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Original Research Article

A study of serum levels of prostate specific antigen, prostate acid phosphatase in prostate cancer patients and its complications on liver

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ABSTRACT

Background: The prostate cancer (PC) is most leading disorders in human beings particularly in males. Prostate specific antigen (PSA) and prostate acid phosphatase (PAP) are tumor markers useful for early detection and diagnosis of PC. In prostate cancer patients more prone to liver and bone cancer metastasis because in these patients elevated levels of serum liver function tests (LFT) and these liver enzymes more specific for early detection of pathological changes in liver and bones.
Methods: This is the case control study was carried out the association of serum levels of PSA/PAP inpatients with prostate cancer and healthy controls. Total 120 subjects included in this study in that 60 PC patients and 60 controls was included and blood was collected. The serum PSA levels are estimated by ELISA, PAP estimated by Kinetic method and LFT Was analyzed by commercial kits.
Results: The present study evaluates the serum levels of LFT, PSA and PAP in patients with prostate cancer and compared with the healthy controls. The statistically significant difference between the PSA, PAP and LFT levels in patients with PC when compared to controls. The positive correlation in between PSA, PAP with LFT (p=0.001).
Conclusions: This study suggesting that the serum PSA, PAP levels sensitive parameters for early detection of prostatic cancer and also for these patients' frequent measurements of serum liver function tests, useful for early detection of significant pathological changes occurs in the liver and bone cancers metastasis from prostate.

Keywords: Prostate specifics antigen, Prostatic acid phosphatase, Liver function tests, Prostate cancer

INTRODUCTION

Prostate cancer (PC) is one of the second most leading disorders in particularly in the males. Several metabolic disturbances occur in prostatitis, prostatic hyperplasia (BPH), and prostate cancer.[1] PC second most dreadful disease in the world particularly in the men. This type of cancer occurs mostly in young people with positive family history. The prostate specific antigen (PSA) and prostate acid phosphatase (PAP) used for early detection and disease progression of PC.[2] PSA is a glycoprotein contain 237 amino acids produced by lumina of the prostate gland and circulated in blood stream exist 2 major forms. The PSA levels useful for the prostate cancer detection and predict prognosis in men with prostate cancer undergoing therapy.[3,4]

PAP is the lysozyme produced mainly in the prostate gland and also some of the research identified it is synthesized in other tissues like erythrocytes, platelets, leukocytes, bone marrow, bone, liver, spleen, kidney, and intestine.[5,6] Elevated levels of serum PAP in prostatic cancer and other malignant such as osteogenic sarcoma, multiple myeloma, and bone metastases of other cancers.[7]

Liver is the one of the major organs sited in right hypochondrium, all metabolisms and detoxification processes occurs. PSA metabolism occurs in the liver, in PC patients' abnormal levels of serum LFT.[8] We aimed that the to evaluate serum PSA, PAP and LFT was useful for early detection and progression of PC and its complications particularly in the liver.

METHODS

This is the case-control study was conducted in Akash institute of medical sciences and research center, Karnataka from 2018-2020. A total 120 subjects included in the present study 60 PC patients and 60 healthy controls. All the subjects were recruited in the study after obtaining their informed consent after obtaining of ethical clearance from the institute (IEC No-463). Patients with prostatic cancer and age more than 30 years were included in the present study. Whoever has with absolute indications for surgical intervention such as: refractory hematuria, recurrent UTI, concomitant bladder stones, second renal insufficiency, UTI, other type of cancers and inguinal hernia excluded from this study. From the all subjects, after overnight fasting (12 hours), 5 ml of venous blood was collected and transferred into plain tube. The collected samples were separated by centrifugation at 4000 rpm for 15 min and stored until biochemical analysis was done.

Serum total bilirubin, serum direct bilirubin, serum aspartate transaminase (AST), serum alanine transaminase (ALT), serum alkaline phosphatase (ALP), serum gamma glutamyl transferase (GGT), serum total protein, serum albumin was measured by laboratory standard methods. Serum PSA was measured by enzyme linked immunosorbent assay (ELISA) and PAP also measured by using commercial kinetic kit (AIA 360 analyzer).

Statistical analysis

The normal distribution of data checked by using Kolmogorov Smirnov test. All the characters descriptively summarized. The mean and standard deviation about the arithmetic mean were used. Variations in the serum PSA, PAP and LFT was analyzed by using student's t-tests (2 tailed). The correlation between the PSA, PAP and LFT was done by using Pearson correlation analysis. The Data was compiled in Microsoft excel spread sheets and analyzed using SPSS for windows version 16.0. A p value<0.05 was considered statistically significant.

