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Short Report

The Study Of Serum Prostate Specific Antigen And Phosphatase Isoenzymes Activity As Diagnostic Parameters In Patients With Prostate Cancer In Nigeria

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Abstract:
Serum activities of Acid Phosphatase (ACP) and Prostatic Acid Phosphatase (PAP) are still employed in most hospitals in Nigeria for the diagnosis of prostate cancer, because of lack of resources for prostate specific antigen (PSA) assay. Serum PSA and activities of phosphatase isoenzymes ACP and PAP, Alkaline Phosphatase (ALP) and Heat stable Alkaline Phosphatase (HSAP) were studied in 71 apparently healthy male controls and 47 proven prostate cancer patients. There were statistically significant increases in the mean serum levels of PSA, PAP, ACP, ALP and HSAP in the prostate cancer patients compared to the controls ($P<0.001$). PSA level was increased above the cut-off level in 85.1% of patients, PAP in 66.0%, ACP in 57.5%, ALP in 34.0% and HSAP in 21.3% of cases. Serum levels of PSA, ACP and PAP were lower and of ALP and HSAP higher in patients with longer duration of the disease ($P<0.05$). The study confirms the relevance of PSA assay over ACP, PAP, ALP and HSAP in the diagnosis of prostate cancer patients. It highlights the need for the inclusion of PSA assay in hospitals for accurate diagnosis of prostatic carcinoma.
Key words: Prostate Cancer, Prostate specific antigen, Acid phosphatase, Nigeria.

Introduction

Prostate cancer is the most common malignant tumour in men over the age of 65 years. It has been declared a public health epidemic in black American men because of its high incidence.[1] Africa was reported in the past to have a low incidence of this disease,[2] however recent studies indicate a high and rising incidence in Nigerians.[3,4]

The measurement of acid phosphatase(ACP) isoenzymes is recommended as a routine screening test for patients whose serum ACP is abnormally high. This is because the isoenzyme study not only indicates the presence or absence of prostate cancer but also whether or not there is bony metastasis.[5] However, with the advent of prostate specific antigen (PSA) measurement, assay of ACP and prostatic acid phosphatase (PAP) in the diagnosis, staging and monitoring of prostate cancer has taken a back-stage.[6] ACP and PAP estimations are still employed in most hospitals in Nigeria because of lack of resources for PSA.[7] On the other hand, heat stable alkaline phosphatase (HSAP), a placenta – type ALP that is expressed in gonadal and urologic cancers[8], including prostate carcinoma and metastatic diseases with bony lesions,[9] may play a role in the diagnosis of prostate cancer in the absence of facilities for PSA. Thus, the need for the evaluation and reappraisal of the combined serum activities of ALP, HSAP, ACP and PAP in the presence or absence of PSA assay in the diagnosis and monitoring of prostate cancer in Nigeria. This may provide a simpler, more common and affordable combined method for the diagnosis of this disease and/or encourage hospital management to improve on the resources necessary for this diagnosis.

Materials and methods

Subjects

Forty-seven (47) prostate cancer patients within the ages of 50-90 years were selected from University of Benin Teaching Hospital, Benin City (UBTH), and Nnamdi Azikiwe University Teaching Hospital, Awka (NAUTH), Nigeria between July 2002 and July 2003. Prostate cancer patients were grouped as <1 year, 1-2 years and >2 years after diagnosis. The control population was made up of 71 male volunteers, who were apparently healthy and prostate cancer asymptomatic. They were selected to match the patients in age and socio-economic status. Informed consent was obtained from all subjects.

Collection of Samples

Five millilitres (5ml) of venous blood was obtained from each of the subjects, dispensed into plain container without anticoagulant, allowed to clot and retract. The serum was separated from the whole blood after centrifugation and stored frozen until the assay. However, sera for ACP and PAP estimations were stabilised using 5mg sodium hydrogen sulphate monohydrate per ml of serum before freezing.

