/m2) and obese women at BMI ≥ 30kg/m2. (13)

Statistical Analysis:

The collected data of both groups (cases and controls) were entered and processed by using the statistical package for social science (SPSS) version 20 .The results were presented as frequencies and proportions for categorical variables and as mean and standard deviation (SD) for continuous variables .

The means of the studied parameters between both groups were compared by using Student's test (independent 2 sample test).Pearson's correlation (bivariate analysis) was used to assess the correlation between serum testosterone , LH/FSH ratio, FGS and PSA levels .The correlation coefficient (r) was calculated , the higher the (r) value indicated the stronger correlation .The cutoff point for PSA in the control group was 0.02 ng / ml. Level of significance was set at P<0.05 as cutoff point for significant differences or correlations .

Results:

Patients and controls matched for age and body mass index (BMI). There were significant increase in serum LH , serum LH/ FSH ratio , serum testosterone in patients comparing to controls .in addition the mean **FGS** of the Patients was significantly higher than controls; (10.6±2.7) and (2.6±1.0) , respectively.(P = 0.0005).(Table 1) .the serum PSA also significant higher in patients with PCOS than controls (Table 2) (Figure 1)

There were statistically significant correlation between PSA and serum LH, serum FSH, serum LH/FSH , serum testosterone and **FGS** (Table3).

There were positive correlation between serum PSA level and degree of hirsutism (Table 4,5)

Table 1. Demographic parameters and hormonal assay of PCOS cases and control group.

Parameters	Case No=50 mean± SD	Control No=50 mean± SD	P value
Age	28.04± 3.6	26.9± 2.1	0.061
BMI (Kg/ m)	24.2±6.3	23.4± 4.7	0.085
FGS	10.6± 2.7	2.6± 1.0	0.0005
LH(IU/L)	11.7± 2.4	7.0± 0.6	0.0005
FSH(IU/L)	5.2± 1.2	5.4± 0.3	0.255
LH/FSH ratio	2.3± 0.4	1.2± 0.1	0.0005
Testosterone ng/ml)(1.5± 0.6	0.3± 0.06	0.0005

Significant difference between two means using Student-t-test for two independent means at 0.05 level of significance.

No. number,SD:Standard deviation,BMI:Body Mass Index,FGS:Ferriman gallewey score,LH:leutinizing hormone,FSH:follicular stimulating hormone.

Table 2&Figure 1:show that the mean serum PSA level in Patient was (0.16±0.09) and it was significantly higher than controls (0.02± 0.003) , (P = 0.0005).

Table 2. Level of PSA in PCOS and control groups

	PCOS Cases No.=50 mean± SD	Control No.=50 mean± SD	P-Value
PSA -ng/ml	0.16± 0.09	0.02± 0.003	0.0005

PSA:prostate-specific antigen.

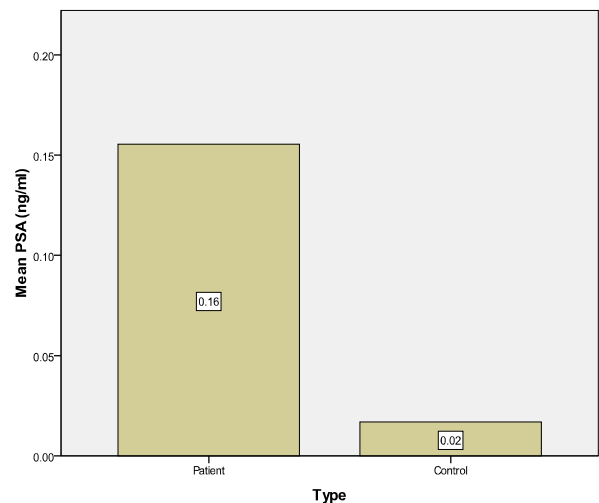


Figure (1) Mean PSA levels for PCOS cases and controls.

Parameters	Pearson correlation of PSA (r)	P Value
Age	0.015	0.919
BMI	0.012	0.652
FGS	0.964	0.0005
LH(IU/L)	0.918	0.0005
LH/FSH ratio	0.988	0.0005
Testosterone(ng/ml)	0.922	0.0005

Table 3 : correlation between PSA and other parameters in PCOS patients**Table 4. The mean PSA level according to the degree of hirsutism that is scored by FGS system in PCOS cases .**

PSA in group I	PSA in group II	P-value
0.07± 0.009	0.1± 0.06	0.0005
PSA in group II	PSA in group III	P-value
0.1± 0.06	0.3± 0.03	0.0005

Table 5. Correlation of serum PSA level with the degree of hirsutism in PCOS cases

Group	No. of patients	FGS	PSA Ng/ml
I	10	4-8	0.07± 0.009
II	34	9-12	0.1± 0.06
III	6	13-16	0.3± 0.03

Discussion:

PCOS appear to be a heterogeneous disorder in which ovarian and adrenal androgen excess is presented by variety of high gonadotropic degrees and metabolic abnormalities(14). PCOS develops when the ovaries are stimulated to produce excessive amount 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 (hyperinsulinemia) in women whose ovaries are sensitive to this stimulus (14,15). The mean FGS in cases group was (10.6 ± 2.7) which was significantly higher than controls (2.6 ± 1.0) . This was in agreement with **Bahceci M et al** who demonstrated significantly higher FGS in cases than controls (16).

