RESEARCH COMMUNICATION

Effects of Aging and Ethnicity on Serum Free Prostate Specific Antigen

Sudip Shah[1*], Bharat Jha[2], Madhav Prashad Khanal[2]

Abstract

Understanding the relationship between ethnicity and free prostate specific antigen (fPSA) could identify the population that should be targeted for intervention and prevention program regarding prostate disease. In this study, we therefore examine the effects of aging and ethnicity on fPSA, measured in serum by chemiluminescent assay (CLIA) method of 351 men visiting Tribhuvan University Teaching Hospital (TUTH) for fPSA test from December to March. Medicinal records abstracts were used to obtain information regarding the ethnicity and age of the cases. Those cases whose age and surname could not be obtained were excluded in our study. The subjects were stratified in four ethnic groups viz; Indo-Nepalese, Tibeto-Nepalese, Indigenous and Other based on the origin. The relationship between age and fPSA level was analysed using bivariate coorelation. The age and the fPSA level of the cases were expressed in Mean ± SEM. The association among different age-group and ethnicity with fPSA were analysed using one way ANOVA. The mean fPSA and mean age of the subjects were 1.74 ± 0.22 and 66.84 ± 0.64 respectively. fPSA level was fairly correlated with the age (r=0.146, p=<0.01). The mean fPSA level (ng/ml) among the four age category (<45, 45-60, 60-75 and >75) were 0.49 ± 0.13, 0.69 ± 0.10, 1.94 ± 0.04 and 2.33 ±0.43 respectively. The difference in mean fPSA level among four different age-groups was statistically significant (p=0.031). Analysis showed no correlation between the fPSA level and the ethnicity. These data suggest that the fPSA level is associated with the age.

Keywords: Age - ethnicity - free prostate specific antigen - Nepalese

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Introduction

There are major variations in the age-specific prevalence of prostate disease between countries. Death rates from invasive prostate cancer (PC) has the widest geographical variations, with 20-fold differences between African-American men living in the US compared with Chinese and Japanese men living in Asia. The prevalence of benign prostate hyperplasia (BPH) also varies between countries, albeit less strikingly (Guess, 1992). Also wide variation in the reported incidence of clinical PC has been reported between different ethnic groups. The reasons for these population differences relating to ethnicity or geography are not well understood, but hormonal, genetic and nutritional factors may be involved. The well established epidemiological determinants of prostate disease are age, exposure to androgens in early manhood, and genetics.

Prostate Specific Antigen (PSA) is concentrated in prostatic tissue, and serum PSA levels are normally very low. Disruption of the normal prostatic architecture in prostate disease (BPH, PC or Prostatitis) allows greater amounts of PSA to enter the general circulation. Elevated serum PSA level leads to a large percentage of false positive screening results of PC. A potential solution to this problem involves the determination of free prostate specific antigen (fPSA) levels and PSA velocity (Partin and Oesterling, 1996). The measurement of free serum PSA in conjunction with total PSA, can improve specificity of prostate cancer screening in selected men with elevated total serum PSA levels, which would subsequently reduce unnecessary prostate biopsies with minimal effects on cancer detection rates (Catalona et al., 1995).

PSA levels can be affected by many factors that might be unrelated to prostate disease, e.g. age and ethnicity (Chia et al., 2008). In the US, other than having a PSA test, the main factors that increases the likelihood of receiving a diagnosis of PC are ageing, race (black race which increases the risk by a factor of ~1.5), and a family history of PC (a history of having an affected first degree relative at least doubles the risk). So, the main aim of my study was to assess the effect of the ageing and the ethnicity on the fPSA level among the Nepalese people.

Men with the prostate disease generally exhibit elevated levels of PSA in their serum; this tumor marker is now frequently used for PC screening, diagnosis and monitoring of the response to therapy. As total PSA and fPSA level depends markedly on age and might be significantly influenced by the ethnicity. An appropriate threshold value in Asian men should be established

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and age-related correlation is needed. To date, studies conducted to establish normal serum PSA values have involved study population that have included North America, Europe, Japan, Korea and China. To our knowledge, there are no reports of population studied involving the South Asian, also in Nepal no reports of such studied have been started. But also, correlation and association of different risk factors and biochemical parameters including tumor markers in prostate disease, age-specific PSA ranges in according to ethnicity should be established.

