RESEARCH COMMUNICATION

Prostate Biomarkers with Reference to Body Mass Index and Duration of Prostate Cancer

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Abstract

Objective: This study was performed to assess prostate biomarkers with reference to body mass index and duration of prostate cancer. Materials and Methods: A hospital based retrospective study was undertaken using data retrieved from the register maintained in the Department of Biochemistry of Manipal Teaching Hospital, Pokhara, Nepal between 1st January, 2009 and 28th February, 2012. Biomarkers studied were prostate specific antigen (PSA), acid phosphatase (ACP) and prostatic acid phosphatase (PAP), alkaline phosphatase (ALP) and gamma glutamyl transpeptidase (γGT). Demographic data including age, duration of disease, body weight, height and body mass index (BMI) were also collected. Duration of disease was categorized into three groups: <1 year, 1-2years and >2 years. Similarly, BMI (kg/m^2) was categorized into three groups: <23 kg/m^2, 23-25 kg/m^2 and >25 kg/m^2. Descriptive statistics and testing of hypothesis were used for the analysis using EPI INFO and SPSS 16 software. Results: Out of 57 prostate cancers, serum level of PSA, ACP and PAP were increased above the cut-off point in 50 (87.5%), 30 (52.63%) and 40 (70.18%) respectively. Serum levels of PSA, ACP and PAP significantly declined with the duration of disease after diagnosis. We observed significant and inverse relation between PSA and BMI. Similar non-signficiant tendencies were apparent for ACP and PAP. Conclusions: Decreasing levels of prostate biomarkers were found with the duration of prostate cancer and with increased BMI. Out of prostate biomarkers, PSA was found to be significantly decreased with the duration of disease and BMI.

Keywords: PSA - ACP - PAP - prostate cancer - BMI - duration of disease

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Introduction

Prostate cancer (PCa) is the most common malignant tumor in male above 60 years however age more than 40 years is the risk factor for prostate cancer (Ceber et al., 2010; Nath et al., 2012). Prostatic biomarkers including prostate specific antigen (PSA), acid phosphatase (ACP) and prostatic acid phosphatase (PAP) can be utilized in the diagnosis, staging and monitoring of prostate cancer (Morote et al., 1989). Serum level of prostatic biomarkers decreases in prostate cancer with longer duration after diagnosis reflects the better indicator of organ's response for the treatment of tumors (Filella et al., 1990). Different documentation from different studies regarding association between body mass index and detection rate of prostate cancer provided great loopholes. Andersson et al. (1997) reported no significant relation between the PCa and BMI, Presti et al. (2004) reported higher incidence of PCa with lower BMI and Schuurman et al. (2000) reported higher incidence of PCa with higher BMI (Andersson et al., 1997; Presti et al., 2004; Schuurman et al., 2000). Chiu et al. (2011) reported a higher BMI was significantly associated with lower PSA levels. To the best of our knowledge, no study regarding prostate biomarker's relation with the duration of PCa and BMI has been reported from Nepal. Thus our objective was to compare the serum level of prostate biomarkers with different grade of BMI and duration of PCa.

Materials and Methods

This hospital based retrospective study was carried out using data retrieved from the register maintained in the Department of Biochemistry of the Manipal Teaching Hospital, Pokhara, Nepal between 1st January, 2009 and 28th February, 2012. The variables collected were age, weight, height, total PSA, PCA, PAP, ALP and γGT. Ethical approval for the study was taken from the institutional research ethical committee. Serum Total PSA was estimated by microtitre well ELISA method (Wajsman Z et al., 1978; Kuriyama et al., 1980). PSA was analyzed using Human reagent kits and with the help of ELISA

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and semi autoanalyser (Humalyser 3500, Germany). Estimation of γGT was done by using Human reagent kits by kinetic method. Estimation of ALP was done by using the method of king and Armstrong (Moss et al., 1987). Serum activity of total ACP and PAP were estimated by King and Kind method using Radox Laboratories Ltd, UK. Laboratory standard operation procedures were maintained for all laboratory analysis. Internal quality control sera, both normal and pathological, were also run for each lot of the test, for the validation of the results. Inclusion criteria- Cases were men with incident, histologically confirmed prostate cancer. Controls were men without clinical cancer who were seen at the same hospital for an annual physical examination. Exclusion criteria- Patients suffering from any other cancer was excluded from our study. Difference for continuous variables was assessed by using the t-test and Mann-Whitney U test. The data was analyzed using Excel 2003, R 2.8.0 Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and the EPI Info 3.5.1 Windows Version.

