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Research Article

CORRELATION OF SERUM PROSTATE SPECIFIC ANTIGEN (PSA) LEVEL IN VARIOUS PROSTATE PATHOLOGY IN ELDERLY MEN

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ABSTRACT

The aim of this prospective study is to correlate the lesions of prostate mainly, Benign prostate hyperplasia, prostate carcinoma and BPH with prostatitis with serum PSA level and find the proportion of benign hyperplasia and prostate cancer in elderly men with enlarged prostate by analyzing prostate tissue received at the Department of Pathology, Dr. Vasantrao Pawar Medical college, hospital and research centre, Nashik during a 2 year period from June 2010 to June 2012. The results are compared with other similar studies. During the 2 year period of this study.

80 prostate tissues were studied and of these 15% (n= 12) were malignant, 1.25% (n=1) showed low grade prostate intraepithelial neoplasia and the remaining 83.8% (n=67) were BPH. The majority (11 cases) of the malignancies were adenocarcinomas, and one case of transitional cell carcinoma and most frequent Gleason score was 7 (in 54.5%) had. The highest incidence of malignancies and hyperplasia occurred between 60 and 69 years of age. The mean serum PSA value in benign cases was 8.90 ng/ml (SD ± 12.77) and in malignant cases was 83.06 ng/ml (SD ± 80.36). Serum PSA in the range of 0-4 ng/ml was significantly associated with benign lesions and value more than 20 ng/ml was significantly associated with malignant lesions.

Key Words: *Benign Prostate Hyperplasia, Prostatitis, Serum Prostate Specific Antigen (PSA), Adenocarcinoma, Gleason Score*

INTRODUCTION

Because of location of prostate gland at bladder neck, enlargement of the gland leads to problems related to urinary obstruction (Epstein, 2010). Incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma increases with age.

Benign prostate hyperplasia, prostate carcinoma and prostatitis are three pathologic processes which frequently affect the prostate gland. Diagnosis of prostatitis is very necessary as they can be successfully treated with antibiotics. Benign prostatic hyperplasia is the usual name applied to a common benign disorder of the prostate that, when extensive, results in varying degrees of urinary obstruction, sometimes requiring surgical intervention (Rosai, 2012). It is extremely common problem in elderly men over the age of 50 years (Epstein, 2010).

Prostate cancer is the leading cause of new cancer in men and is second only to lung cancer as a leading cause of cancer-related deaths in men (Rosai, 2012). Several factors, including age, race, family history, hormone levels, and environmental influences are suspected to play a role in pathogenesis.

This study includes description of incidence of various lesions of prostate, their clinical manifestations, serum prostate specific antigen (PSA) level, classification and grading of prostate tumors.

MATERIALS AND METHODS

This is a prospective study of lesions of prostate and their correlation with serum PSA level. The present study includes 80 prostate specimens from patients, for histopathological examination and their serum

PSA level, coming to the department of pathology, Dr. Vasantrao Pawar Medical college, hospital & research centre, Nashik during the period of June 2010 to June 2012. After receiving the specimen, detailed macroscopic examination was done. The received specimens were fixed in 10% formalin. In cases of TURP approximately 5-6 grams of tissue was processed in one cassette and embedded. The sections were cut at 3-5 micron thickness and subsequently stained by haematoxylin and eosin stain. Special stains like Periodic acid Schiff (PAS), Ziehl Neelson were performed whenever required. All the lesions of prostate were classified into neoplastic and non-neoplastic lesions on microscopy. The tumors of prostate were classified according to WHO classification (Eble *et al.*, 2004) and the cases of prostatic adenocarcinoma were graded using Gleason grading system (Rosai, 2012). All these lesions were correlated with serum PSA level. Serum PSA of the patient was measured by chemiluminescene immunoassay (CLIA) method using Lumax - CLIA strip reader (by Monobid Inc.). Kit used was Acculite CLIA VAST enabled kit containing individual tracer component and calibrator sets.