Materials and Methods

The study population included men from different parts of Nepal prescribed for the fPSA test in Tribhuvan University Teaching Hospital from December 2010 to March 2011. Blood samples were obtained for serum fPSA concentration. Those cases whose age and surname could not be obtained were excluded in our study. Cases who fulfilled the criteria (n=351) were stratified in four ethnic groups based on the origin viz; Indo-Nepalese (n=237), Tibeto-Nepalese (n=49), Indigenous (n=50) and Other (n=15). The cases of varied ages were included in the analysis. Subjects were divided into four age categories of <45 (n=16), 45-60 (n=72), 60-75 (n=153), >74 (n=110) All serum samples were assayed for fPSA in the same laboratory to prevent inter laboratory variation in measurements. The fPSA level was assayed using an immunometric assay (EKONCLIA F- PSA kit, Bio-Ekon Biotechnology, China). The EKONCLIA fPSA standards (provided by Manufacturer Company) were calibrated against National Standard of P.R. China for free Prostate Specific Antigen (150544-0004). 1ng/ml EKONCLIA fPSA Standards =1ng/ml fPSA NS 150544-0004

The relationship between serum fPSA level and age was assessed using Pearson correlation. Association of mean of continuous data between cases was tested by one way ANOVA if comparison was done in four groups. Data are expressed as the mean and SEM, all the p- value were two-tailed, and those <0.05 (95% Confidence Interval) was considered as statistically significant. All the data of cases and controls were entered into Microsoft Excel (Microsoft Office 2007) and Statistical Package for Social Service (SPSS for Windows Version; SPSS 17.0, Inc, Chicago, IL).

Results

Some 351 cases were recruited for our study. Those subjects who were excluded with missing PSA level data were not statistically different with regards to age or ethnicity.

Table 1 and Table 2 shows the characteristics of the study subjects by ethnic and age groupings.

The Indo-Nepalese subjects constituted the majority (67.52%); with Tibeto-Nepalese, Indigenous and Others forming the remaining, at 13.96%, 14.25% and 4.27% respectively (Table 2). The "Others" group is made up of ethnic minorities in Singapore. 37.61% of all the study's subjects had fPSA levels of 0.42ng/ml or less. There

Table 1. Basal Characteristics of the Cases Regarding Their Age

Age-groups	No of cases, n(%)	Mean±SE	p-value
<45	16 (4.6)	0.49±0.13	
45-60	72 (20.5)	0.69±0.10	0.031
60-75	153 (43.6)	1.94±0.40	
>74	110 (31.3)	2.33±0.43	

Table 2. Basal Characteristics of the Subjects Regarding their Ethnicity

Ethnic division	No of subjects, n(%)	fPSA Mean ± SEM	p-value
Indo-Nepalese	237 (67.5)	1.85 ± 0.30	
Tibeto-Nepalese	49 (14.0)	1.70 ± 0.48	0.840
Indigenous	50 (14.3)	1.45 ± 0.28	
Other	15 (4.27)	1.05 ± 0.31	

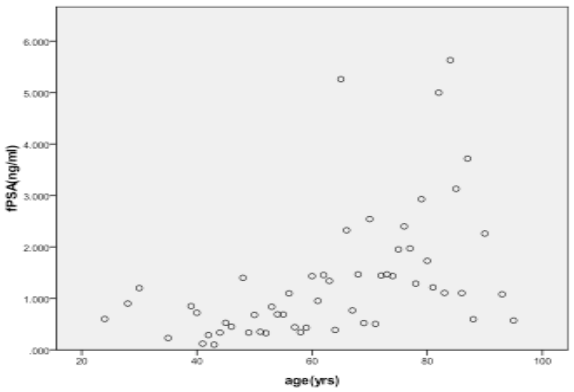

Figure 1. Relation Between fPSA (ng/ml) and Age (years)

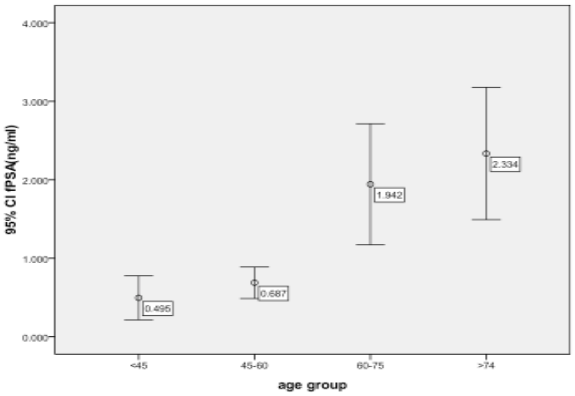

Figure 2. Mean and 95% Confidence Interval (CI) of fPSA Levels by Age- groups

were no significant differences (p=0.840) in the means of fPSA levels of Indo-Nepalese (1.85 ± 0.30 ng/ml), Tibeto-Nepalese (1.70 ± 0.48), Indigenous (1.45 ± 0.28) and Others (1.05 ± 0.31) using the one-way analysis of variance (ANOVA).

fPSA levels were fairly associated with age (Spearman's r= 0.146, p<0.01). fPSA level increased with the increase of the age. Figure 1.