Results

Table 1 shows the distribution of prostate cancer cases with serum prostate biomarkers above the cut-off points. Out of 57 prostate cancer patients, 50 (87.7%) had serum PSA level more than cut-off point. Similarly, 40 (70.18%) and 30 (52.63%) of prostate cancer cases had serum PAP and ACP level respectively more than cut-off point. PSA showed higher reliability prostate biomarker followed by PAP and ACP. Besides prostate biomarker, 15 (26.32%) and 11 (19.3%) cases of prostate cancer had ALP and γGT respectively more than cut off point.

Table 2 shows the comparison of mean value of prostate biomarkers between the cases and controls. Mean value of serum PSA, ACP and ALP were found to be increased in cases when compared with control (p-value <0.001). Mean value of serum γGT level were also increased in cases when compared with controls (p-value 0.015). However, significant differences were not found in serum level of ALP (p-value 0.098) and BMI (p-value 0.895) between the cases and controls.

Table 3 shows the comparison of mean value of each prostate biomarker in prostate cancer cases with respect to duration from the date of diagnosis. The serum level of PSA (P-value 0.007), ACP (p-value <0.001) and PAP (p-value <0.001) were decreased with the duration of prostate cancer. However, the mean value of ALP (p-value 0.199), γGT (p-value 0.483) and BMI (p-value 0.628) were not significantly changes with the duration of disease.

Table 4 shows the comparison of mean value of each prostate biomarker in prostate cancer cases with respect to different group of BMI. The serum level of PSA (p-value 0.001), ACP (p-value 0.677) and PAP (p-value 0.822) were decreased with the increased level of BMI in prostate cancer. Similarly, the mean value of ALP (p-value 0.64) was also decreased with the increased level of BMI in prostate cancer. However, the mean value γGT (p-value 0.032) was increased with the increased level of BMI in prostate cancer.

Table 1. Distribution of Patients with Biochemical Values above the Cut-Off (Upper-Limit of Normal)

Parameter	Number of Patients (%)	Cut-off Point
PSA (ng/ml)	50 (87.70)	04.0
ACP (U/L)	30 (52.63)	4.50
PAP (U/L)	40 (70.18)	0.80
ALP (U/L)	15 (26.32)	310
γGT (U/L)	11 (19.30)	50.0

Table 2. Comparison of Different Parameters in Prostate Cancer Patients and Controls

Parameter	Patients (n = 57)	Controls (n = 57)	P-value
PSA (ng/ml)	7.8±3 (6.96-8.56)	1.9±0.98 (1.6-2.1)	<0.001
ACP (U/L)	4.8±1.8 (4.34-5.28)	3.1±0.6(2.9-3.2)	<0.001
PAP (U/L)	2.0±1.7 (1.58-2.5)	0.5±0.2 (0.4-0.5)	<0.001
ALP (U/L)	265±69 (247-283)	246±53 (232-260)	0.098
γGT (U/L)	38±11.7 (35-41)	33.5±8.3 (31-36)	0.015
BMI	23.8±2.9 (23-24.6)	23.9±3 (23-25)	0.895

Table 3. Comparison of the Mean Levels of the Biochemical Parameters in Prostate Cancer Subjects with Respect to Duration from Diagnosis

Parameter	Duration of prostate cancer after diagnosis			P-value
	<1year (n = 25)	1-2 years (n =18)	>2 years (n =14)	
PSA (ng/ml)	9.00±3.60 (7.5-10.5)	7.330±2.21 (6.23-8.44)	6.030±1.40 (5.2- 6.84)	0.007
ACP (U/L)	5.90±1.70 (5.2- 6.6)	4.250±1.56 (3.47-5.03)	3.620±1.06 (3.0- 4.23)	<0.001
PAP (U/L)	3.00±1.80 (2.2- 3.7)	1.460±1.33 (0.79-2.10)	1.100±1.10 (0.5- 1.74)	<0.001
ALP (U/L)	255 ±49.0 (234-275)	289.4±72.5 (253- 325)	253.6±88.7 (202-305)	0.199
γGT (U/L)	39.6±11.9 (35-44.5)	38.72±12.4 (32.5-44.9)	34.92±10.5 (28.9- 41)	0.483
BMI	23.5±3.30 (22-24.8)	24.08±2.59 (22.8-25.4)	24.40±3.10 (22.6- 26)	0.628

