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RESEARCH ARTICLE

Assessment of Incidence and Prevalence of Prostate Cancer in Middle Aged Male Patients of Western Nepal Using Prostate-specific Antigen and Digital Rectal Examination that Underwent Prostate Biopsy

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ABSTRACT

This study was conducted to evaluate the incidence of prostate cancer (PCa) in male patients with increased prostate-specific antigen (PSA), and normal or abnormal digital rectal examination (DRE) that underwent a prostate biopsy. From March 2018 to November 2018, a total of 98 consecutive males suspected of having PCa due to increased PSA levels underwent transrectal ultrasonography (TRUS)-guided sextant biopsy of the prostate. The total PSA (tPSA), demographic data, the incidence of PCa, benign prostate hyperplasia (BPH), and prostatitis were assessed. The patients were divided into two groups according to their PSA values (Group A serum tPSA level, 4–10 ng/mL; and Group B serum tPSA level, 10.1–20.0 ng/mL). Of the 98 biopsied cases, 56% had PCa, 23% had BPH, and 21% had prostatitis. The mean PSA and the age of the carcinoma group were significantly higher than those of the benign group ($P < 0.01$). The biopsy results were grouped as PCa, BPH, and prostatitis. The incidence of PCa for Group A and Group B cases was 51% and 65%, respectively. In the case of PCa, BPH, and prostatitis, the mean PSAs were 10.02 ng/mL, 8.76 ng/mL, and 8.41 ng/mL, respectively ($P < 0.40$). In conclusion, TRUS-guided prostate biopsy and interpretation by a skilled team are highly recommended for early detection of PCa or its ruling-out. Due to the very high incidence of PCa in the patients with PSA >10 ng/mL, TRUS-guided biopsy is indicated, whatever the findings on DRE and/or LUTS, since the PCa detection rate is high.

Keywords: Benign prostate hyperplasia, digital rectal examination, lower urinary tract symptoms, prostate biopsy, prostate carcinoma, prostate-specific antigen

INTRODUCTION

Prostate cancer (PCa) is one of the most common cancers in the male population and is the second leading cause of cancer death for men in the USA.[1] It is a major cause of morbidity and mortality in Nepal,[2] yet there are few studies determining the relation between prostate-specific antigen (PSA) levels and the risk of PCa. The mortality of PCa on the basis of geographic area differs. In the Scandinavian area and Southern Europe its prevalence is high, and in Eastern Asia, its prevalence is the least. Its prevalence is directly related to age. PSA and digital rectal examination (DRE) are good screening tools of PCa. In this retrospective study, we evaluated PCa prevalence in Nepalese male patients of western region that was referred to our center for transrectal prostate biopsy due to increased PSA level.

Unfortunately, in Nepal, most PCa is already associated with non-organ-confined disease or bone metastasis at detection. Therefore, focusing research on methods of its early detection has developed.[2]

PSA is secreted by the epithelial cells lining the acini and the ducts of the prostate gland in both normal and malignant conditions.[3,4] The serum levels of PSA are elevated in PCa and benign prostate hyperplasia (BPH).[5-7] Prostate biopsy has been usually performed in clinical practice in cases with increased PSA levels. Although a serum PSA level of 4.0 ng/mL is used as a cutoff point for PCa screening, it is relatively difficult to differentiate prostate adenocarcinoma from benign prostatic hyperplasia (BPH) in patients with gray-zone PSA levels (4–10 ng/mL).[8-12]

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PCa early detection guidelines are mainly based on data from the USA and Europe and may not be relevant to other geographic areas or ethnic groups.[12]

This study was designed to evaluate the significance of total PSA (tPSA) in the PSA of 4–10 ng/mL and its comparison with PSA levels of 10–20 ng/mL for discrimination between benign and malignant prostate disease in middle-aged Nepalese men.