RESULTS

Table 1 shows the mean values and SD of patient's characteristic's and various biochemical parameters studied in prostate cancer and healthy controls. Significant difference was observed serum AST (38.15±20.72, p=0.001*), ALT (40.51±31.92, p=0.012*), ALP (111.54±30.66, p=0.001*), GGT (23.50±10.29, p=0.007*), albumin (4.62±0.49, p=0.017*), PSA (6.68±2.11, p=0.001*) and PAP (5.48±1.62, p=0.001*). Significantly higher levels in between serum AST, ALT, ALP, GGT, albumin, prostate specifics antigen and PAP in patients with PC when compared with healthy controls (p<0.001).

Table 2 shows the positive correlation of serum prostate specifics antigen and PAP with serum AST (r=0.277 and 0.275, p=0.002*), serum ALT (r=0.236 and 0.188, p=0.010*), serum ALP (r=0.602 and 0.610, p=0.001*), serum GGT (r=0.201 and 0.300, p=0.028*, 0.001*), serum albumin (r=0.246 and 0.249, p=0.007*, 0.006*) and negative correlation between the serum total bilirubin (r=0.040 and 0.020, p=0.663, 0.828), direct bilirubin (r=0.030 and 0.020, p=0.747, 0.824), total protein (r=0.009 and 0.058, p=0.920, 0.530) in patients with prostate cancer.

Figure 1 shows that the scattered plots in between serum ALP and serum PSA and PAP ratio, X axis showed: serum PSA and PAP ratio and Y-axis showed serum ALP concentrations. Positive correlation between serum ALP and serum PSA/PAP, (p value of 0.05) when compared with prostate cancer patients.

Table 1: Comparison of biochemical parameters in patients with prostate cancer and healthy controls.

Variables	Controls	Prostate cancer	P value
Age (years)	51.63±8.37	51.51±7.19	0.935
T BIL (mg/dl)	0.83±0.31	0.80±0. 35	0.686
D BIL (mg/dl)	0.28±0.14	0.26±0.13	0.513
AST (mg/dl)	24.38±17.36	38.15±20.72	0.001*
ALT (mg/dl)	27.15±25.24	40.51±31.92	0.012*
ALP (mg/dl)	90.25±35.07	111.54±30.66	0.001*
GGT (mg/dl)	28.78±10.71	23.50±10.29	0.007*
T. protein (g/dl)	7.42±0.47	7.44±0.56	0.876
Albumin (g/dl)	4.41±0.45	4.62±0.49	0.017*
PSA (ng/Ml)	2.13±1.56	6.68±2.11	0.001*
PAP (ng/Ml)	1.01±0.56	5.48±1.62	0.001*

Data expressed as mean ± SD, *Median (Inter quartile range), ns=non-significant.
TBIL: Total bilirubin, DBIL: Direct bilirubin, AST: Aspartate transaminase, ALT: Alanine transferase, ALP: Alkaline phosphate, T. PROTEIN: Total protein, PSA: Prostate specific antigen, PAP: Prostate acid phosphatase. Mg/dl: Milligram per deciliter, g/dl: Grams per deciliter, ng/mL: Nano grams per deciliter.

Table 2: Pearson correlation in between serum PSA/PAP with liver function tests.

Parameter		R value	P value
PSA	T BIL (mg/dl)	0.040	0.663
	D BIL (mg/dl)	0.030	0.747
	AST (mg/dl)	0.277	0.002*
	ALT (mg/dl)	0.236	0.010*
	ALP (mg/dl)	0.602	0.001*
	GGT (mg/dl)	0.201	0.028*
	T. protein (g/dl)	0.009	0.920
	Albumin (g/dl)	0.246	0.007*
PAP	T BIL (mg/dl)	0.020	0.828
	D BIL (mg/dl)	0.020	0.824
	AST (mg/dl)	0.275	0.002*
	ALT (mg/dl)	0.188	0.040*
	ALP (mg/dl)	0.610	0.001*
	GGT (mg/dl)	0.300	0.001*
	T. protein (g/dl)	0.058	0.530
	Albumin (g/dl)	0.249	0.006*

Data expressed as Rho values (r values), *non-significant, p-Probability values.

TBIL: Total bilirubin, DBIL: Direct bilirubin, AST: Aspartate transaminase, ALT: Alanine transferase, ALP: Alkaline phosphate, T. protein: Total protein, PSA: Prostate specific antigen, PAP: Prostate acid phosphatase, Mg/dl: Milligram per deciliter, g/dl: Grams per deciliter, ng/mL: Nano grams per deciliter.