The mean fPSA of the subjects between the different age groups was found to be statistically significant (p=0.031) (Table1). The highest mean fPSA level are seen in the age category 60-75 and >74. There were significant differences in the mean fPSA levels for different age

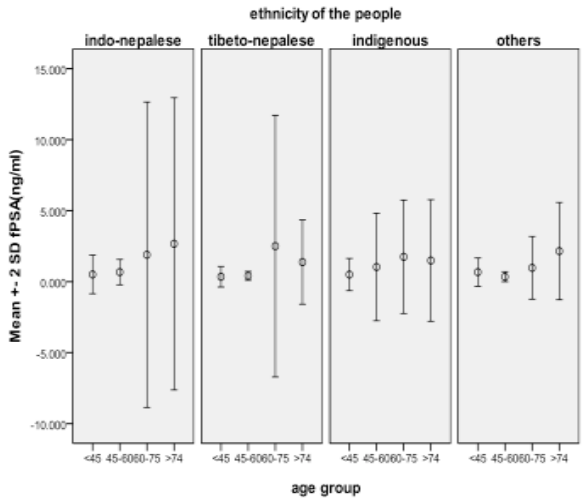

Figure 3. Mean and ± 2 Standard Deviatin of fPSA Levels by Ethnicity and Age group

groups (Figure 2). There was generally a progressive increase in the mean fPSA levels for each of the age groups within the Indo-Nepalese and Other. However, in the ethnic group Tibeto-Nepalese and Indigenous, the mean fPSA is highest in the age group 60-75 (Figure 3).

Discussion

The prevalence of prostate disease varies markedly in different regions of the world, but the reason for such geographical and/or ethnic disparities are poorly understood. Since PSA is a prostate tumor marker, its level can be affected by many factors that might be unrelated to prostate disease, eg. age and ethnicity. So, the main aim of my study was to assess the effect of the ageing and the ethnicity on fPSA levels among the Nepalese people.

In our study, we observed that 67.52% of the subjects were the Indo-Nepalese. The other ethnic groups (Tibeto-Nepalese, Indigenous and Other) comprises 13.96%, 14.25% and 4.27% respectively. In the four different age groups (<45, 45-60, 60-75 and >75) we found 4.56%, 20.51%, 43.59% and 31.34% of the total participants respectively. The figure of the studied population does not reflect Nepalese ethnic distribution and thus the study of fPSA levels cannot be extrapolated to the entire population.

We revealed that fPSA levels were positively associated with age. The association between the age and the fPSA was ($r=0.146$, $p<0.01$) which means fairly correlated. The positive association between age and the fPSA levels found in the present study is consistent with other recent studies.

Chia et al. (2007; 2008) analyzed data from the Singapore Prostate Awareness Week (PAW) 2005 involving 2410 Chinese men. They found that PSA was significantly correlated with age (correlation coefficient, $r=0.27$, $p<0.001$). They reported that mean PSA levels had a trend of increasing with the increment of the age which was quite similar to that of the Nepalese men in the present study.

In our study, we stratified serum fPSA levels into seven groups (<0.43, 0.43-0.75, 0.75-1.0, 1.0-1.50, 1.50-3.0, 3.0-6.0, >5.9) to see the fPSA levels trend across the different age groups. The prevalence of fPSA level >0.43ng/ml in the age group <45 and 45-60 years were 1.97% and 9.95% respectively. In the 60-75 and >74 age group the prevalence of fPSA level >0.43ng/ml rose rapidly to 28.46% and 21.68%. Since fPSA is produced in the prostate and the prostate generally enlarges after the age 50, the increase in the fPSA levels with age is understandable.

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The positive association between the age and the PSA ($r=0.27$, $p<0.01$) was also observed by Chia et al. [4] 3486 cases were observed and found that PSA levels increased with the each 10 year age group and these trends were significant ($p<0.001$) across both PSA group levels and age grouping. In the ≤50 and >50-60 years age groups the prevalence of the PSA levels >4ng/ml were 1.1% and 3.7% respectively. This figure increased to 11.3% and 23.5% for age groups >60-70 and >80 years respectively.

The mean fPSA level of the four ethnic groups (Indo-Nepalese, Tibeto-Nepalese, Indigenous and Other) were 1.85 ± 0.30ng/ml, 1.70 ± 0.48ng/ml, 1.45 ± 0.28ng/ml and 1.05 ± 0.31ng/ml respectively. The difference in mean fPSA level among four different ethnic groups was statistically non-significant ($p=0.840$).