RESULTS AND DISCUSSION

Results

80 specimens were received for histopathological examination, out of which, 69 (86.3%) were transurethral resection of prostate (TURP), 6 (7.5%) were needle biopsies and 5 (6.3%) were open prostatectomy specimens. Out of total 80 cases studied, 48 cases (60%) were reported as BPH without prostatitis (Figure 1), 18 cases (22.5%) as BPH with chronic prostatitis (Figure 2) and one case (1.25%) as BPH with granulomatous prostatitis (Figure 3), together constituting 83.75% of total cases.

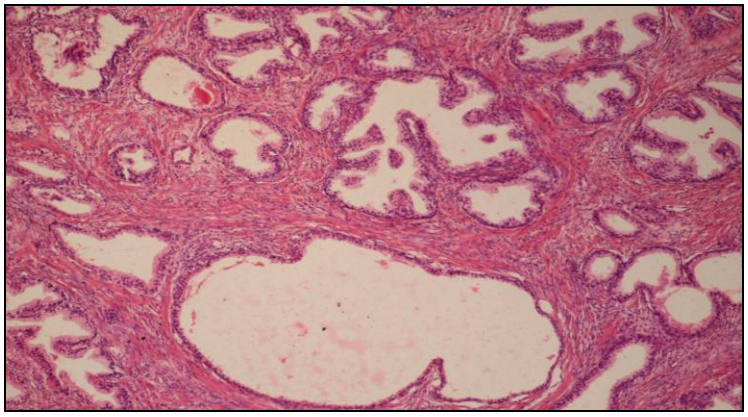


Figure 1: Benign prostatic hyperplasia with glandular and stromal proliferation and dilated gland (H & E, 100X)

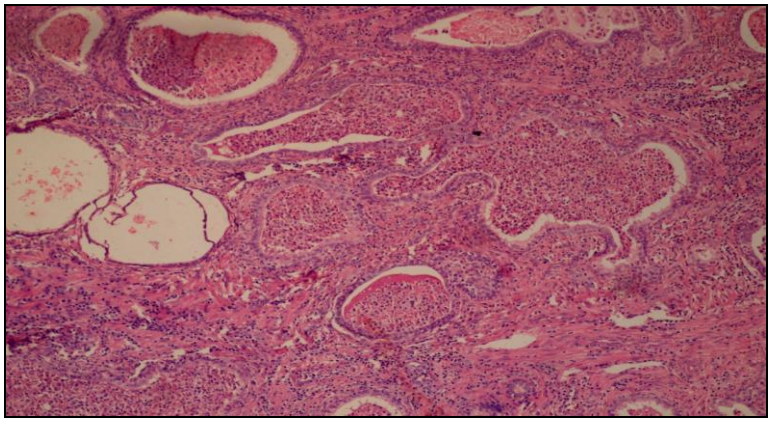


Figure 2: Chronic prostatitis showing infiltration of lymphocytes, plasma cells, histiocytes in the stroma and secretions and neutrophils in lumen (H & E, 100X)

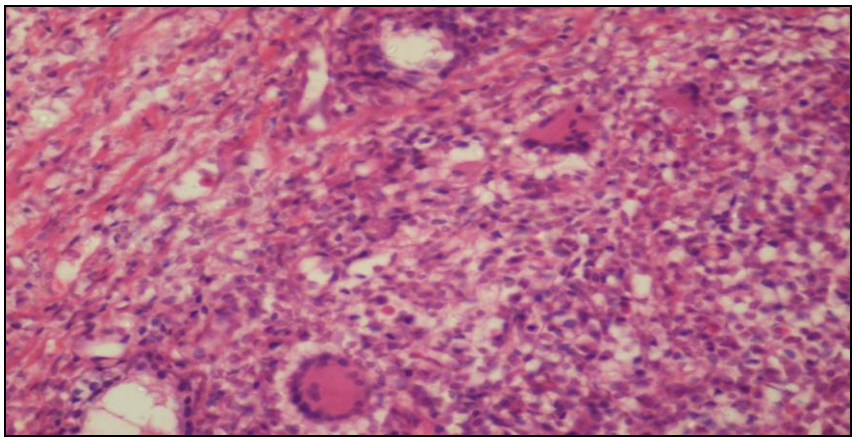


Figure 3: Granulomatous prostatitis showing epitheloid cell granulomas and giant cells (H & E, 400X)

One case (1.25%) was associated with low grade prostatic intraepithelial neoplasia (LGPIN).
Malignant cases constituted 12 cases (15%), out of which 11 cases were of adenocarcinoma (Figure 4) and one case was of transitional cell carcinoma (Figure 5).

