RESEARCH ARTICLE

Prostate Cancer Screening in a Healthy Population Cohort in Eastern Nepal: an Explanatory Trial Study

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Abstract

Background: Prostate cancer features a substantial incidence and mortality burden, similarly to breast cancer, and it ranks among the top ten specific causes of death in males. Objective: To explore the situation of prostate cancer in a healthy population cohort in Eastern Nepal. Materials and Methods: This study was conducted in the Department of General Surgery at B. P. Koirala Institute of Health Sciences, Dharan, Nepal from July 2010 to June 2011. Males above 50 years visiting the Surgical Outpatient Department in BPKIHS were enrolled in the study and screening camps were organized in four Teaching District Hospitals of BPKIHS, all in Eastern Nepal. Digital rectal examination (DRE) was conducted by trained professionals after collecting blood for assessment of serum prostatic specific antigen (PSA). Trucut biopsies were performed for all individuals with abnormal PSA/DRE findings. Results: A total of 1,521 males more than 50 years of age were assessed and screened after meeting the inclusion criteria. The vast majority of individuals, 1,452 (96.2%), had PSA ≤4.0 ng/ml. Abnormal PSA (>4 ng/ml) was found in 58 (3.8%). Abnormal DRE was found in 26 (1.72%). DRE and PSA were both abnormal in 26 (1.72%) individuals. On the basis of raised PSA or abnormal DRE 58 (3.84%) individuals were subjected to digitally guided trucut biopsy. Biopsy report revealed benign prostatic hyperplasia in 47 (3.11%) and adenocarcinoma prostate in 11 (0.73%). The specificity of DRE was 66.0% with a sensitivity of 90.9% and a positive predictive value of 38.5%. The sensitivity of PSA more than 4ng/ml in detecting carcinoma prostate was 100% and the positive predictive value for serum PSA was 19.0% Conclusions: The overall cancer detection rate in this study was 0.73% and those detected were locally advanced. Larger community-based studies are highly warranted specially among high-risk groups.

Keywords: Screening - prostate cancer - PSA - DRE - trucut biopsy - Eastern Nepal

Asian Pacific J Cancer Prev, **14 (5)**, 2835-2838

Introduction

Prostate cancer (PCa) is the second most common cause of cancer and the sixth leading cause of cancer death among men worldwide with an estimated 899,000 new cases and 258,000 new deaths in 2008. Out of this 72% of the cases and 53% of the deaths were found in developed countries representing <20% of the world population. Prostate cancer incidence rates varied 24-fold worldwide in 2008 with the highest estimated rates in Australia/ New Zealand, western Europe, North America, and the Caribbean and the lowest in south central Asia, northern Africa, and eastern Asia (Ferlay et al., 2010).

Screening for prostate cancer aims to decrease mortality and morbidity from the disease by increasing the chances of successful treatment through early detection (Rabah and Arafa, 2010). Total PSA is the most useful screening test for the diagnosis of prostate cancer and the addition of DRE improves the detection rate of prostate cancer over PSA alone (Ahmed et al., 2009).

The ERSPC trial showed a relative risk reduction of 21% in favor of prostate-cancer screening in the intention-to-screen analysis and 29% among screened men after adjustment for noncompliance (Schröder et al., 2009).

In Nepal, to the best of our knowledge (after extensive search on PUBMED, CINAHL, ERIC, and CIJE) though accurate data regarding prevalence of prostate cancer has not been published, Annual Report 2009-2010 from B.P. Koirala Memorial Cancer Hospital, Bharatpur shows that out of 170 genitourinary malignancies, 31 (18.23%) were carcinoma prostate. Among the 31 carcinoma prostate detected 4 underwent radical prostatectomy for early carcinoma prostate and 27 received Androgen ablation/ hormone therapy for advanced disease. Another similar data from the study 'Clinico-Epidemiological study of genitourinary malignancies at B. P. Koirala Institute of Health Sciences (2006-2008)' done in B. P. Koirala Institute of Health Sciences, Dharan, Nepal revealed that

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out of 139 cases of genitourinary carcinoma, 24 (17.26%) were carcinoma prostate (Hai et al., 2008). So this study was undertaken as a trial to explore the situation of prostate cancer in a cohort of healthy population of Eastern Nepal and also to assess the feasibility of screening of cancer prostate.

Materials and Methods

This study was conducted in the Department of General surgery at B. P. Koirala Institute of Health Sciences, Dharan, Nepal in Surgical Outpatient Department, its Teaching District Hospitals (Dhankuta, Inaruwa, Bhadrapur and Rangeli) representing four different regions of Eastern Nepal, through health camps from July 2010 to June 2011. The Study was approved by "The Institute Protocal and Ethical Committees"of B.P.K.I.H.S.

