Original Research Article

A Study On Correlation of Various Prostate Pathology With Serum Prostate Specific Antigen At A Tertiary Care Centre In Bihar

Awadh Kumar[1], Md Muntaka[2*], Neeraj Kumar Rajak[3], Gaurav[4], V S Prasad[5]

[1]Associate Professor, Department Of General Surgery, Darbhanga Medical College and Hospital, Laheriasarai, Bihar, India

[2]3rd Year Junior Resident, Department Of General Surgery, Darbhanga Medical College and Hospital, Laheriasri, Bihar, India

[3]3rd Year Junior Resident, Department Of General Surgery, Darbhanga Medical College and Hospital, Laheriasri, Bihar, India

[4]3rd Year Junior Resident, Department Of General Surgery, Darbhanga Medical College and Hospital, Laheriasri, Bihar, India

[5]Associate Professor, Department Of General Surgery, Darbhanga Medical College and Hospital, Laheriasarai, Bihar, India

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Abstract

Introduction: Diseases primarily inflicting prostate gland are inflammation, benign nodular enlargement, and tumors. Serum prostate-specific antigen (PSA), a marker for prostatic carcinoma has high sensitivity, specificity, and compliments histopathological diagnosis. Gleason's microscopic grading is a paramount feature and with PSA are important for diagnosis, management, and prognosis of carcinoma. **Methodology:** Clinicopathological study of 100 prostatic biopsies was conducted in the Department of General Surgery, Darbhanga Medical college and Hospital, Darbhanga, Bihar, India, over a period of One year from January 2020 to Dcember 2020. The study was approved by the Institutional Ethical Committee and all patients gave informed written consent. All patients presenting with LUTS underwent DRE and were worked up with USG KUBP, Serum PSA and biopsy (if indicated) after obtaining consent. **Results:** A total of 100 patients were included in the study. The mean age in our study was 62.5 years [range 50-90 years]. The majority of the patients in the study group were in the age group of 61-70 years. PSA levels of the patients were compared according to their age. The mean serum PSA for age group 50-60 years was 3.9 ng/ml, for age group 61-70 was 15.2 ng/ml, for age group 71-80 was 11.3ng/ml, for age group 81-90 was 11.4 ng/ml. The mean serum PSA for the whole group was 13.2 ng/ml. The mean serum PSA level was found to increase with each decade, starting from 50 years up to 90 years ($p< 0.05$). **Conclusion:** Mean serum PSA levels rises with increasing age. Serum PSA levels has a significant correlation with International prostate symptom severity scoring wherein mean serum PSA level rises with severity of LUTS. However, serum PSA levels do not show significant correlation with Gleason score or clinical stage of prostate cancer.

Key Words: Correlation, Prostate Pathology, Serum Prostate Specific Antigen.

Introduction

Diseases primarily inflicting prostate gland are inflammation, benign nodular enlargement, and tumors[1]. Worldwide benign prostatic hyperplasia (BPH) affects 210 million males and is common over the age of 50 years[1, 2]. Carcinoma of the prostate is most common nonskin cancer in the west and the second leading cause of cancer death among men[2, 3]. Carcinoma is a disease of elderly men occurring at age 65 years and above; with increasing trend in Asian countries in last 25 years. In India, carcinoma of prostate occupies 2nd to 10th rank among cancers in men, in various metro cities as per national cancer registry[4, 5].

Among the carcinomas, the majority are adenocarcinomas that develop from the acini of the ducts. Other rare histological subtypes include small cell carcinomas, signet ring carcinoma, adenoid cystic carcinoma, neuroendocrine tumor, transitional cell carcinoma, which account for about 5%.

*Correspondence
Dr. Md Muntaka
3rd Year Junior Resident, Department Of General Surgery, Darbhanga Medical College and Hospital, Laheriasri, Bihar, India.
E-mail: muntakamun@gmail.com

A possible precursor lesion of prostatic malignancy is prostatic intraepithelial neoplasia, which is dysplasia of the epithelium lining the prostatic glands. Studies have shown that the appearance of prostatic intraepithelial neoplasia may precede carcinoma by 10 or more years[6].

Digital rectal examination (DRE) and transrectal ultrasonography are a preliminary practical diagnostic method but has low specificity and sensitivity[1, 7].

A transrectal biopsy is essential to confirm the diagnosis. Most popular is Gleason's microscopic grading system development of Donald *F* Gleason in 1966[8]. Gleason's grading system is superior and the best predictor of disease progression and outcome. Serum prostate-specific antigen (PSA), a marker for prostatic carcinoma has high sensitivity, specificity, and compliments histopathological diagnosis. Gleason's microscopic grading is a paramount feature and with PSA are important for diagnosis, management, and prognosis of carcinoma[7, 8].

Methodology

Clinicopathological study of prostatic biopsies was conducted in the Department of General Surgery, Darbhanga Medical college and Hospital, Darbhanga, Bihar, India, over a period of One year from January 2020 to Dcember 2020. The study was approved by the Institutional Ethical Committee and all patients gave informed written consent.