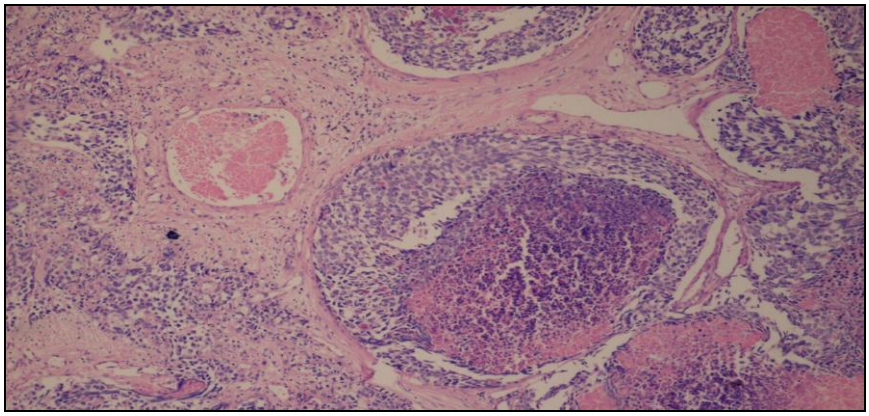


Figure 4: Prostatic adenocarcinoma – Gleason pattern 5 with central comedo necrosis (H & E, 100 X)

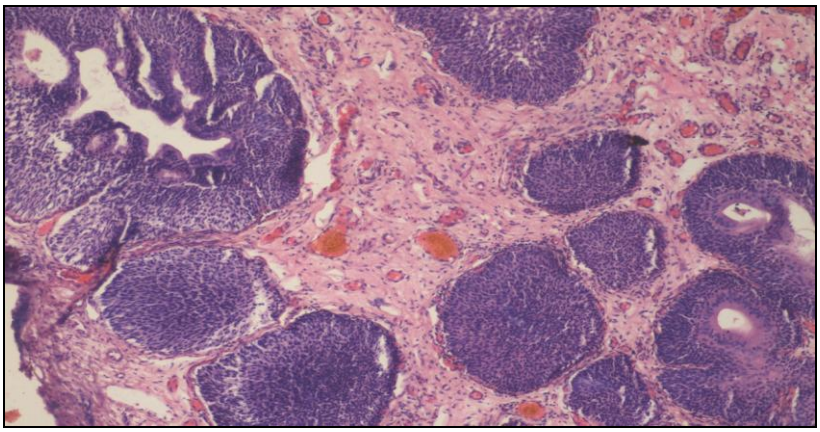
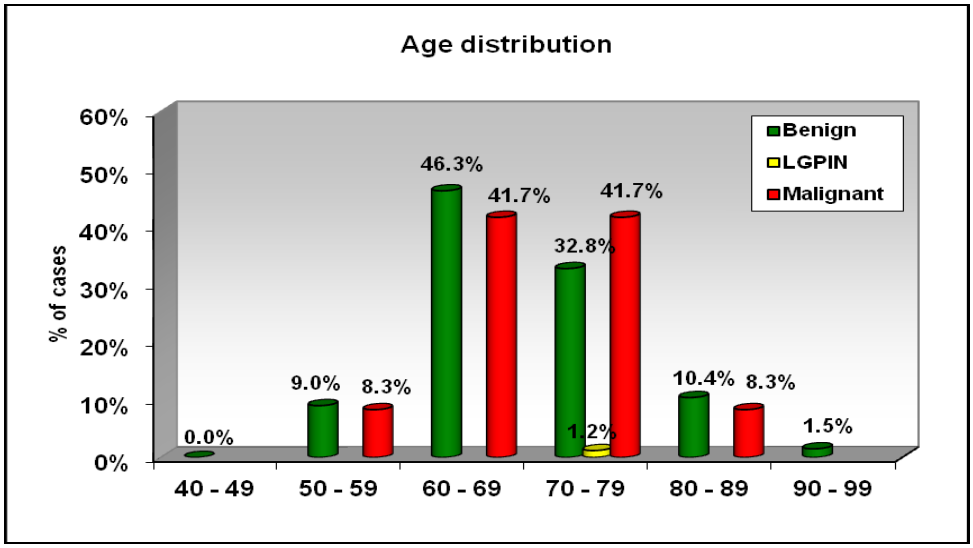