Inclusion criteria

All males above 50 years of age attending outpatient department of surgery in B.P.K.I.H.S, teaching district hospitals and screening camps.

Exclusion criteria

All males who were already diagnosed to have carcinoma prostate, who did not give consent for enrollment, who did not give consent for trucut biopsy of prostate, and who had a history of coagulopathies or sepsis were excluded from the study.

Males above 50 years visiting Surgical Outpatient Department in BPKIHS were enrolled in the study. Screening camps were organized in the selected Teaching district hospitals of BPKIHS. Standing posters regarding information about carcinoma prostate were displayed in the study settings. Information was also broadcasted via local radio centers asking men to participate actively in the study. Men above 50 years were invited to participate in the study and were explained the nature, objectives and benefits of the study. Written consent was taken from each of them regarding their willingness to be enrolled in the study. A total of 1521 males were assessed and screened after meeting inclusion criteria. For all subjects a predesigned proforma were filled. Blood samples were collected from all individuals included in the study prior to Digital rectal examination (DRE). Three ml of blood was taken in a plain vial, centrifuged and the serum was stored at -20 degree Celsius until analysis. PSA was estimated using Chemicluminescence Assay (CLIA) method (Acculite Kit, by Monobind, California, USA). Serum prostatic specific antigen (PSA) above 4ng/ml was considered abnormal. In DRE prostate was considered abnormal if the consistency of prostate was hard, there was evidence of nodularity, induration, asymmetry and absence of median sulcus. Trucut biopsy was done for all individuals with abnormal PSA or DRE or both findings. Glycerine suppository enema was given prior to the biopsy. Adequate antibiotic coverage was given with oral Metronidazole and Ofloxacin for 5 days.

Focussed group discussions were conducted in the camps to assess the feasibility of screening carcinoma prostate. Any patient diagnosed with prostate cancer was offered treatment according to its stage and grade as well as the general health condition of the patient. The patient was made aware of all the treatment options, including watchful waiting, radical prostatectomy, and radiation therapy. Those with a negative biopsy were offered continued annual screening.

Estimation of sample size

The sample size was calculated based on the basis of prevalence of 1% for carcinoma prostate in the general population. This study considered precision of 5% and confidence interval of 95%. The sample size came out to be 1521 subjects.

Primary data analysis

Collected data were entered in Microsoft excel-2007 and imported into SPSS 11.5 version for statistical analysis. For descriptive statistics mean, standard deviation, proportion, percentage and diagrammatic presentation was done. For inferential statistics chi-square test, t-test were carried out to find out the significant differences between the dependent and independent variables where level of significance was considered p=0.05.

Results

The study population was 1521 healthy males with age more than 50 years. Out of these 98% were married, 10% of the participants were having secondary schooling and 5% of the participants were having higher secondary education. Among the enrolled population only 1510 individuals were analysed as five did not come for follow

Table 1. Age and PSA Distribution

Age (years)	PSA (ng/ml)		
	≤4	4.0-10	>10
50-60	673	7	2
61-70	468	14	7
>70	311	12	16
Total	1452	33	25

Table 2. PSA and HPE Report

PSA	HPE	
	Negative	Positive
≤4.0	0	0
≥4.0	47	11

Table 3. PSA and DRE Findings

DRE Findings	PSA (ng/ml)		
	≤ 4	4.0-10.0	>10
Positive	0	1	9
Negative	1452	32	16
Total	1452	33	25

Table 4. DRE and HPE Report

DRE	HPE		P value
	Negative	Positive	
Negative	31	1	<0.001
Positive	16	10	

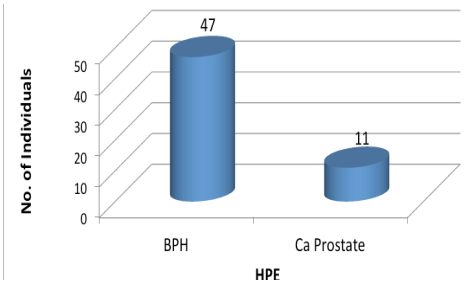

Figure 1. PSA Distribution in the Screening Population

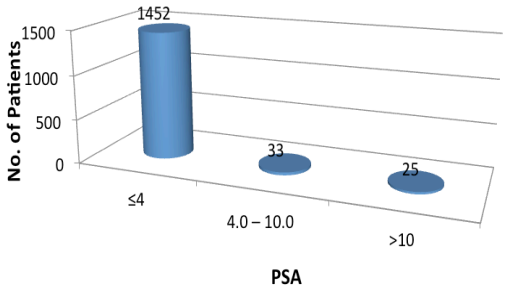

Figure 2. Trucut Biopsy Report

Figure 3. People Attending a Screening Camp

up and six did not give consent for Trucut biopsy. These 11 individuals had high PSA.