Methods

Serum ALP and HSAP activities were determined using the methods of King and Armstrong,[10] and Moss and Whitby[11] respectively, employing reagent kits supplied by Randox Laboratories Ltd, UK. Total ACP and PAP activities were determined using King and Kind Method[12] with reagent kits supplied by Randox Laboratories Ltd, UK. PSA was determined by the use of AxSYM PSA (Abbott Diagnostics) automated microparticle enzyme immunoassay technique.[13]

Statistical Analysis

Statistical methods included student's two – tailed test for unpaired data and analysis of variance (ANOVA) for continuous variables. These were carried out with SAS software (SAS Institute Inc. Cary, North Carolina). The 5% ($P<0.05$) level of significance was adopted for significant findings.

Results

The distribution of prostate cancer patients with serum biochemical values above the cutoff points for the various parameters is shown in Table 1. PSA showed higher reliability as tumour marker (85.1%), followed by PAP (66.0%), ACP (57.5%), ALP (34.0%) and HSAP (21.3%).

Table 1: Distribution of patients with biochemical values above the cut-off (upper-limit of normal)[14,15]

Parameter	Number of Patients (%)	Cut-off point
PSA (ng/ml)	40 (85.1)	4
ACP (U/L)	27 (57.5)	5.5
PAP (U/L)	31 (66.0)	1.0
ALP (U/L)	16 (34.0)	130
HSAP (U/L)	10 (21.3)	0.0

Serum PSA concentration as well as the activities of ACP, PAP, ALP and HSAP were significantly increased in the prostate cancer patients compared with controls (P<0.001; Table 2).

Table 2: Serum biochemical values in prostate cancer patients and controls

Parameter	Patients (n = 47)	Controls (n = 71)	P value
PSA (ng/ml)	10.6 ± 4.4	2.2 ± 0.8	<0.001
ACP (U/L)	64.2 ± 35.4	7.96 ± 3.4	<0.001
PAP (U/L)	59.3 ± 34.5	2.6 ± 2.2	<0.001
ALP (U/L)	251.7 ± 61.2	133.3 ± 55.0	<0.001
HSAP (U/L)	2.0 ± 1.6	0.13 ± 0.09	<0.001
Values are mean ± SD			

Table 3 shows the comparison of each parameter in prostate cancer subjects with respect to duration from date of diagnosis. The serum PSA, ACP and PAP levels were significantly lower (P<0.01) in patients with longer duration from diagnosis (>2years) comapred to those with shorter duration from diagnosis (<1year). On the other hand, the serum activities of ALP and HSAP were significantly higher in patients with diagnosis >2years compared to those with duration of <1year after diagnosis (P<0.01).

Table 3: Comparison of the mean levels of the biochemical parameters in prostate cancer subjects with respect to duration from diagnosis

Parameter	Duration		
	<1year (n = 20)	**1-2 years (n = 14)**	**>2 years (n = 13)**
PSA (ng/ml)	12.7± 5.1^{a}	10.1 ± 2.8^{b}	7.8 ± 2.6^{b}
ACP (U/L)	82.7 ± 41.7^{a}	51.8 ± 23.0^{b}	49.1 ± 19.1^{b}
PAP (U/L)	78.0 ± 41.5^{a}	48.4 ± 19.7^{b}	44.2 ± 17.1^{b}
ALP (U/L)	222.2 ± 61.7^{a}	250.8 ± 50.3^{a}	298.1 ± 42.5^{b}
HSAP (U/L)	0.9 ± 0.6^{a}	1.3 ± 0.9^{a}	4.3 ± 2.3^{b}
Values are mean ± SD			
Values with different superscripts per row are statistically significant (P<0.05)			

Comparison of serum PSA and phosphatase isoenzymes activity shows that for each age group, (Table 4) the values were significantly higher in patients than in controls (P<0.01 and P<0.001).

