Original Article

Community Screening of Prostate Cancer in Eastern Nepal

Narayan Belbase[1], C S Agrawal[2]
[1]Department of Surgery, College of Medical Sciences, Bharatpur, [2]Professor, Department of Surgery, BPKIHS, Dharan

ABSTRACT

Background: Prostate cancer incurs a substantial incidence and mortality burden, and it ranks among the top ten specific causes of death in males.

Objectives : To explore the situation of prostate cancer in a cohort of healthy population in Eastern Nepal .

Methods: This study was conducted in the Department of General surgery at B. P. Koirala Institute of Health Sciences, Dharan, Nepal in the department of surgery from July 2010 to June 2011. Males above 50 years visiting Surgical Outpatient Department in BPKIHS were enrolled in the study. Screening camps were organized in four Teaching district hospitals of BPKIHS in Eastern Nepal. Digital rectal examination (DRE) was done by the trained professionals after collecting blood for serum prostatic specific antigen (PSA). Trucut biopsy was done for all individuals with abnormal PSA, DRE or both findings.

Results: A total of 1521 males more than 50 years of age were assessed and screened after meeting inclusion criteria. Maximum individuals 1452 (96.2%) had PSA ≤ 4.0 ng/ml. Abnormal PSA (> 4 ng/ml) was found in 58 (3.8%) individuals. Abnormal DRE was found in 26 (1.72%) individuals . Both DRE and PSA was 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%) individuals and adenocarcinoma prostate in 11 (0.73%) individuals. The specificity of DRE was 65.95% sensitivity 90.9% and positive predictive value 38.46%. The sensitivity of PSA more than 4ng/ml in detecting carcinoma prostate was 100% and the positive predictive value for serum PSA was 18.96%.

Conclusion: 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.

INTRODUCTION

Prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males, accounting for 14% (903,500) of the total new cancer cases and 6% (258,400) of the total cancer deaths in males in 2008.[1] Descriptive epidemiology has shown wide ethnic/racial differences in the incidence of Prostate carcinoma. The highest incidence rate group (100/100,000/year) includes African Americans in the United States; intermediate rates (20–50/100,000/year) are observed in Canada, South America, and European countries; and lowest rates (10/100,000/year) in Japan, China, and India.[2] Screening for prostate cancer aims to decrease mortality and morbidity from the disease by increasing the chances of successful treatment through early detection.[3] Evidences clearly supports the use of PSA screening in conjunction with DRE as a means of early detection of Prostate cancer. Such screening has decreased the incidence of metastatic disease at diagnosis and paralleled the decrease of the mortality rate from Prostate cancer. [4]

In Nepal, to the best of our knowledge, though accurate data regarding prevalence of prostate cancer has not been published, Annual Report 2009 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. [5] Another similar

Correspondence
Narayan Belbase , *Dept of Surgery, College of Medical Sciences, Bharatpur*

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 out of 139 cases of genitourinary carcinoma, 24 (17.26%) were carcinoma prostate.[6] 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 1521subjects.

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 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 4ng/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 than10 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 no. 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.[7,8,9]. 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 78% – 100%.[10,11] The reported positive predictive value of PSA in screening studies was 28% - 35% percent.[12] 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 45%-58%; the specificity of DRE ranges from 96%-97%;and positive predictive value ranges from 28%-34**.** The cancer detection rate using DRE ranges from 1.3%-1.4%.[13,14] 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.[11,15,16,17] 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%.[3,18,19] 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%.[3,14,20,21] 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.

RESULTS

Table 1: Age and PSA distribution

Age (Years)	PSA(ng/ml)			P value	Remarks
	PSA ≤ 4	PSA 4.0 – 10	PSA >10		
50-60	673	7	2	< 0.001	Significant
61-70	468	14	7		
>70	311	12	16		
Total	1452	33	25		

Table 2: PSA and HPE

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

Table 3: Relation between PSA and abnormal DRE

DRE Findings	PSA (ng/ml)			P value	Remarks
	≤ 4	4 .0 - 10.0	>10		
Positive	0	1	9	< 0.001	Significant
Negative	1452	32	16		
Total	1452	33	25		

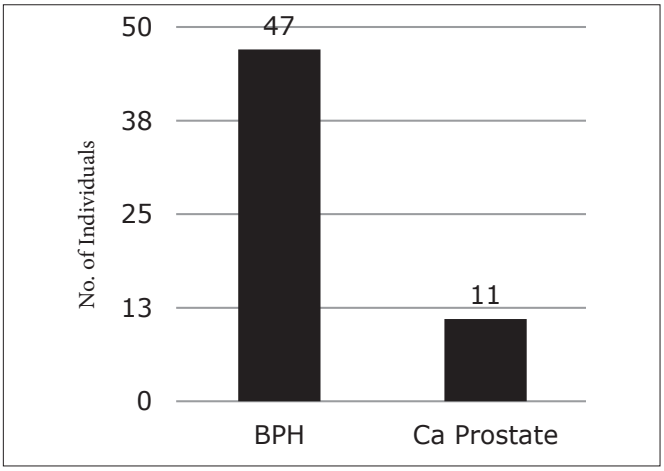

Figure 1: Trucut biopsy report

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.

