ORIGINAL RESEARCH PAPER

Biochemistry

STUDY OF SERUM PROSTATE SPECIFIC ANTIGEN AND AGE SPECIFIC DISTRIBUTION IN BENIGN ENLARGEMENT OF PROSTATE AND CARCINOMA OF PROSTATE.

KEY WORDS:

Dhananjay Bhale MBBS.,MD . Professor and Head Biochemistry, MGM MC Aurangabad India

D. M. Vaishnav MBBS,MD . Associate Professor Biochemistry, MGM MC Aurangabad India

Ruta Anandgaonkar* MBBS, D.P.B.,MD.Tutor in Biochemistry, MGM MC Aurangabad, India *Corresponding Author

ABSTRACT

INTRODUCTION: Benign prostatic hyperplasia is the most common neoplastic disorder affecting the aging male population worldwide.

AIMS AND OBJECTIVES: To study Serum PSA levels in patients of benign enlargement of prostate and cancer of prostate .

MATERIAL AND METHODS: The present study was carried out in Department of Biochemistry in collaboration with Central Laboratory and Department of Urology, MGM Medical College, Aurangabad from November 2015 to November 2017. Serum PSA levels were measured on VITROUS 5600 by Enhanced Chemiluminescence method. In the present study, the mean PSA in Group B was 19.21±11.95 ng/ml which was comparatively higher than Group A. This mean difference of PSA between two groups was found to be statistically significant (p<0.0001). The mean age of Group A was 66.02±10.05 years whereas in Group B the mean age was 68.38± 8.49 years.

SUMMARY AND CONCLUSION: In this study, higher serum PSA levels were observed in the benign and malignant group both suggesting a potential correlation between prostate inflammation and prostate cancer.

INTRODUCTION

Benign prostatic hyperplasia is the most common neoplastic disorder affecting the aging male population worldwide. Prostate specific antigen (PSA), neutral serine protease secreted exclusively by prostatic epithelial cells, has a number of applications in the management of men with prostatic carcinoma. Screening programs for prostate cancer will increase the percentage of localized prostate cancer, which can be cured by radical prostatectomy.[1]

Prostate specific antigen is used as a prescreening marker , followed by DRE and TRUS . When PSA is abnormal, it is highly efficient in detecting prostate cancer at a localized (potentially curable) stage since 99% of the cancers diagnosed were at such a localized stage, thus practically eliminating the diagnosis of metastatic and non-curable prostate cancer.[2]

In light of these findings, we analyzed Serum PSA to know role of inflammation in BEP and cancer prostate .

AIMS AND OBJECTIVES

1. To study levels of serum prostate specific antigen (PSA) levels in patients of benign enlargement of prostate and cancer of prostate.
2. To study age specific distribution in patients of benign enlargement of prostate and cancer of prostate.

Materials and Methods

The present study was carried out in Department of Biochemistry in collaboration with Central Laboratory and Department of Urology, MGM Medical College, Aurangabad. The Study was approved by Institutional Ethical and Research Committee to use human subjects in research study. Informed consent was taken from patient / relative conducted after getting ethical committee clearance from MGM MC and Hospital ethical committee. The study was conducted from November 2015 to November 2017.

ELIGIBILITY CRITERIA :

a) Inclusion Criteria :

a. Newly diagnosed Patients of BEP and prostate cancer medically and histopathologically diagnosed.
b. Serum PSA levels >4 ng/ml
c. Age Group >55 years.
d. Those who are willing to participate in study.

b) Exclusion Criteria: According to history given by patient

a. Acute infections
b. Rheumatoid arthritis
c. Gout
d. Asthma
e. Chronic lung disease
f. Myocardial infarction

STUDY DESIGN :

It is an observational cross sectional study.

A total of 114 patients were enrolled in this present study. These were divided in two groups .Each group contain 57 patients.

