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

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 carcinoma 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 Protocol 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 truncut 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 Chemiluminescence 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. Truncut 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) | ≤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 | ≤4 | ≥4 | HPE |
|     | 0 | 47 | 11 |

| Table 3. PSA and DRE Findings |
| DRE Findings | ≤4 | 4.0-10 | >10 |
| Positive     | 0  | 1   | 9 |
| Negative     | 1452 | 32 | 16 |
| Total        | 1452 | 33 | 25 |

| Table 4. DRE and HPE Report |
| DRE | ≤4 | HPE | P value |
|     | 31 | 1 | <0.001 |
| Positive | 16 | 10 |
forms. Normal PSA values are those ≤4 ng/mL. Current
uncomplexed (free or unbound) or complexed (bound)
malignant prostate tissues. It circulates in the serum as
up. Details of result are shown in Table 1-4 and Figure 1.

PSA and DRE findings were advised for regular follow
in this study was 0.73%. Cancers detected were locally
100% and positive predictive value for the combination
be 100% and positive value for the combination of both
that misses a substantial proportion of cancers and detects
when treatment is less likely to be effective. The sensitivity
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 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%;
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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
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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.

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 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).

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
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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.

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being present in an individual. When DRE and PSA are
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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.

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