MATERIALS AND METHODS

This is a retrospective study in which males with increased PSA levels (4 ng/dL) that referred to transrectal ultrasound (TRUS) prostate biopsy were evaluated. In this study, a total of 98 males with increased PSA values with or without positive DRE (4–20 ng/mL) were evaluated from March 2018 to November 2018. The mean age of these patients was 65.81 years, ranging from 45 to 87 years, with a standard deviation (SD) of 8.50. This study was performed in the Department of Urology, Gandaki Medical College, Nepal and got approval from the Ethical Committee, Gandaki Medical College. Before DRE and tPSA were measured for all of these patients. None of them had current urinary tract infections, clinical prostatitis, and history of prior prostate surgery (transurethral resection of the prostate or open prostatectomy). A sextant biopsy was performed from the apex and base of the right and left parasagittal planes of the prostate with 10 core biopsies. If hypoechoic areas were noted on TRUS, a specimen was taken from each of these areas.

Demographic data including age, PSA level, prostate volume, and pathology result were evaluated. PSA was measured using the Tandem-R assay. Prostate volume was calculated using the following formula:

$$\Pi/6 \times L \times W \times H, \qquad \text{Equation 1}$$

where L = length, W = width, and H = height.

The patients were divided into two groups: Group A, with a PSA level between 4 and 10 ng/dL and Group B, with a PSA level between 10 and 20 ng/dL. On the basis of prostate weight, the mean, median, SD, and variance were 56.48 cm^3, 49 cm^3, 27.34, and 747.94, respectively.

The total number in Group A was 65.3% and Group B was 34.7%. One experienced pathologist performed the histopathological examinations. Atypical small acinar proliferation and prostate intraepithelial neoplasia were excluded from the study. Demographic and clinical characteristics of patients with and without prostate adenocarcinoma were compared with the use of statistical *t*-test.

Statistical analysis

The statistical analysis of the collected data was performed using SPSS Statistics, version 16.0 (SPSS Inc, Chicago, IL) software.16 The values of continuous variables were demonstrated as mean ± SD. Comparisons of variables (age, prostate volume, PSA, and pathologic diagnosis) were done with the *t*-test. $P < 0.05$ was considered significant.

RESULTS

The overall final pathologic diagnosis was prostate adenocarcinoma in 56%, BPH in 23%, and prostatitis – subacute or chronic – in 21%. The group-specific pathologic diagnosis was as follows: For Group A, prostate adenocarcinoma in 51%, BPH in 26%, and prostatitis – subacute or chronic – in 23%; and for Group B, prostate adenocarcinoma in 65%, BPH in 17.5%, and prostatitis – subacute or chronic – in 17.5%. The mean (and SD) for the age of Group A and Group B was 64.38 years (8.134) and 68.5 years (8.56), respectively.

The mean (and SD) prostate volume for Group A and Group B was 55 cm^3 (23.963) and 59.5 cm^3 (32.702), respectively. The mean prostate volume for PCa cases was 46.09 cm^3. The mean prostate volume for prostatitis cases was 64.67 cm^3, with SD of 26.304. The mean prostate volume for BPH cases was 74.06 cm^3, with SD of 33.51. The mean PSA level for PCa was 10.02 ng/dL, with a SD of 4.37. The mean PSA level for prostatitis was 8.76 ng/dL, with a SD of 3.72. The mean PSA level for BPH was 8.41 ng/dL, with a SD of 3.56. The mean (and SD) age for PCa, prostatitis, and BPH was 67.63 years (8.98), 62.34 years (6.83), and 64.58 years (7.52), respectively. The mean Gleason score for Group A was 6.5 and for Group B was 6.7 ($P \leq 0.05$). The statistical relationship between the PSA level and PCa was significant ($P < 0.40$).

ANOVA test was used for the determination of the relationship between the age and PCa; moreover, it was significant ($P < 0.01$). With this test, the relationship between PCa and BPH was significant ($P < 0.01$). The relationship between age and PSA was significant ($P > 0.01$). Based on our study, the positive predictive value for PCa in Group A was 51% and for Group B was 65%.