The mean serum Testosterone level in cases group was (1.5 ± 0.6) ng/ml which was significantly higher than controls (0.3 ± 0.06) ng/ml. This finding agreed with the results of a study done by **Burelli A et al** 2006, which showed significantly higher hormonal level of testosterone in cases than controls(17). Insulin and insulin-like growth factor -I (IGF-I) enhance ovarian androgen production by potentiating the

stimulatory action of LH on ovarian androstenedione and testosterone secretion. Since IGFBP levels are lower in women with PCOS, this leads to increased bioavailable IGF-I, which increases stimulation of the theca cells in combination with LH to produce higher levels of androgen production(12,13). The mean LH / FSH ratio in PCOS cases was (2.3 ± 0.4) which was significantly higher than the controls (1.2 ± 0.1) , this finding was consistent with that reported by **Metawie M S et al** who found significantly higher LH / FSH ratio in PCOS cases than controls (2.7 ± 0.2) versus 1.2 ± 0.2 , respectively(18). In this study we found elevated serum PSA level in PCOS cases mean PSA value was (0.16 ± 0.09) which was significantly higher than mean of controls (0.02 ± 0.003) , this finding was in consistent with **Mardanian F et al** who demonstrated that PCOS cases exhibited significant higher mean PSA value than normal control group.(19) The mean PSA value in PCOS cases was (0.19 ± 0.1) in comparison to mean PSA value in controls (0.03 ± 0.04) , this goes also with **Bahceci M et al** .(16) These findings disagree with that reported by **Saleh et al** who found that in PCOS case, the mean PSA value was comparable with that of controls (20). In the current study there was no positive correlations between serum PSA, age and BMI, these findings were in agreement with that reported by **Kocak M et al** who demonstrated that PSA level was independent of age and BMI in PCOS cases(21). The above result might be attributed to some degree of insulin resistance occurs in most women with PCOS even those of normal weight(13). In the current study there was positive correlations between serum PSA and FGS, LH / FSH ratio and testosterone in PCOS cases, these findings was in agreement with **Vural et al** who demonstrated elevated serum PSA level in PCOS cases and positive correlations between serum PSA and FGS, LH / FSH ratio, serum testosterone and no correlation between PSA and age(22).

These findings also goes with **Mardanian F et al** who found positive correlation of PSA with LH / FSH ratio, FGS and testosterone level in PCOS cases (19). The finding of positive correlations between serum PSA and testosterone was also reported by **Guohong W et al** (23). A direct correlations were concluded in this study between serum PSA with degree of hirsutism as evaluated by FGS, as there was significant differences for serum PSA between 1st group (FGS 4-8) and 2nd group (FGS 9-12), 2nd and 3rd group (FGS 13-16). This goes with study conducted by **Metawie M et al** who demonstrated a strong correlation between serum PSA with the degree of hirsutism evaluated by FGS (18).

Conclusions:

Prostate – specific antigen level is significantly higher in women with PCOS and positively correlate with LH/ FSH , testosterone and Ferriman – Gallway score . it is also concluded that the higher score of hirsutism correlates with higher serum PSA level.

Author's contributions:

WidadMahmood: Iraqi board student who perform the study protocol including selection of patients, examination, doing concerned tests.
WasanWajdi:supervisor who help the student in performing , data collection and interpretations.
Raya Khalid: data anaysis and critical revision

References:

