International Journal of Pharmaceutical Science Invention
ISSN (Online): 2319 – 6718, ISSN (Print): 2319 – 670X
www.ijpsi.org Volume 3 Issue 1‖ January 2014 ‖ PP.36-40

Serum Total Prostatic Specific Antigen and Prostatic Acid Phosphatase Measurement Discriminating Prostate Carcinoma from Benign Prostatic Hyperplasia in Sudanese Patients

Haala M. Gabra[1*]; Adbelgadir A Elmugadam [2]; Badereldein H Elabid [3]; Ghada A.Elfadil[2], Mohamed H. Arbab [4];Elmutuz H.Elssaig [5];

[1,]*Clinical Chemistry, Laboratory department, Fedail Hospital.*
[2,]*Clinical Chemistry, department of FMLS, Sudan University of Science and Technology.*
[3,]*Chemical Pathology, department of FMLS, University of Science and Technology.*
[4,]*Medical Microbiology, department of FMLS, Omduraman Ahlia University.*
[5,]*Clinical Chemistry, department of FMLS, Al-Zaiem Al-Azhari University.*

ABSTRACT : *This is a prospective, analytical, hospital based, case control study. The aim of this study was to evaluate the clinical utility of total prostate specific antigen (TPSA) and prostatic acid phosphatase (PAP) for distinction between prostate carcinoma (PCa) and Benign prostatic hyperplasia (BPH) in Sudanese patients in Khartoum state.This study was carried out in Fedail Medical Hospital during the period of 2010 to 2012. It was performed on 200 patients as the study group and 100 healthy volunteers as the control group. The age for the control group and the study group were matched. Serum level of TPSA was measured by Roche immunoassay cobas e411 and serum PAP level was measured spectrophotometericaly.The mean level of serum TPSA was (42.6±27.2) and (7.8±5.1) for PCa & BPH respectively (p<0.01). While mean of PAP value were (37.5±24.5) and (8.81±7.05) for PCa & BPH respectively. PAP was elevated in 65% of the patients with cancer confined to the prostate, TPSA in 90%. In those patients with metastatic spread, PAP was elevated in 80% compared with 92% for PSA. In the BPH group, PAP levels were raised in 35% and for PSA in 81%.In conclusion, the results indicated that marked elevation of serum PSA suggests prostate carcinoma and that serum TPSA can discriminate prostate carcinoma from prostatic benign hyperplasia better than serum PAP.*

KEY WORDS : *Total Prostate Specific Antigen, Prostatic Acid Phosphatase, Benign Prostatic Hyperplasia, Prostate Cancer, and Sudanese.*

I. INTRODUCTION

Prostate cancer is the second leading cause of cancer-related deaths for men in the United States **(1)**. It has been suggested that screening for prostate cancer may have reduced prostate cancer mortality rates, but this remains controversial **(2)**. Current American Cancer Society guidelines for prostate cancer screening recommend a digital rectal examination and prostate-specific antigen (PSA) measurement annually for all men 50 or older if they have a minimum life expectancy of 10 years **(3)**.Prostate specific antigen (PSA) is a protein manufactured solely in the prostate. The prostate gland manufactures this protein in large quantities. The PSA level in the blood can vary by about 20% from day to day **(4)**. The Food and Drug Administration (FDA) in 1994 approved serum PSA to be used as an early detection of prostate cancer. Like so many serum tumour markers, it is produced by both normal and cancerous glands. In men with prostate cancer, the serum levels can be elevated in both localized and advanced or disseminated disease. PSA levels are generally proportional to the size of the tumour. However, there is a significant overlap between PSA levels found in cancer and benign prostatic hyperplasia cases (BPH) **(5)**. Prostatic acid phosphatase is an enzyme produced by several types of tissue, including normal prostate tissue. PAP is one of the major proteins secreted by prostate columnar epithelium secretory cells following puberty. In healthy individuals, PAP serum levels are low, on the order of 1-3ng/ml, whereas serum levels are elevated in many individuals with metastatic prostate cancer **(6, 7)**. Prostatic specific antigen (PSA) and prostatic acid phosphatase (PAP) are the tumor markers of prostatic carcinoma and have been used for confirming and monitoring prostate cancer **(8, 9)**. The clinical utility of PSA and PAP for early detection of prostate cancer is hampered by elevation of serum PSA levels in men with prostate benign hyperplasia **(10, 11)**.

II. MATERIALS AND METHODS:

2.1.Study design

This study was prospective, analytical, hospital based, case control study conducted in Fedail Hospital, Khartoum state, Sudan during the period of December 2010 to March 2012.