Figure 5: Primary transitional cell carcinoma of prostate (H & E, 100 X)

Final histopathological diagnosis:

Final histopathological diagnosis	**Number of cases (%)**
1) Benign conditions	
a) BPH without prostatitis	48 (60)
b) BPH with chronic prostatitis	
c) BPH with granulomatous prostatitis	18 (22.5)
	01 (1.25)
2) Low Grade Prostatic Intraepithelial Neoplasia (LGPIN)	01 (1.25)
3) Malignant	
a) Adenocarcinoma	11 (13.75)
b) Transitional cell carcinoma	01 (1.25)
Total	80 (100)

Maximum benign cases i.e. 31 (46.3%) were seen in the age group 60-69 years. Youngest benign case was 50 years old and oldest case was 90 years old patient. One low grade PIN (LGPIN) case was reported in a 72 years old patient. Peak occurrence of malignant cases was distributed in two age groups, i.e. in 60-69 and 70-79 years, each group having 5 cases (41.7%) each. Youngest patient with malignancy was 55 years and oldest patient was 80 years old.



In the present study, we got 7 cases (8.75%) associated with various metaplasias. The maximum cases were of transitional metaplasia (5 cases). We also got 1 case each of squamous metaplasia and intestinal metaplasia.

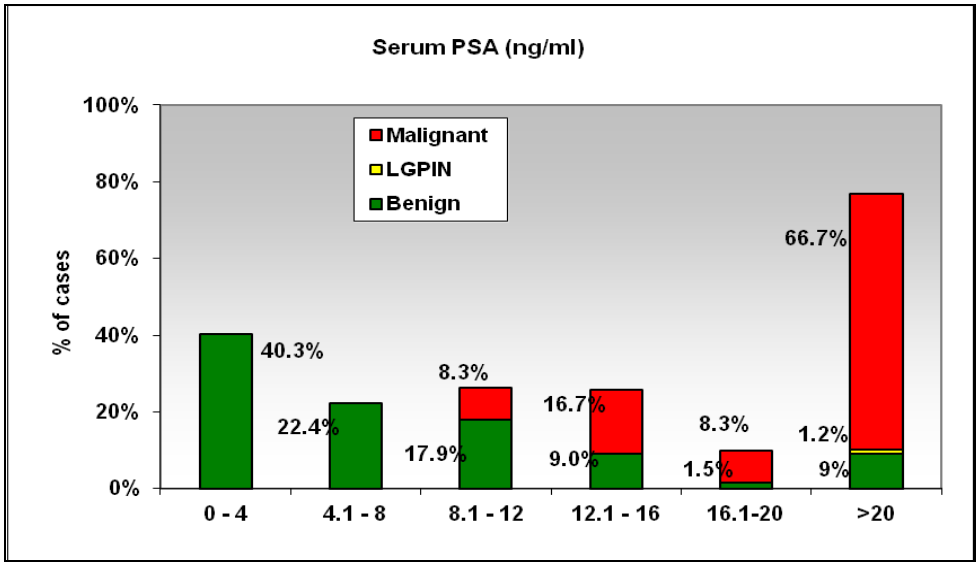
In our study, serum PSA was done in all cases. Maximum benign cases (27 cases) had serum PSA in the range of 0-4 ng/ml. 15 benign cases (22.4%) had modest elevation in serum PSA, in the range of 4.1-8 ng/ml and 12 benign cases (17.9%) had serum PSA in the range of 8.1-12 ng/ml. We also got 6 benign cases (9%) with severe degree of serum PSA elevation with value more than 20 ng/ml. The mean serum PSA value in benign cases was 8.90 ± 12.77 ng/ml

One case of low grade PIN (LGPIN) had serum PSA 26.6 ng/ml which was severely elevated.