Chia et al. (2007)examined the distribution of PSA levels among Chinese (92.8%), Malays (3.0%), Indians (2.5%) and Others (1.8%), taking the effect of age into consideration. He obtained the mean PSA levels of Chinese (1.60ng/ml), Malays (1.39ng/ml), Indians (1.23ng/ml) and Others (1.70ng/ml). Although there were differences in the mean PSA levels between the four ethnic groups, these differences were not significant ($p<0.05$). This observation was also true for the different ethnic groups stratified by their 10 years age group. He had claimed that the sample sizes in each of the age groups for the Malays and Indians were small so it would be premature to make any inference regarding their mean PSA levels.

Similarly, in our study there were numerically differences in the mean fPSA level between the four ethnic groups. But the differences were not statistically significant. So, we found no association between them. As we had considered a single factor, cast, to find the relationship between fPSA and ethnicity which might be insufficient. There is a complex relationship between PSA and ethnicity that cannot be explained by any single factor. Ethnicity may be associated with the fPSA, taking the fPSA test repetitions rate into consideration because repetition of the tests can be correlated with the socio-economic status (SES) and ethnicity. Ethnicity and SES must be examined simultaneously to find the relation of the

ethnicity with the prostate disease and PSA because of high prevalence of poverty among ethnic minorities. Intuitively, different cultural backgrounds could predispose patients to certain treatment preferences (Knight et al., 2004). The maximum mean fPSA in the ethnic group Indo-Nepalese was at the age group >74 with mean fPSA 2.667. In the ethnic group Tibeto-Nepalese and Indigenous, the peak mean fPSA was 2.50 and 1.74 respectively at the age group 60-75. By the previous studies it has been proven that, these are the age groups that are in more risk of the prostate disease. For subjects aged >60 it would be pertinent to evaluate their fPSA levels with added attention and further investigation might be warranted if there are other grounds for suspicion.

Lin et al. (2010) took a total of 7,803 participants without clinical evidence of prostate cancer. The median PSA value (95th percentile range) was 0.896ng/ml (3.329) for men 50-59 years old; 1.151ng/ml (5.114) for men 60-69 years old; 1.623ng/ml (6.237) for men 70-79 years old and 1.754ng/ml (6.613) for men older than 80 years. The serum PSA values correlated with age ($r=0.3078$, $p<0.001$). There were small changes in the median and 95th percentile PSA values in men younger than 50 years old, but large increase in those older than 50 years.

PSA was found to be elevated with the age because with the age, the prostate gland is found to be enlarged. Accordingly prostate volume (PV) too is found to be increased. Prostate condition such as BPH, prostatitis and PC become more common with the increase of the age, mainly after the age 50. The cancerous prostate tissue usually releases more PSA into the blood than normal healthy tissue does. Anatomical transition zone of the prostate where the nodular BPH originates is the most hormonally sensitive region of the human prostate. It is also the fastest growing region during the middle life and later life in men.

As reported by Pradhananga et al. (2009), Nepal has lower PC rates than does India and Pakistan. In Nepal, PC lies on the 8th position in the order of frequency of cancer in the age group >64. It is not known how much of this variation is due to differences in inherited susceptibility associated with genetic factors, environmental etiology, compared with differences in life styles characteristics such as diet and physical expenditure.

In our study, there was no systematic sampling of the subjects and thus biases could be introduced. But all biochemical assays were performed within the same laboratory. These precautions assure that all of the study end points were measured as accurately and reproducibly as possible. The men who participated in the study were not aware that we are studying the relationship between ethnicity and fPSA levels, so the cast of the men would not have affected the study finding through selection bias. Subjects included in the study could possibly have different types of prostate diseases. PSA levels in these subjects could reflect underlying prostate disease (e.g. BPH, PC, etc).

Since our study is the hospital based study, these figures do not generalize the data of the prevalence of the prostate disease in Nepal but can provide the knowledge and awareness regarding fPSA utility in prostate disease screening in Nepalese society. Many men have annual PSA test. However given the slow rate of growth of early PC, longer intervals between tests might be more appropriate. Decision analyses have supported the use of screening every two years (Carter et al., 1999; Ross et al., 2000). They have also suggested the possible benefits of starting testing as an earlier age, 40 or 45 year and stopping of testing at the age of 75 or even 65 years in men with persistently low levels of PSA (0.5-1.0ng/ml).

In conclusion, the age of the subject plays the vital role in the fPSA level as we found fairly positive correlation between those two variables.The ageing and the longer life expectancy of men have made prostate disease a major health issue. Since age is one of the key factors for the prostate disease, with the increment of the age, susceptibility towards the disease too increases. So it is recommended to measure the PSA of men when the increment of age is towards the midlife and more.

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