Study Groups :

- Patients were divided in to 2 groups i.e. Group A and Group B.
- **Group A :** Benign enlargement of prostate (BEP) n= 57
- **Group B:** Carcinoma prostate n= 57

Collection of Blood Sample and Laboratory Method :

Total 5 ml of venous blood sample (fasting) was collected from antecubital vein under all aseptic precautions in plain bulb .It was then allowed to clot and will be then centrifuged for 10 min at 3000 r.p.m. for serum separation. Serum was used for the analysis of PSA. The tests were carried out on same day after serum separation. Serum PSA levels were measured on VITROUS 5600 by Enhanced Chemiluminescence method.

Estimation of Serum Prostate Specific Antigen (P.S.A) :[20]

METHOD :

Enhanced Chemiluminescence

PRINCIPLE :

The VITROS Total PSA II test is performed using the VITROS Total PSA II Reagent pack & the VITROS Total PSA Calibrators on the VITROS 5600 Immunodiagnostic System using intellicheck technology. An Immunometric Immunoassay techniqueis used which involves the reaction of Total PSA present in the sample with a biotinylated antibody and a horseradish peroxidase (HRP) labeled antibody conjugate. The antigen antibody complex is captured by streptavidinon the wells. Unbound materials are removed by washing.

The bound HRP conjugate is measured by a luminescent reaction. A reagent containing luminogenic substances and an electron transfer agent, is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminal derivative, producing light. The electron transfer agent increases the level of light produced and prolongs its emission. The light signals are read by the system. The amount of HRP conjugate bound is directly

proportional to the concentration of total PSA present.

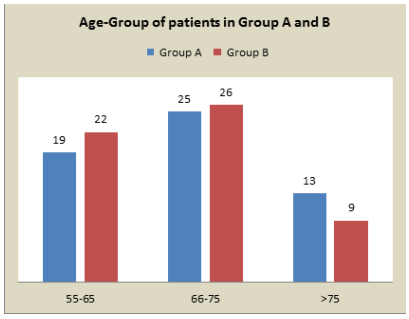
OBSERVATIONS AND RESULTS

The present study was carried out in Department of Biochemistry in collaboration with Central Laboratory and Department of Urology, MGM Medical College, Aurangabad. Total 114 subjects were studied from November 2015 to November 2017, of which 57 were cases of BEP and 57 were cases of carcinoma prostate.

OBSERVATIONS AND RESULTS:

Table 1 : Age-Group of patients in Both Groups

Age-Group	Group A		Group B	
	No. of cases	Percentage	No. of cases	Percentage
55-65	19	33.3%	22	38.6%
66-75	25	43.9%	26	45.6%
>75	13	22.8%	09	15.8%
Total	57	100%	57	100%
Mean±SD	66.0210.05		68.388.49	

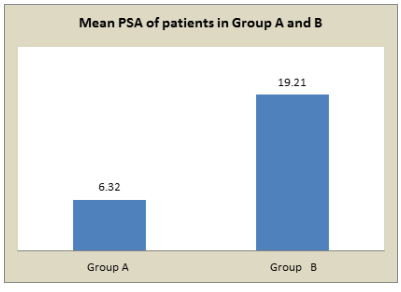


Bar diagram 1 : Showing group wise distribution of age in group A and B

Table 2 : Comparison of Mean PSA of patients in Groups

PSA	Mean±SD ng/ml	z-value	p-value
Group A	6.32±2.12	8.07	P<0.0001 S
Group B	19.21±11.95		

In the present study, the mean PSA in Group B was 19.21±11.95 ng/ml which was comparatively higher than Group A. This mean difference of PSA between two groups was found to be statistically significant (p<0.0001).



Bar diagram 3 : Showing mean PSA (ng/ml) in Group A and B

DISCUSSION

Prostate cancer is the most prevalent cancer found in men above the age of fifty years and is frequently diagnosed in men between 45 and 89 years of age with a median age of 72 years. Benign enlargement of prostate (BEP) is a universal phenomenon in aging men. The disease affects men over the age of 45 and increases with advancing age. By the eighth decade, more than 90% of men have prostatic hyperplasia and it remains a leading cause of morbidity in elderly men. Prostate cancer among adult males is the most common neoplasm in western countries. Prostate specific antigen (PSA) is now a well established tumor marker that aids in the early detection of localized prostate cancer. Increased PSA concentrations are found in the serum of patients with benign prostatic hyperplasia or patients with prostate cancer, respectively. The incidence of prostate cancer varies worldwide , with highest rates reported in USA , and lowest in parts of Asia. The prostate cancer incidence rates are 1.6 to 1.9 times higher and mortality rates are 2 to 3 times higher among African-American men than Caucasian –American men. In regions where PSA screening is not readily available prostatic cancer is locally advanced or metastatic and therefore incurable in most cases. Racial differences in stage at presentation and therapy indicate the need for greater prostate cancer awareness and education among patients and physicians. More widespread use of PSA for early detection in men at increase risk of prostate cancer is needed.[3]