All patients presenting with LUTS underwent DRE and were worked up with USG KUBP, Serum PSA and biopsy (if indicated) after obtaining consent. DRE was carried out with the patient lying in left lateral position and the following were assessed: size of the prostate gland with any asymmetric enlargement of the lateral lobes, tenderness of the prostate gland, consistency of the prostate gland (Firm/Hard/Variable consistency), surface nodularity and the consistency of these nodules, mobility of the rectal mucosa over the prostate gland and the tone of the anal sphincter.

A trans-abdominal ultrasound examination was done to assess the size of the prostate gland. Size was graded as follows. Grade I was less than 25 cmm, Grade II was 26 to 50 cmm, Grade III 51 to 75 cmm and Grade IV more than 75 cmm. Serum PSA specimen were collected in 5 ml sterile EDTA tubes (BD vacutainers®). The samples were centrifuged within 20 minutes of collection at 2000 g for 10 min and sera was frozen at -20o c until tested. The total prostate specific antigen (tPSA) was assessed at the hospital pathology lab using IRMA technique (Diagnostic System Laboratories Inc, Texas, U.S.A.)

Patients with suspicious DRE finding (defined as hard nodular fixed prostate) or increased Serum PSA levels (defined as more than 4 ng/ml) underwent prostate biopsy. Other patients were followed up with serum PSA levels, thereby dividing patients into two groups. Group 1 with suspicious DRE or elevated serum PSA underwent biopsy. Group 2 who had benign feel of prostate on DRE and normal serum PSA levels were only followed up. Patients of both groups were followed up every 3 months and clinical, ultrasonological and biopsy findings were recorded in the study performa.

Biopsy specimen collection and processing was done starting with Sodium phosphate enema at 0600 hrs on the day of biopsy and oral antibiotic cover (single oral dose of tab ciprofloxacin (500 mg)-Tinidazole (500 mg) in the morning 2 hrs prior to biopsy to patients. Patients were placed in the left lateral decubitus position with knees and hips flexed 90 degrees. An arm board was attached parallel to the table and a pillow placed between the knees. Ultrasound was done using ultrasonography unit and a transrectal 7.5 MHZ biplane probe under local anesthesia (2% lignocaine jelly). 12 cores (6+6) of tissue targeting the peripheral zone at the apex, midgland, and base, as well as laterally directed cores on each side of the prostate were taken. The cores biopsies were taken using automated biopsy gun with a disposable 18G Core needle (C. R. Bard Inc, New Jersey, U.S.A). The specimen obtained was sent in two bottles labelled as Right and Left separately to the hospital Pathology Lab and reported upon by one of the institutional pathologists. A written consent was obtained prior to the prostate biopsy. Pre biopsy workup and investigations were done in all patients prior to biopsy. Investigations included were complete blood counts, coagulation profile, blood sugar, urine examination and culture, blood culture. Vital parameters including pulse, BP, temperature and respiratory rate were recorded pre and post biopsy. The post-biopsy patients were kept for observation for 06 hours and discharged accordingly with the advice to continue antibiotic for 48 hours and to attend OPD or emergency room in case symptoms of fever, dysuria, hematuria, hematospermia or bleeding per rectum arises. Patients were followed up firstly at 3 months interval and after 6 months interval.

Data were analyzed using Statistical Package of Social Sciences (SPSS) ver 21.0. Chi square test was performed to establish association and a p value of < 0.05 was considered significant.

Results

A total of 100 patients were included in the study. The mean age in our study was 62.5 years [range 50-90 years]. The majority of the patients in the study group were in the age group of 61-70 years. PSA levels of the patients were compared according to their age. The mean serum PSA for age group 50-60 years was 3.9 ng/ml, for age group 61-70 was 15.2 ng/ml, for age group 71-80 was 11.3 ng/ml, for age group 81-90 was 11.4 ng/ml. The mean serum PSA for the whole group was 13.2 ng/ml. The mean serum PSA level was found to increase with each decade, starting from 50 years upto 90 years ($p< 0.05$).

Among 100 patients, 51 had IPSS score in the range of 1-7 (mild), 45 had IPSS between 8- 19 (moderate) whereas only 4 patients had IPSS>19 (severe). Mean serum PSA in patients with mild, moderate and severe LUTS were 4.2 ng/ml, 6.5 ng/ml and 13.2 ng/ml respectively. The range of serum PSA in patients with IPSS score of mild, moderate and severe were from 0.6 to 42 ng/ml, 0.4 to 30.1 ng/ml and from 12.2 to 16.3 ng/ml respectively ($p< 0.05$).

The mean Serum PSA amongst patients with DRE suspicious of malignancy was 14.7 ng/ml, whereas in the benign DRE finding group, the mean serum PSA was 1.9 ng/ml ($p<0.05$).