In the present study 66.7% (8 cases out of 12) malignant cases had severely elevated serum PSA levels more than 20 ng/ml. Two malignant cases had serum PSA in the range of 12.1-16 ng/ml and one case each in the range of 8.1-12 ng/ml and 16.1-20 ng/ml. In our study we did not get any malignant case

having serum PSA in the range of 0-8 ng/ml. The mean serum PSA value in malignant cases was 83.06 ± 80.36 ng/ml.

When serum PSA levels in benign and malignant cases were compared, serum PSA in the range of 0-4 ng/ml was significantly associated with benign lesions, P value = 0.007 and serum PSA more than 20 ng/ml was significantly associated with malignant lesions, P value < 0.0001.



6 cases (54.5%) of adenocarcinoma had Gleason score 7. We found 3 cases (27.3%) with Gleason score 8 and 1 case each with Gleason score 9 and 10.

Discussion

Prostate lesions are common in the geriatric age group. Benign hyperplasia and carcinoma of the prostate are increasingly frequent with advancing age and are uncommon before the age of 40.

In the present study, majority of the cases (83.8%) were benign, of which BPH without prostatitis constituted 60% of the cases, followed by 15% cases of carcinoma of prostate.

In a study by Mittal *et al.*, (1989) showed 92.98% of benign cases, followed by 7.02% malignant cases.

In cases of chronic non-specific prostatitis, lymphocytes, plasma cells and macrophages were seen in the stroma and lumen of the ducts showed secretions and neutrophils.

Abdel-Meguid *et al.,* (2009), in their study, found prevalence of prostatic inflammation with BPH about 20.1% cases.

In the present study, one case of granulomatous prostatitis was noted, which showed well formed epitheloid cell granulomas with giant cells. There was no evidence of caseation and special stain for AFB was negative.

Epstein *et al.,* (1984), in a study of 62 patients of granulomatous lesions of prostate, found 9 cases of specific granulomatous prostatitis which were caused by mycobacterium tuberculosis, 31 cases of nonspecific granulomatous prostatitis, 13 cases of post-transurethral resection granulomatous prostatitis who had recently undergone prostatic surgery and remaining 9 cases were associated with varied causes like malakoplakia, sarcoid, foreign body-type granulomas.

Mittal *et al.*, (1989), showed granulomatous prostatitis in 1.62% of cases.

Prostatic Intraepithelial Neoplasia (PIN)

In the present study, one case of LGPIN was observed constituting to 1.25 % of total cases. Shakya *et al.*, (2003), found 2 cases (1.88%) PIN in their study of 106 cases.

Prostatic intraepithelial neoplasia is most commonly found in the peripheral zone and HGPIN not commonly found in transurethral resection specimen. Low incidence of PIN in our study may be due to

majority of the specimens we received were TURP (86.3%) and some pathologist prefer not to report low grade PIN, recognizing the difficulty in separating this lesion from benign epithelium and reactive atypia.

Prostate Carcinoma

In the present study, incidence of prostate carcinoma was 15%. Among all malignant lesions, commonest lesion was prostatic adenocarcinoma accounting to 91.66%. In two cases perineural invasion was seen.

One rare case of transitional cell carcinoma of prostate was encountered in the present study. Cystoscopy revealed normal bladder and urethral mucosa. Primary transitional cell carcinoma is a rare tumor, representing 1 to 4 % of all primary prostate carcinoma. Ende and associates (Nicolaisen *et al.,* 1984) described 7 cases of primary transitional cell carcinoma, hypothesizing that the site of origin was the distal periurethral ducts within the prostate.

Age Specific Distribution of BPH

Present study showed 67 BPH cases which formed the major type of lesion in the study. These cases were maximum in the age group of 60-69 years having 46.3% of cases. Youngest benign case was 50 years and oldest case was 90 years old patient.