2.2.Subjects

This study was performed on 200 male patients as the study group, 100 of them diagnosed with prostatic carcinoma and another 100 diagnosed with benign prostatic hyperplasia. The mean age for them was 68.8.0±8.3 years. The study, also, included 100 healthy males as the control group with matched mean age 66.7.0±8.1 year. Interviews with the patients were done to obtain the clinical data. Also, a questionnaire was designed to collect data from the patients. Permission of this study was obtained from the authorized personnel in Fedail hospital. The nature of the study was explained to all participants in this study. Informed consent was obtained from each participant.

2.3.Sample

In a sterile condition by using a local antiseptic for skin, 5 ml of venous blood was collected in serum separating gel tubes from patients and controls. The blood samples were separated after complete clotting by centrifugation at 4000 rpm for 5 minutes and serum was collected and stored in tubes at -20°C for the analysis of TPSA while for PAP the serum was analyzed immediately after separation.

2.4. Measurements of TPSA & PAP

Serum for TPSA was measured by Electrochemiluminesent (ECL) immunoassay on Roche analyzer cobas e411, while the serum for PAP level was measured spectrophotometericaly. All samples were analyzed in the laboratory of Fedail Hospital.

2.5. Statistic evaluation

The data obtained were expressed as mean values ± SD. Statistical analysis was performed using SPSS 17 (Statistical Package for Social Sciences). The means were compared using Independent sample t.test. Pearson's correlation analysis was used for correlation of parameters measured. Analysis using two-tailed and a p-value ≤ 0.05 was considered as statistically significant.

III. RESULTS:

Serum TPSA (42.6±27.2ng/ml) in the PCa group was found to be higher than that in BPH group (7.8±5.1ng/ml). The difference between the two means was highly significant at $p<0.01$. PAP in the PCa group was significantly higher than that of BPH group (4.26±0.24 and 3.02±0.97) respectively ($p<0.01$).Then the study groups were subdivided according to the level of TPSA (<4ng/ml, 4-10ng/ml, 10-20ng/ml and >20 ng/ml) as shown in tables I and II, the TPSA was highly significant than PAP in all ranges.

TableI : Comparison between TPSA in PCa group and BPH group according to the level of TPSA

TPSA ranges	PCa mean±SD	P value	BPH mean±SD	P value
TPSA <4ng/ml	2.87±1.16	0.00	1.35±0.37	0.00
TPSA4-10 ng/ml	6.42±1.75	0.00	6.25±1.54	0.00
TPSA10-20ng/ml	14.2±3.13	0.00	13.2±2.9	0.00
TPSA >20ng/ml	59.1±26.6	0.00	25.6±4.2	0.00

Table II: Comparison between PAP in PCa group and BPH group according to the level of TPSA

TPSA ranges	PCa mean±SD	P value	BPH mean±SD	P value
TPSA <4ng/ml	4.26±0.25	0.002	3.02±0.97	0.029
TPSA 4-10 ng/ml	6.94±2.3	0.00	7.55±4.98	0.00
TPSA10-20ng/ml	17.3±10.4	0.33	11.61±5.8	0.00
TPSA >20ng/ml	44.8±19.5	0.174	24.9±12.6	0.089

The PCa group were sub divided according to Gleason score to well differentiated (2/10, 3/10 and 4/10), moderate differentiated (5/10, 6/10 and 7/10) and poor differentiated (8/10, 9/10, 10/10). TPSA levels were highly significant in all stages of prostate cancer while the PAP was only significant in the moderate differentiated group of the PCa as shown in table III.

Table III: Comparison between TPSA and PAP in PCa group according to Gleason score.

PCa Stages		TPSA	PAP
Well differentiation	Mean ± SD	7.7 ± 7.5	27.1 ± 23
	P value	0.00	0.37
Moderate differentiation	Mean ± SD	27 ± 23	23.9 ± 22
	P value	0.00	0.00
Poor differentiation	Mean ± SD	42.6 ± 33	37.5 ± 33
	P value	0.00	0.236

There were strong positive and significant correlations between TPSA and PAP in PCa group (r=0.836, P=0.00) (figure 1) and also there were strong positive and significant correlations between TPSA and PAP in BPH group (r=0.702, p=0.00) (figure 2).