Table 4: Age-wise distribution of serum biochemical values in prostate cancer patients and controls

Parameter	Age Groups											
	51-60 years			61-70 years			71-80years			81-90 years		
	Patients (n = 6)	Controls (n = 22)	P value	Patients (n = 18)	Controls (n = 20)	P value	Patients (n = 21)	Controls (n = 19)	P value	Patients (n = 2)	Controls (n = 10)	P value
PSA (ng/ml)	7.3 ± 2.7	2.5 ± 0.9	<0.01	9.3 ± 3.0	2.3 ± 0.5	<0.001	11.9 ± 4.0	1.9 ± 0.7	<0.001	18.0 ± 8.0	2.1 ± 0.7	<0.01
ACP (U/L)	61.4 ± 33.8	8.8 ± 4.3	<0.001	60.1 ± 26.5	8.4 ± 3.5	<0.001	66.8 ± 40.4	6.7 ± 2.2	<0.001	82.2 ± 44.1	7.7 ± 2.3	<0.001
PAP (U/L)	57.6 ± 33.9	3.1 ± 2.7	<0.001	53.5 ± 24.4	2.9 ± 2.2	<0.001	62.9 ± 39.7	1.8 ± 1.9	<0.001	77.8 ± 42.4	2.2 ± 1.3	<0.001
ALP (U/L)	206.2 ± 92.9	153.1 ± 63.2	>0.05	249.8 ± 55.2	117.2 ± 51.9	<0.001	263.7 ± 54.9	120.6 ± 45.8	<0.001	279.9 ± 0.5	145.8 ± 51.7	<0.01
HSAP (U/L)	0.4 ± 0.3	0.00 ± 0.0	<0.01	1.0 ± 0.9	0.0 ± 0.0	<0.001	2.6 ± 1.2	0.0 ± 0.0	<0.001	4.6 ± 2.1	0.0 ± 0.0	<0.001
Values are mean ± SD												

Discussion

Results of this study indicate significant elevations in serum PSA concentrations as well as ACP, PAP, ALP and HSAP activities in prostate cancer patients compared to controls. It shows that PSA remains a potent marker for diagnosis of prostate cancer. However, ALP and HSAP, and of course ACP and PAP may be effective markers for prostate carcinoma with reliability in the range of PSA (85.1%) > PAP (66.0%) > ACP (57.5%) > ALP (34.0%) > HSAP (21.3%). The higher reliability shown by PSA, PAP, and ACP may be due to the fact that they are prostate specific proteins.[16,17] The continued use of ACP and PAP assays due to the absence of PSA assay facility may account for the reported low incidence of prostate carcinoma in Nigeria.[18]

Higher levels of ALP and HSAP activities in patients with longer duration of prostatic cancer corroborates the finding that increases in serum levels of ALP occur with concomitant advancement of prostate cancer.[19] This may be due to, not only elevation in serum HSAP, but also increase in the concentration of bone and liver ALP isoenzymes in advanced prostate carcinoma with bone and liver metastasis respectively.[20] Increase in ALP and HSAP with advanced prostate cancer may make ALP and HSAP as markers of relapse during treatment. Elevated levels of HSAP appear to occur in prostate cancer patients with metastatic disease that are clinically progressive as well as those apparently responding to chemotherapy.[8,21] The lower mean values of PSA, PAP and ACP in the prostate cancer subjects with longer duration after diagnosis may indicate that these may be better indices of the organ's response to treatment of the tumour. Therefore PSA is a useful marker in the management of patients with prostate carcinoma and it surpasses PAP in this regard.[22]

An age-adjusted study of the mean PSA, ACP, PAP, ALP and HSAP values in the prostate cancer patients showed higher levels with higher age of the subjects. The mean values of PSA, PAP and ACP showed statistically significant higher values in the prostate cancer patients compared to control subjects in all age groups, while the increase in ALP was not statistically significant in the youngest age group (51-60 years). This further confirms the greater reliability of PSA, PAP and ACP in the prostate cancer monitoring over ALP. The significant increases observed among the older age

groups may be attributed to the finding that prostrate cancer is the most common malignant tumour in Nigerian men of average age 71 years.[7]

This study has confirmed that PSA measurement remains a more reliable method compared to ACP, PAP, ALP and HSAP assays for the diagnosis of prostate cancer. It also points to the issue that spectrophotometric measurement of PAP and ACP, and may be ALP and HSAP could be relevant in the monitoring of patients with prostate cancer. It calls for the inclusion of PSA measurement in the litany of tests run in most hospitals in Nigeria for the diagnosis of prostate cancer. This will help bring into focus the exact incidence of prostate cancer in Nigeria for adequate management and planning.

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