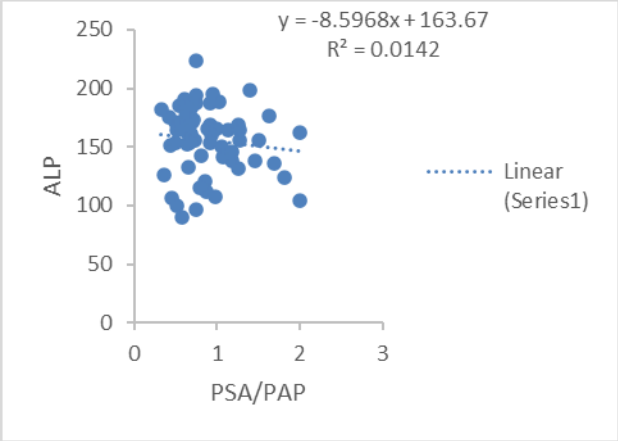

Figure 1: Scattered plots in between serum ALP and serum PSA and PAP.

ALP: Alkaline phosphatase, PSA: Prostate specific antigen, PAP: Prostate acid phosphatase, X-axis: ratio of PSA/PAP and Y-axis: ALP concentrations.

DISCUSSION

Prostate specific antigen synthesized from the epithelium of prostate gland and secreted into seminal fluid to maintain liquefaction of seminal fluid.[9] In circulation this will present in two major forms, complexed form bound with alpha 1-antitrypsin and another form free form. The normal serum levels of total PSA less than 4 ng/L.[10] The measurement of serum PSA levels useful for the early detection and progression of prostatic cancer.[11]

In the present study, serum prostate specific antigen levels were measured in patients with prostate cancer and healthy controls. There is a positively increased levels (Table 1; 2 tailed student's t-test's observed in patients with PC when compared with healthy controls. Similarly, another study found positively elevated levels of PSA levels found in prostatic cancer and compared with the controls.[12] Previous studies were done a systemic review on PSA screening, the elevated levels are useful for early detection and progression of prostate cancer when compared with the controls.[13] Men are with strong family history of prostate cancer and PSA Screening can reduce the mortality from prostate cancer.[14]

PAP is the hydrolytic enzyme and act as a glycoprotein synthesized from the lysosomes of prostatic epithelial cells. There are two different forms of PAP is there in human beings, cellular form (cPAP mostly present in prostatic cells) and another form is secretory form (sPAP present in both prostate and seminal fluid).[15,16] The physiological functions of cPAP effects like growth suppressing because it is cellular protein has tyrosine phosphate activity in the prostate tissue. Whenever reduced levels of cPAP in the body the extracellular signal-regulated kinase (ERK)/-and mitogen-activated protein kinase (MAPK) signaling pathway decreased. This leads to loss of androgen sensitivity and increase growth rate and tumorigenicity.[17,18]

The present study evaluates the PAP was measured significantly increased levels observed in patients with prostate cancer and compared to healthy controls (2 tailed student t-test) p=0.001. Similarly, previous study reported that the PAP is the positive subtype showed easier metastasis, larger tumor size, more localized tumor numbers, higher pathological grade, and shortened survival duration. PAP is one of the important progressions of prostate cancer.[19] We found that the most of the prostatic cancer patients' metastasis to bone, similarly another study was found that the PAP detection is prostate cancer patients used for metastasis of bone related problems particularly osteoblast lesions.[20]

Elevated levels of serum AST, ALT, ALP, GGT and albumin levels observed in prostatic cancer patients and compared with the healthy controls. Significantly increased levels of LFT in prostatic cancer patients leads to pathological changes in the liver, results increased enzymes activity. Particularly significantly increased ALP levels when compared with PSA and PAP by Pearson correlation (r=0.610 and p=0.001*) in patients with prostate cancer and compared to healthy controls. Another study also reported bone metastasis occurs from the prostate cancer particularly in men. In prostatic cancer patients elevated levels of serum ALP may be leads to early detection of bone metastasis in prostate cancer patients.[21,22] This study also suggests to frequent

measurement of serum PSA, PAP and LFT in prostate cancer patients useful for early detection of bone metastasis.

Serum prostate specific antigen and prostate specific acid phosphatase are synthesized from the prostate gland and if any pathological changes occur in the prostate gland these levels are elevated in the blood, to measure serum PSA and PAP levels are useful for early detection and progression of prostatic cancer. The prostate cancer patients are more prone to metastasis of liver and bone cancers, this study evaluated that the serum liver function tests are more significantly difference between prostate cancer patients and healthy controls. This study suggests to frequent checking of serum PSA, PAP and LFT levels more significantly useful for early detection of metastasis of liver and bone cancers in prostatic cancer patients.

Limitations

The present study was small sample size and randomly selected prostate cancer patients. This study suggests large sample size and follow-up studies are required.

CONCLUSION

Serum PSA and PAP elevated in serum useful for early detection and progression of prostate cancer and also these levels are significantly correlating with serum liver function tests results frequent monitoring of these tests useful for early detection of metastasis of liver and bone cancers in patients with prostate cancer.

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