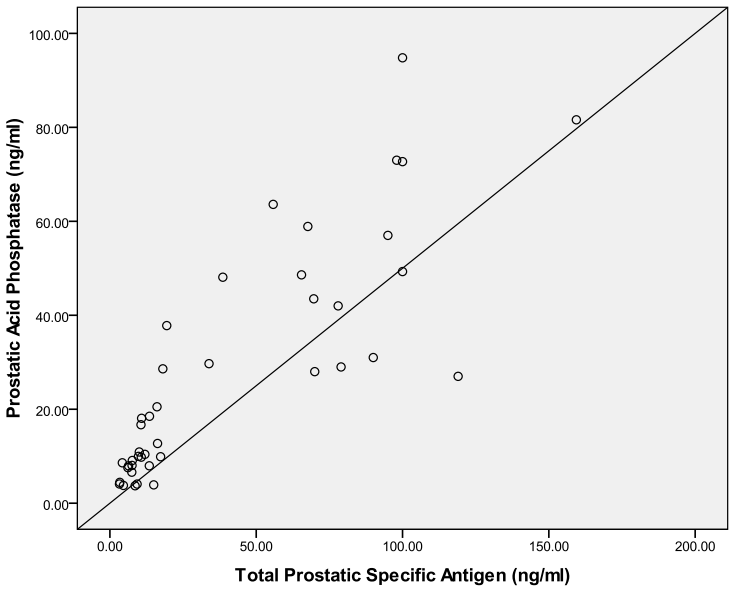

Figure1: A scatter plot shows correlation between TPSA & PAP in the PCa study group

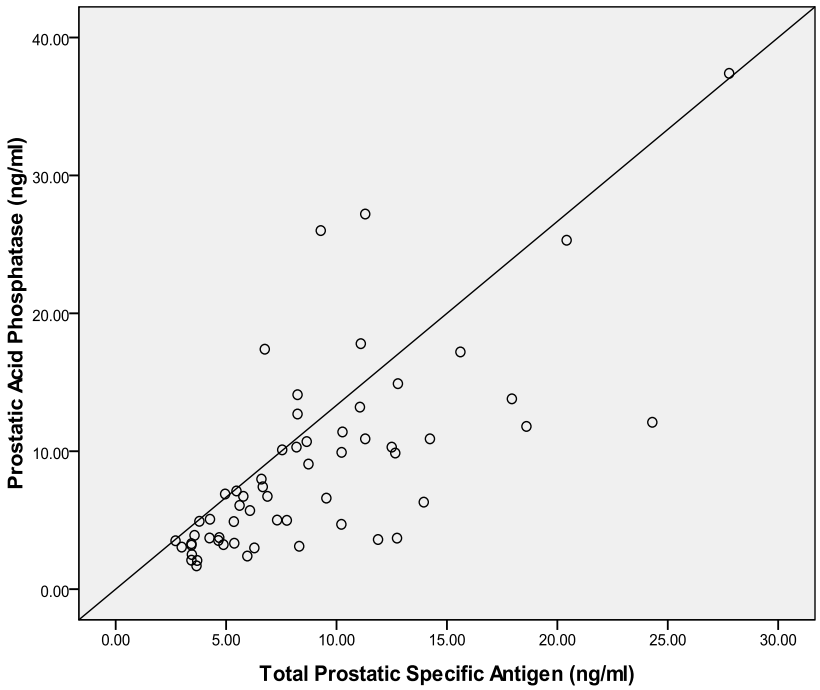

Figure2: A scatter plot shows correlation between TPSA & PAP in the BPH study group

TableIV: The sensitivity, specificity, PPV & NPV for TPSA & PAP

Parameter	TPSA	PAP
Sensitivity	95%	77%
Specificity	96%	91%
Positive Predictive Value	0.96	0.89
Negative Predictive Value	0.95	0.81

Efficiency of discrimination of prostate carcinoma from benign prostatic hyperplasia by PAP assay, as indicated in tables V and VI, is inferior to that of TPSA assay.

Table V: TPSA measurement discrimination of prostatic cancer from benign prostatic hyperplasia

Parameter	No. of PCa	No. of BPH
TPSA <4 ng/ml	25%	75%
TPSA 4-10 ng/ml	32%	68%
TPSA 10-20 ng/ml	58%	41%
TPSA >20 ng/ml	91%	9%

*Normal range is 0- 4 ng/ml.

Table VI: PAP measurement discrimination of prostatic cancer from benign prostatic hyperplasia

Parameter	No. of PCa	No. of BPH
PAP <5 ng/ml	14%	38%
PAP 5-10 ng/ml	26%	25%
PAP >10 ng/ml	59%	35%

*Normal range is 0- 5 ng/ml.