Shakya *et al.,* (2003), in their study of 106 BPH cases, found 47.16% of cases between 71-80 years followed by 33.96% cases in 61-70 years.

Age Specific Distribution of Prostate Carcinoma

In the present study, malignant cases showed peak in two age groups, i.e. in 60-69 years and 70-79 years, each having 41.7% of cases. The youngest patient with prostate carcinoma was 55 years and oldest patient was 80 years old.

Prostate cancer is a disease associated with aging. About 60% of all prostate cancer cases are diagnosed in men aged 65 years. The probability of developing prostate cancer increases from 0.01% among individuals aged < 39 years to 2.63% for those aged 40 to 59 years; 6.84% for those aged 60 to 69 years and 12.54% for those aged 70 years and older (Cancer Facts & Figures, 2012).

Anunobi *et al.,* (2011), showed prostate carcinoma in an age range of 40 to 98 years, with a mean age of 66 years and peak prevalence in the 60-69 year age group.

The incidence of prostate cancer varies worldwide, with the highest rates found in the United States, Canada, and the lowest rates found in China and other parts of Asia including India. These differences are caused by genetic susceptibility, exposure to unknown external risk factor or differences in health care and cancer registration, or even a combination of these factors (Quinn *et al.,* 2002). Also the advent of screening for serum PSA has increased detection of preclinical disease, affecting cancer incidence.

Serum PSA

Normal levels of serum PSA vary according to the age of the patient. Also in several disease processes like prostate cancer, prostatic intraepithelial neoplasia, and prostatitis, the protective layers between prostatic lumen and capillary may be broached resulting in elevation of serum PSA level (Brawer, 1999).

In the present study, 40.3% of the benign cases had serum PSA < 4 ng/ml. 22.4% benign cases had modest elevation in serum PSA, in the range of 4.1-8 ng/ml and 17.9% had serum PSA in the range of 8.1-12 ng/ml. 9% of benign cases had severely elevated serum PSA with value more than 20 ng/ml, probably due to associated conditions like chronic prostatitis, granulomatous prostatitis. According to a study by Nadler *et al.,* (1995), acute and chronic inflammation of prostate is more commonly associated with high serum PSA. Kiehl and associates (2001) in their study also concluded that BPH and prostatitis is associated with PSA elevation when glandular epithelium is disrupted.

Prostate needle biopsy causes dramatic increase and digital rectal examination causes a modest increase in serum PSA (Ornstein *et al.,* 1997).

Stamey *et al.,* (1982) found 68% of patients with BPH with PSA > 4.0ng/ml. In present study we got about 59.7% of patients with elevated serum PSA (> 4.0ng/ml).

In the present study, 66.7% malignant cases had severely elevated serum PSA levels more than 20 ng/ml. 16.7% malignant cases had serum PSA in range of 12.1-16 ng/ml. One malignant case each was present in range of serum PSA 8.1-12 ng/ml and 16.1-20 ng/ml.

Narayan *et al.,* (1995) found 24% of prostate adenocarcinoma patients with serum PSA >20 ng/ml. In a study by Lekili *et al.,* (1994), 8 out of 25 (32%) prostate adenocarcinoma patients had serum PSA value >20ng/ml.

Conclusion

Thus in conclusion, the commonest pathology encountered in the prostates studied was BPH (83.8%). Incidence of carcinoma was 15%. Prostatitis was encountered in 23.3% of cases and associated metaplastic change was seen in 8.75% of total cases. Also one case of LGPIN was observed.

Benign cases were common in the age group of 60-69 years (46.3%). One case of LGPIN was reported in a 72 years old patient. Malignant cases showed peak in two age groups, i.e. in 60-69 years and 70-79 years (each 41.7%).

The mean serum PSA value in benign cases was 8.90 ng/ml (SD ± 12.77). The mean serum PSA value in malignant cases was 83.06 ng/ml (SD ± 80.36). Serum PSA in the range of 0-4 ng/ml was significantly associated with benign lesions and value more than 20 ng/ml was significantly associated with malignant lesions.