Table 4. Comparison of Serum Biochemical Values among BMI Groups in Prostate Cancer

Parameters	BMI group (Kg/m^2)			P-Value
	<23	23-25	>25	
PSA (ng/ml)	9.49±3.46 (7.96-11.03)	7.05±2.56 (5.77-8.32)	6.28±1.36 (5.570-6.98)	0.001
ACP (U/L)	5.01±1.75 (4.24-5.79)	4.83±2.15 (3.76-5.91)	4.50±1.38 (3.79-5.220)	0.677
PAP (U/L)	2.15±1.53 (1.47-2.83)	2.12±2.13 (1.06-3.18)	1.82±1.53 (1.03-2.610)	0.822
ALP (U/L)	276 ±71.8 (244.5-308)	258 ±62.0 (228-289.7)	258 ±73.2 (220-295.57)	0.640
γGT (U/L)	33.4±10.5 (28.7-38.1)	39.5±7.60 (35.7-43.3)	42.9±14.6 (35.43-50.5)	0.032

Discussion

In this study, we found that significant elevation of PSA, ACP, PAP and γGT in prostate cancer cases compared with normal control group. However, there was no significant difference of serum level of ALP and BMI between prostate cancer cases and normal healthy controls. In current study, PSA was found to be potent biomarker for the detection of prostate cancer. The serum level of PSA, ACP and PAP were found to be elevated in 87.7%, 52.63% and 70.18% of prostate cancer respectively. PSA and PAP are the predominant proteins found in prostate glands and most of the part of ACP is covered by PAP in prostate cancer. Due to this reason, PSA, PAP and ACP have shown higher reliability in prostate cancer (Bauer et al., 1988; Angelis et al., 2007). Moreover, PSA overcome the low incidence of detection of prostate cancer using PAP and ACP alone. We found that 26.32% of prostate cancers have the elevation of serum ALP level. However, there was not significant elevation of serum ALP level among the prostate cancer. Higher activity of serum ALP with the advancement of prostate cancer indicates the advances of bone and liver metastasis (Wajsman et al., 1978). 19.3% of prostate cancers had serum γGT level more than cut off point. Moreover, γGT level was significant elevated among the prostate cancer cases. Though γGT is not specific for prostate, its concentration is found be high in prostate glands. Higher mean values of PSA, PAP and ACP in earlier period after diagnosis and low mean values with the longer duration after diagnosis reflecting the high detecting efficacy of prostate cancer. Moreover, suppresses of these markers after treatment indicates better marker for the management and follow-up of prostate cancer to know the efficacy of treatment (Filella et al., 1990; Sfoungaristos et al., 2011). Significant elevation of serum level of PSA and PAP with the advances of age indicates that incidence of prostate cancer is higher among the advanced age. In our study, we observed higher serum level of PSA and PAP above 70 years of age. In this study, we found that mean value of serum PSA, ACP and PAP were decreased with the increased level of BMI. Significant decreasing of prostatic biomarkers with the increasing BMI reflects a greater cancer detection rate in patients having relatively lower BMI. Our result is similar to the study done by Presti et al (Presti et al., 2004). McGrowder DA et al reported that some components of the metabolic syndrome such as obesity, an abdominal fat distribution, and hyperinsulinemia have been associated with the risk of prostate cancer (McGrowder et al., 2012). The exact mechanism between the BMI and prostate cancer detection has not been documented. Some hypotheses have proposed to explain the relationship between BMI and prostate cancer (Freeman et al., 2004; Presti et al., 2004). One of the possible hypotheses is due to effect of hormones. Higher level of estrogen and lower level of testosterone is usually found in excessive adipose tissues. This condition is well matched with the detection of cancer in patients having low BMI. According to lipid-raft theory, cholesterol accumulates in solid tumor cells and interruption of cholesterol homeostasis in prostate with aging and with the transition to malignant state (Freeman et al., 2004). Mittal A et al showed significant association between hypercholesterolemia in prostate cancer (Mittal et al., 2011). However, the hypothesis of utilization of fat is related to prostate cancer risk which is not properly matched with lower BMI and greater cancer detection. In conclusion, decreasing the level of prostate biomarkers found with the increasing level of BMI indicates higher amount of detection rate of prostate cancer found in lower BMI. Level of prostate biomarkers (PSA, PAP ACP) decrease with the duration of prostate cancer after having treatment indicate its specificity to prostate glands and can be utilized for diagnosis and management of prostate cancer.

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