Age was correlated positively with tPSA in both the PCa group and the BPH group in all tPSA ranges (0.001). This means that in our cases, the proportion of males with PSA levels above the cutoff value increased with age. The mean PSA value (range, SD) in all men with PCa was 10 ng/mL (4–20 ng/mL, 4.37), in those with BPH was 8.4 ng/mL (4–20 ng/mL, 3.56), and in those with prostatitis was 8.7 ng/mL (4–20, 3.72) ng/mL ($P < 0.001$).

DISCUSSION

The incidence of PCa in Nepal is significantly less than those in developed countries and similar to eastern Mediterranean regions.[13-15] PCa is the most frequently reported malignancy in Iranian males after stomach cancer.[16,17] Among genitourinary cancers, it is the second most common cancer after bladder cancer, with an incidence of 33.4%.[18-20] The lowest recorded PCa rate is 0.4 per 100,000 in Nepal.[13,21] Nepal men are ethnically and racially different from most of the Asian men,[21,22] so the biochemical parameters of PCa should be different. In a study by Khezri *et al*.,[23,24] in a large healthy male population, the serum PSA concentration correlated directly with the subject's age and prostatic volume. Based on this study, the age-related PSA cutoff point was 2.61 ng/mL for 50–59 years, 3.59 ng/mL for 60–69 years, and 4.83 ng/mL for 70–79 years. The serum PSA levels and prostate volume are age- and race-dependent. For this reason, we chose the cutoff point of 4 ng/mL for prostate biopsy. In another study by Mehrabi *et al*., the PSA cutoff level in the males >69 years is 4.4 ng/mL.[24,25]

In our study, patients with serum PSA levels between 4 and 20 ng/mL, only 56% had pathologically diagnosed PCa, which is much lower than the values used in Western countries. This can be explained by a widely different geographical prevalence of PCa.[25] Amirrasouli *et al*.[25] evaluated 332 men with serum tPSA levels of 4–20 ng/mL. After TRUS prostate biopsy, they detected PCa in 15% of their patients. Incidence of PCa for serum tPSA level 10 ng/mL and serum tPSA level of 10.1–20.0 ng/mL was 6.7% and 39.5%, respectively. Catalona *et al*.[26-28] found positive findings on prostate biopsy in <50% of the patients with PSA of 4–10 ng/mL.

Several studies showed an advantage of using PSAD compared with tPSA alone.[11,12,27,29,30] Lam *et al*.[31] recommended a PSAD cutoff of 0.15 ng/mL for detection of PCa, which spared half of the patients from undergoing unnecessary biopsies. In spite of its value, we did not consider the role of PSAD in this study.

Although several studies showed that PSA screening had a beneficial effect, the results of the selected studies were inconsistent, and mass screening is not warranted.[32,33] Both PSA and DRE were not recommended for population-based screening programs, but they could be conducted individually.[32]

Hua *et al*.[34] studied the prostate biopsy results in 295 Chinese cases with PSA levels ≥4 ng/mL; the positive detection rate of PCa was 19.7%. In our Iranian cases, the positive detection rate was 56%. We observed, like Gohji *et al*.,[35] in the patients with PCa, the prostate volume was smaller, and the age was higher than in the patients with BPH or prostatitis. In the Safarinejad study,[13] the detection rate of PCa in males using PSA alone was reported at 3.5%, which reflects an increase in its incidence. In addition, Safarinejad detected 17.5% PCa in cases with PSA 4–10 ng/mL and 47.6% in cases with PSA 10–20 ng/mL.

CONCLUSION

Comparing our study results with others, we found that PSA alone can be used efficiently as a first and/or repeat the test for PCa screening of Nepalese males. In addition, we found that the chance of PCa increases with increasing age, the lesser weight of prostate, and increased tPSA. There was no difference in the Gleason score in our two groups of different PSA levels (4–10 and 10–20 ng/mL).

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