IV. DISCUSSION:

The results in this study showed that in the BPH group, PAP was raised in 35% and 81% for PSA. PAP was elevated in 65% of the patients with cancer confined to the prostate, TPSA in 90%. In those patients with metastatic spread, PAP was elevated in 80% compared with 92% for PSA. TPSA results show highly statistically significance (P value < 0.01) in the PCa group & BPH group even when the TPSA stratified to levels (<4, 4-10, 10-20 & >20 ng/ml). However PAP shows highly significance in PCa group only when TPSA in the range of (< 4 & 4-10 ng/ml) while in the BPH group it was statistically significant in all ranges (P value <0.01) except when TPSA > 20 ng/ml it was statistically insignificant (P value >0.05).In the PCa group and according to the Gleason´s score TPSA shows highly significance in all stages (P value <0.01), however PAP shows only highly significance in the moderate differentiated group (P value <0.01).Results in this study indicate that prostate carcinoma can be discriminated from Benign Prostatic Hyperplasia by serum TPSA with 95% sensitivity and by PAP with only 77 % sensitivity. The combined use of PSA and PAP do not give a greater accuracy in the screening of prostate cancer when compared with the sole use of PSA. This finding was consistent with the results reported by Bogdanowicz, et al (12) and Shih, et al (13). Although Bogdanowicz, et al (12) reported that PAP was elevated in only 4 patients when PSA was normal; however, in this study, the results obtained indicate that PAP was elevated in only one patient when PSA was normal.In conclusion, the study showed that PAP was a less sensitive than TPSA in screening of the prostate cancer. TPSA was superior to PAP for the detection of prostatic cancer. PAP does not give a greater accuracy in the screening of prostate cancer when compared with the TPSA. Prostatic specific antigen measurements can be used for discrimination of Benign Prostatic Hyperplasia from Prostatic Carcinoma, since PSA measurements are simple, painless, and relatively inexpensive procedures.

REFERENCES:

[1] Jemal, A; Siegel, R; Ward, E; Murray, T; Xu, J and Thun M J. (2007). Cancer statistics.CA Cancer J Clin. ;57:43-66.

[2] Hoffman, RM. Viewpoint. (2006). limiting prostate cancer screening. Ann Intern Med.; 144:438-440.

[3] Smith, R; Cokkinides, V and Eyre, HJ. (2004). American Cancer Society guidelines for the early detection of cancer.CA Cancer J Clin.; 54:41- 52.

[4] Sölétormos, G; Semjonow, A; Sibley, PEC; Lamerz, R; Petersen, PH; Albrecht, W; Bialk, P; Gion, M; Junker, F; Schmid, HP and Poppe HV. (2005). Biological Variation of total prostate-specific antigen: A Survey of published estimates and consequences for clinical practice. Clin Chem; 51: 1342-1351.

[5] Carter, HB; Epstein, JI and Partin, AW. (1997). Influence of age and prostate-specific antigen on the cancer of curable prostate cancer among men with nonpalpable disease. Urology; 53: 126-130.

[6] Ahmann, FR and Schifman, RB. (1987). Prospective comparison between serum monoclonal prostate specific antigen and acid phosphatase measurements in metastatic prostatic cancer. J Urol ; 137: 431-434.

[7] Robles, JM; Morell, AR; De Torres, JA and Rosello, AS. (1989). Clinical behavior of prostatic specific antigen and prostatic acid phosphatase: a comparative study. Int J Biol Markers; 4: 87- 94.

[8] Hudson, MA; Bahnson, RR and Catalona, WJ. (1989). Clinical use of prostate specific antigen in patients with prostate cancer J Urol.; 142:1011-1 017.

[9] Stamey, TA; Yang, N; Hay, AR; McNeal, JE; Freiha, FS and Redwine, E. (1987). Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. N Engl J Med.; 317:909-916.

[10] Ercole, CJ; Lange, PH; Mathisen, M; Chiou, RK; Reddy, PK and Vessella, RL. (1987)Prostatic specific antigen and prostatic acid phosphatase in the monitoring and staging of patients with prostatic cancer. J Urol.; 1 38:1181-1 184.

[11] Heaney, JA; Allen, MA; Keane, T and Duffy, MJ. (1987). Prostate specific antigen superior serum marker for prostatic carcinoma. IrJ Med Sci.; 156:138-141.

[12] Bogdanowicz, JF; Bentvelsen, FM; Oosterom, R and Schroeder, FH. (1991).Evaluation of prostate-specific antigen and prostatic acid phosphatase in untreated prostatic carcinoma and benign prostatic hyperplasia Scand J Urol Nephrol Suppl. 138:97-103.

[13] Shih, W-J; Collins, J; Mitchell, B and Wierzbinski. (1994). Serum PSA and PAP measurements discriminating patients with prostate carcinoma from patients with nodular hyperplasia J Nati Med Assoc.; 86:667-670.