The ranges of serum PSA for grade I, grade II, grade III and grade IV prostate enlargement were from 0.6 to 5.2 ng/ml, 0.8 to 15.1 ng/ml, 0.2 to 33.2 ng/ml and 0.8 to 47.4 ng/ml respectively. The mean Serum PSA amongst patients with prostate sizes 75 gms were 1.6 ng/ml, 2.9 ng/ml, 7.2 ng/ml and 11.2 ng/ml respectively ($p< 0.05$).

A total of 42 patients underwent biopsy on the basis of either DRE suspicion or raised serum PSA levels, out of which 24 had benign disease, whereas 18 had adenocarcinoma. Remaining 58 patients did not undergo biopsy.

Amongst the malignancy group, the number of cases of serum PSA levels <4 ng/ml,4-10 ng/ml and >10 ng/ml were 3, 4 and 11 respectively. The range of serum PSA in malignancy group was from 2.5 ng/ml to 48.7 ng/ml. The mean Serum PSA in malignancy group was 15.7ng/ml. Amongst the benign group, (BPH as well as prostatitis) the number of patients of serum PSA levels graded as 10 ng/m1 were 4, 19 and 1 respectively. The range of serum PSA in benign group was from 1.1 ng/ml to 9.3 ng/ml.

Amongst 18 patients with biopsy proven adenocarcinoma, 9 patients had Gleason score <7, 6 had score of 7 and rest 3 had score of >7. The range of Gleason score noted was 6 to 8. The range of serum PSA was from 3.2 ng/ml to 48.4 ng/ml. No significant correlation was seen between serum PSA values and Gleason grade of prostate cancer. ($p > 0.05$)

Amongst the 18 patients with adenocarcinoma 1 had cT1c disease, whereas cT2 and cT3 were seen in 15 and 2 patients respectively. For cT1c, the patients had PSA level of 4-10 ng/ml. For cT2, the number of patients of serum PSA<4 ng/ml,4-10 ng/ml and >10 ng/ml was 6, 4 and 5 respectively. For cT3, both the patient had serum PSA >10 ng/ml. Clinical stage T2 formed majority of biopsy proven adenocarcinoma cases. However, there was no significant correlation between serum PSA levels and clinical stage of prostate cancer ($p>0.05$).

Discussion

The mean age in our study was 62.5 years [range 50- 90years]. This compares favorably with the study done by Sunanda De et al who found mean age of study group to be 66 years[9]. Josephine et al found mean age to be 65 years[10]. Our study shows that with the increase in age group, there is increase in serum PSA levels. The results of our study were comparable with PSA best

practice statement 2009 age specific PSA range for Asian population[11]. According to their study, serum PSA levels showed an increasing trend with age. There was significant correlation between the IPSS and serum PSA levels Our study was comparable to study done by Park et al who showed significant linear correlation of PSA with IPSS[12]. The high serum PSA in our study can be attributed to higher levels of serum PSA in Asian population[13]. In our study mean size of prostate was 52.8cc. There was a significant correlation noted between theprostate size and Serum PSA. Our study was comparable to study by Carvalho GF et al and Baruah et al[14, 15]. Correlation of serum PSA levels in detection of Adenocarcinoma prostate was significant. 18 patients had biopsy provenprostate cancer. The mean Serum PSA in malignancy group was 15.7 ng/ml. Results of our study were comparable to numerous studies which showed higher incidence of Adenocarcinoma with higher Serum PSA levels. Anushree et al found patients with PSA values >20.1 were 8.21 times more likely to be malignant than benign on biopsy[16]. Sunanda De et al found that for serum PSA >10.0 ng/ml, sensitivity was 85%, specificity was 72.5% and PPV was 60.7%, for detection of carcinoma prostate[9].

In our study, amongst 18 patients who were biopsy, Gleason scores were not significantly correlated. In a study by Lima, NG et al the PSA levels were higher in the groups with Gleason score of 7 and >7($p<0.05$). However, there was no significant correlation between mean PSA level and Gleason score of <7($p>0.05$)[17]. Dobruch et al also found weak correlation of Gleason score of serum PSA in their study on 377patients with LUTS who underwent TRUS guided prostatic biopsy[18]. In our study out of 16 patients who were biopsy provenprostate carcinoma, among 18 patients with biopsy proven adenocarcinoma, 1 patient had cT1cdisease, whereas cT2 and cT3 were seen in 15 and 2 patients respectively. This is comparable to the study done by Dobruch et al who found cancercon fined to the prostate in 330 (87.5%) cases[18]. However, we found poor correlation with prostate cancer stage of serum PSA levels, p value was 0.07.

Conclusion

Mean serum PSA levels rises with increasing age. Serum PSA levels has a significant correlation with International prostate symptom severity scoring wherein mean serum PSA level rises with severity of LUTS. Serum PSA levels has a significant correlation with prostate size measured by trans-abdominal ultrasonography where in serum PSA levels rises with grade of prostatomegaly. However, serum PSA levels do not show significant correlation with Gleason score or clinical stage of prostate cancer.

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