Limitations of the Study

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.

Acknowledgement

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).

REFERENCES

1. Jemal A, Bray F,Melissa M et al. Global Cancer statistics. CA: A Cancer Journal for Clinicians 2011; 61(2): 69–90.
2. Watanabe M, Tsuyoshi N, Taizo S, et al Comparative studies of prostate cancer in Japan versus the United States, a review. Urologic Oncology. 2000; 5(6): 274–83.
3. DM and Arafa MA. Prostate cancer screening in a Saudi population: an explanatory trial study. Prostate Cancer and Prostatic Diseases 2010;13(2): 191–4.
4. Tenke P, Horti J, Balint P, Kovacs B. Prostate cancer screening. Recent Results Cancer Res.2007;175:65-81.
5. Annual Reports 2009. B.P.Koirala Memorial Cancer Hospital, Bharatpur, Nepal, 2009.
6. Hai MA, Agrawal CS and Agarwal R.Clinico-Epidemiological Study of Genitourinary Malignancy at B.P.Koirala Institute of Health Sciences, Nepal, 2006-2008. (Thesis).
7. Liu ZY, Sun YH, Xu CL, et al. Age- specific PSA reference ranges in Chinese men without prostate cancer. Asian J Androl. 2008 ;11: 100–03.
8. Lee S.E., Kwak C., Park M.S., Lee C.H., Kang W., Oh S.J. Ethnic differences in the age-related distribution of serum prostate-specific antigen values: a study in healthy Korean population. Urology. 2000; 56: 1007–10.
9. Malati T, Kumari G. Racial and ethnic variation of PSA in global population: age specific reference intervals for serum prostate specific antigen in healthy South Indian males. Indian J Clin Biochem 2004;19: 132–37.
10. Harvey, Basuita A, Endersby, et al. A systematic review of the diagnostic accuracy of prostate specific antigen. BMC Urology 2009; 9:14.
11. Catalona WJ, Hudson MA, Scardino PT,et al. Selection of optimal prostate specific antigen cut offs for early detection of prostate cancer: Receiver operating characteristic curves. J Urol 1994; 152: 2037.
12. Woolf SH. Screening for Prostate Cancer with Prostate-Specific Antigen —An Examination of the Evidence. NEJM 1995; 333:1401-05.

13. Lee F, Littrup PJ, Torp-pederson S et al. Prostate cancer:comparison of transrectal US and digital rectal examination. Radiology 1988; 168:389-94.
14. Mettlin CJ, Lee F, Drago J, Murphy GP, et al.The American Cancer Society National Prostate Cancer Detection Project: Findings on the detection of early prostate cancer in 2425 men. Cancer 1991; 67, 2949-58.
15. Littrup PJ, Kane RA, Mettlin CJ, et al. Cost-effective prostate cancer detection. Cancer 1994; 74: 3146.
16. Stone NN, DeAntoni EP, Crawford ED. Screening for prostate cancer by digital rectal examination and prostate-specific antigen: Results of prostate cancer awareness week, 1989-1992. Urology 1994; 44:18.
17. Schroder FH, van der Maas P, Beemsterboer P, et al: Evaluation of the digital rectal examination as a screening test for prostate cancer. Rotterdam section of the European Randomized Study of Screening for Prostate Cancer. J Natl Cancer Inst 1998; 90:1817
18. Catalona, Smith DS, Ratliff TL, et al. Measurement of prostate specific antigen in serum as a screening test for prostate cancer. NEJM 1991; 324(17):1156-61.
19. Niang L, Kouka CN , Jalloh M, Gueye MS. Screening for Prostate Cancer by Digital Rectal Examination and PSA Determination in Senegal. ISRN Oncology 2011.
20. Galic J, Karner I, Tucak A, et al. Comparison of digital rectal examination and prostate specific antigen in early detection of prostate cancer. Coll Antropol 2003; 27 suppl 1:61-6.
21. Ganpule AP, Desai MR, Manohar T, Bapat S. Age-specific prostate specific antigen and prostate specific antigen density values in a community-based Indian population. Indian J Urol 2007;23:122-5.