Age ranged from 50 to 100 years with the mean age of 63.63±9.76 years. Abnormal DRE was found in 26 (1.72%) individuals and abnormal PSA was seen in 58 (3.8%) individuals.The sensitivity of PSA more than 4 ng/ml in detecting carcinoma prostate was 100% and the positive predictive value for serum PSA was 18.96%. Of the 11 detected carcinoma prostate 10 were having PSA more than 10 ng/ml. The specificity of DRE was 65.95%, sensitivity 90.9% and positive predictive value 38.46%. The sensitivity of DRE in combination with PSA was 100% and positive predictive value for the combination of both was 42% which was more than that detected by PSA or DRE alone. The overall cancer detection rate in this study was 0.73%. Cancers detected were locally advanced. All those having negative biopsy but positive PSA and DRE findings were advised for regular follow up. Details of result are shown in Table 1-4 and Figure 1.

Discussion

PSA is a serine protease produced by benign and malignant prostate tissues. It circulates in the serum as uncomplexed (free or unbound) or complexed (bound) forms. Normal PSA values are those ≤4 ng/mL. Current detection strategies include the efficient use of the combination of DRE, serum PSA, and TRUS with systematic biopsy. PSA is widely known to be associated with age. Since PSA is produced in the prostate and prostate generally enlarges after age 50, the increase in PSA levels with age is understandable. Studies conducted in China, Korea and India revealed increasing PSA with age (Lee et al., 2000; Malati and Kumari, 2004; Liu et al., 2008). In our study also, increase in age was associated with rise in PSA which was statistically significant (p value<0.001).

The effectiveness of PSA as a screening method for prostate cancer is debated. However, it has been proved that use of PSA increases detection rates of prostate cancer and leads to the detection of prostate cancers that are more likely to be confined when compared with detection without the use of PSA. For PSA >4 ng/ml sensitivity for detecting prostate cancer ranges from 66.67%-100% (Harvey et al., 2009). The reported positive predictive value of PSA >4ng/ml in screening studies was 17%-57% (Mistry and Cable, 2003). In our study the sensitivity of PSA was 100% and positive predictive value was 18.96%. Possible cause for the low positive predictive value is the unavailability of TRUS guided biopsy facility.

Digital rectal examination is a test with only fair reproducibility in the hands of experienced examiners that misses a substantial proportion of cancers and detects most cancers at a more advanced pathologic stage, when treatment is less likely to be effective. The sensitivity of DRE in detection of prostate cancer ranges from 49%-69.20%; the specificity of DRE ranges from 50%-99.54%; and positive predictive value ranges from 17%-33.06% (Mistry and Cable, 2003). The cancer detection rate using DRE ranges from 1.3%-1.4% (Lee et al., 1988; Mettlin et al., 1991). In our study the sensitivity for DRE was 90.9%, specificity was 65.95%, positive predictive value was 38.46% and the cancer detection rate was 0.67%. This difference may be due to lack of TRUS guided biopsy in our study.

The combination of DRE and serum PSA is the most useful first-line test for assessing the risk of prostate cancer being present in an individual. When DRE and PSA are used as screening tests for prostate cancer detection, detection rates are higher with a combination of the two tests (Catalona et al., 1994; Littrup et al., 1994; Stone et al., 1994; Schroder et al., 1998). In our study also the sensitivity of DRE in combination with PSA came out to be 100% and positive value for the combination of both was 42% which was more than that detected by PSA or DRE alone.

The yield of trucut biopsy for prostate cancer using TRUS ranges from 30.6%-39.3% (Catalona et al., 1991; Rabah and Arafa, 2010; Niang et al., 2011) In our study the trucut biopsy for prostate cancer was positive in 18.97% of the total biopsies. This difference is because our trucut biopsy was digitally guided which has lesser sensitivity compared to TRUS guided biopsy.

Prostate cancer detection rate in different screening studies ranged from 1%-3.7% (Mettlin et al., 1991; Galic et al., 2003; Ganpule et al., 2007; Rabah and Arafa, 2010). In our study it was only 0.73%. The detection rate in our

study was less because our sample size was smaller than the study groups and we did not had the facility of TRUS guided biopsy of the prostate.

In conclusion, the Prostate cancer detection rate in a cohort of healthy population of Eastern Nepal is 0.73%. The prevalence rate of prostate cancer among our studied cohort detected by screening was relatively lower than expected and that detected were locally advanced. This study should be considered as the basic approach to build on for other community-based larger studies, among high-risk population.

The unavailability of TRUS and TRUS guided biopsy was one of the important limiting factor as its absence hampered the cancer detection rate in biopsy.

Acknowledgements

The study was supported by all those participants who volunteered to be the subjects of the study and Nepal Health Research council (NHRC PG grant 2011; Ref. no.1213).

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