1. BalenA. Polycystic ovary syndrome and secondary amenorrhea. In: Edmonds K (ed). *Dew hurts Textbook of Obestetrics&Gynaecology.8th ed., London: Wiley-Blackwell; 2012.PP. 517- 519.*
2. ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long –term healthrisks related to polycystic ovary syndrome. *Fertile Steril.* 2004;81: 19-25.
3. ShaikhN ,Dadachanji R , Mukherjee S . *GeneticMarkers ofPolycystic Ovary Syndrome :Emphasis on insulin Resistance. International Journal Of Medical Genetics.2014 ,pages 10*
4. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, FutterweitW,et al. *The Androgen Excess and PCOSociety criteria for the polycystic ovary syndrome: the complete taskforce report .FertilSteril. 2011 Feb;91(2):456-88.*
5. Denis A .Magoffin. *Ovarian Steroidogenic Abnormalities in the Polycystic Ovary Syndrome.Androgen Excess Disorders in Women:Polycystic Ovary Syndrome and Other Disorders , Second Edition 2011 ,Chapter 18 :P.203-210.*
- 6.AdamsJ,Polson . *Polycystic ovarian syndrome and hyperandrogenismwilliam Textbook of obstetrics and gynecology for postgraduate ,Blackwell science 2010; chapter 17: 383.*
7. Jonard S, Robert Y, Cortet- Rudelli C. *Ultrasound examinationof polycystic ovaries: it is worth counting the follicles. Hum Reprod2003; 18(3):598-603.*
8. Nelson VL, Qin KM, RosenfieldRL. *The biochemical basis for increased testosterone production in theca cells propagated from patients with polycystic ovary syndrome. ClinEndocrinolMetab. 2001;8633- 5925.*
9. Ghosh D, Griswold J, Eman M&. *Structural basis for androgenspecificity and oestrogen synthesis in human aromatase.Nature. 2009;457(7226): 219-23.*
10. Yildiz B O, Bolour S, Woods K. *Visually scoring hirsutism.Hum. Reprod .Update.2010;16, 51-64.*
11. Stura EA, Muller BH, BossusM, Michel S, Jolivet-Reynaud C,Ducancel F. *"Crystal structure of human prostate- specific antigen in a sandwich antibody complex". J. Mol. Biol.2011;414(4): 530– 44.*
12. GopalakrishnapillaiAnilkumar , Jason J. Christiansen . *Is prostate-specific antigen a multifunctional protien ? . American Journal ofPhysiology .2009 ;288(5):975-981.*
13. Taheripanah R., Sepahvandi M, EntezariA,Amiri Z, Samani E.*Evaluation of Serum PSA after cyproterone compound treatment compared with oral contraceptive pill in hirsute polycystic ovarysyndrome patients. Middle East Fertility Society J.2013;15(3):159 162.*
14. Huang A, Brennan K and Azziz R. *Prevalence of hyperandrogenism in the polycystic ovary syndrome diagnosed by the National InstitutesofHealth 1990 criteria. Fertil Steril.2012;93, 1938-1941.*
15. Hussain N K, Rzaiz ZF. *Evaluation of PSA tumor marker in someIraqi women with Polycystic Ovarian Syndrome.Iraqi J. Embryosand Infertil. Res. 2012; 2(4): 22-24.*
16. Bahceci M, Bilge M, Tuzcu A, Tuzcu S, Bahceci S. *Serum prostate specific antigen levels in women with polycystic ovary syndrome and the effect of flutamide+desogestrel/ethinyl estradiol combination.JEndocrinol Invest. 2004;27(4):353-6.*
17. Burelli A, Rineladi E, Cionini R, Benelli E, Pinchera A, Pucci E. *Serum levels of PSA do not change in healthy premenopausal and imnenopausal women, but are increased in subjects with polycystic syndrome (PCOS) Endocrine 2006;11:685.*
18. Metawie M AH, El Sarafy T, El-Kattan S, Azab H, El-Biely M. *Serum-Prostatic specific antigen level as a promising marker in infertile women with polycystic ovarian disease. Middle East Fertility Society. 2008; 13(1):28-32.*
19. Mardanian F, HeidariN . *Diagnostic value of prostate-specific antigen in women with polycystic ovary syndrome. J Res Med Sci. 2011 August; 16(8): 999-1005.*
20. Saleh B.O, Abid G.H. and Al-Rawi J.R *.Hormonal InvestigationsofIdiopathic Hirsute Women: A comparison studywith poly cystic ovarysyndromeHirsuteWomen. J. Res. Nurs. Midwifery 2014 (34):73-77.*
21. Kocak M, Tarcan A, Beydilli G, et al. *Serum levels prostate specific antigen and androgens after nasal administration of agonadotropin releasing hormone agonist in hirsute women. GynecolEndocrinol. 2005; 18(4):179-85.*
22. Vural B, Ozkan S, Bodur H. *Is prostate-specific antigen a potential new marker of androgen excess in polycystic ovary syndrome?J ObstetGynecol Res. 2007;33(2):166-73.*
- 23.Guohong W; Ruiji X; Zhongshu Z. *The Serum Level of Prostate Specific Antigen in Polycystic Ovary Syndrome. PLA Research Institute of Clinical Labrotary Medicine. 2010;43(37): 286-288.*