PSA is most important test used in diagnosis and management of prostate cancer. Its level increases approximately in proportion to the volume of prostate cancer. However, elevated serum levels of PSA do not always result from prostate cancer. Benign conditions, such as bacterial prostatitis, urinary retention, and benign prostatic hyperplasia (BPH), may also cause elevations in serum PSA levels.

REFERENCES

Abdel-Meguid TA, Mosli HA and Al-Maghrabi JA (2009). Prostate inflammation. Association with benign prostatic hyperplasia and prostate cancer, *Saudi Medical Journal* **30**(11) 179-83.

Anunobi CC, Akinde OR, Elesha SO, Daramola AO, Tijani KH, Ojewola RW (2011). Prostate diseases in Lagos, Nigeria: a histologic study with tPSA correlation. *Nigerian Postgraduate Medical Journal* **18**(2) 98-104.

Brawer MK (1999). Prostate-Specific Antigen: Current Status. *CA: A Cancer Journal for Clinicians* **49**(5) 264-81.

Cancer Facts & Figures (2012). Atlanta, GA: American Cancer Society 66.

Eble JN, Sauter G, Epstein JI and Sesterhenn IA (2004). Tumours of the prostate. In: World Health Organization Classification of Tumours: Pathology & genetics of tumours of the urinary system and male genital organs, Lyon: IARC Press 159-215.

Epstein JI and Hutchins GM (1984). Granulomatous prostatitis: distinction among allergic, nonspecific, and post-transurethral resection lesions. *Human Pathology* **15**(9) 818-25.

Epstein JI (2010). The lower urinary tract and male genital system. In: Kumar V, Abbas AK, Fausto N, Aster JC (editors), Robbins and Cotran pathologic basis of disease 8th edition, Philadelphia: Saunders an imprint of Elsevier 971-1004.

Kiehl R, Lemos LD, Stavale JN and Ortiz V (2001). Correlation between chronic prostatitis and prostate specific antigen values. *Brazilian Journal of Urology* **27**(1) 42-45.

Lekili M, Zengin M, Postaci H and Ayder AR (1994). Relationship between histologic grading and serum prostate specific antigen in prostatic carcinoma. *International Urology and Nephrology* **26**(6) 665-68.

Mittal BV, Amin MB and Kinare SG (1989). Spectrum of histological lesions in 185 consecutive prostatic specimens. *Journal of Postgraduate Medical Institute* **35**(3) 157-61.

Nadler RB, Humphrey PA, Smith DS, Catalona WJ and Ratliff TL (1995). Effect of inflammation and benign prostatic hyperplasia on elevated serum prostate specific antigen levels. *Journal of Urology* **154**(2) 407-13.

Narayan P, Gajendran V, Taylor SP, Tewari A, Presti JC Jr and Leidich R *et al.*, (1995). The role of transrectal ultrasound-guided biopsy-based staging, preoperative serum prostate-specific antigen, and biopsy Gleason score in prediction of final pathologic diagnosis in prostate cancer. *Urology* **46**(2) 205-12.

Nicolaisen GS and Williams RD (1984). Primary transitional cell carcinoma of prostate. *Urology* **24**(6) 544-49.

Ornstein DK, Rao GS, Smith DS, Ratliff TL, Basler JW and Catalona WJ (1997). Effect of digital rectal examination and needle biopsy on serum total and percentage of free prostate specific antigen levels. *Journal of Urology* **157**(1) 195-98.

Quinn M and Babb P (2002). Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons. *BJU International* **90**(2) 162–73.

Rosai J (2012). Male reproductive system. In: Rosai and Ackerman's surgical pathology 10th edition, St. Louis: Mosby an imprint of Elsevier 1287-1398.

Shakya G, Malla S and Shakya KN (2003). Salient and co-morbid features in benign prostatic hyperplasia: a histopathological study of the prostate. *Kathmandu University Medical Journal (KUMJ)* **1**(2) 104-09.

Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS and Redwine E (1987). Prostate–specific antigen as a serum marker for adenocarcinoma of the prostate. *New England Journal of Medicine* **317**(15) 909-16.