Prostate cancer is the most prevalent cancer found in men above the age of fifty years and is frequently diagnosed in men between 45 and 89 years of age with a median age of 72 years. The age of Indian patients of prostate cancer varies from 32-86 years with an average age of 43.5 years, which is much lower when compared to the average age of patients in western countries. Prostate cancer is the third most common cancer in men and number two cancer killers above the age of seventy years. Individuals with positive family history are likely to develop disease at younger age compared to the people without family history of cancer.[4]

Benign prostate hyperplasia (BPH) is a universal phenomenon in aging men. The disease affects men over the age of 45 and increases with advancing age. By the eighth decade, more than 90 per cent of men have prostatic hyperplasia and it remains a leading cause of morbidity in elderly men. Histology alone could give final diagnosis of Cancer Prostate approximately in 67% of cases whereas 33% are diagnosed with the help of other modalities. At the time of presentation at the hospital, 42.3% of patients already had extensive multiple bone metastases, whereas 31% had loco regional spread and rest 27% had localized tumor. Hence prevention and early detection of prostate cancer is a valuable life saving and cost effective health strategy. For early detection of prostate cancer, the American Urological Association (AUA) and Food and Drug Administration (FDA) have recommended combined use of digital rectal examination and serum PSA estimation annually in all men at the age 50 years without any family history of cancer and at the age of 40 years with family history of prostate cancer .[5]

In our study out of 114 patients 57 patients were of Benign enlargement of prostate (Group A) and 57 patients were of Cancer of prostate (Group B). In Group A out of 57 patients maximum patients i,e. 25 (43.86%) were from age group 66-75 years. And 13 patients (22.81%) patients were from age group more than 75 years. Also in Group B maximum patients were from age group of 66-75 years i.e. 26 (46.61%) and minimum 9 (15.78%) patients were from age group of more than 75 years (Table 1).

The mean age of Group A was 66.02±10.05 years whereas in Group B the mean age was 68.38± 8.49 years (Table 1). Our finding were correlated with previous findings (Elsberger B et al17 and Catlow J et al[18]).

The mean PSA in Group B was 19.21±11.95 ng/ml, which was comparatively higher than Group A. In Group A it was 6.32±2.12 ng/ml. This mean difference of PSA between two groups was found to be statistically significant (p<0.0001) (Table 3).

Prostate Specific Antigen in BEP and cancer of Prostate :

PSA, a serine protease synthesized by benign and malignant prostatic epithelium, is a sensitive serum marker for prostatic hypertrophy and cancer. In fact, increased PSA levels are often seen in carcinomas of the prostate, but have also been reported in benign inflammatory disorders of the prostate.[6]

PSA, a useful tumor marker is a single chain glycoprotein consisting of 93% amino acids and 7% carbohydrates. In healthy males, the prostate epithelium synthesizes and secretes PSA and efficiently prevents the escape of the protease into the circulation. However, minor amount of PSA does enter into the blood circulation. Hence it is worthwhile to determine serum PSA

concentrations in patients of benign and malignant conditions of prostate, which could help in differential diagnosis.[7]

The use of prostate-specific-antigen in the early detection of prostatic carcinoma results in a 2-3 times increase in prostatic carcinoma detection rate. 15-35% of all operated localized prostatic carcinoma have a normal PSA. A biopsy is indicated in men with a life expectancy of more than 10 years when the PSA value is above 10 ng/ml and/or digital-rectal examination is suspicious. In men with a minimal elevated PSA-value of 4-10 ng/ml, 25% will have a prostatic carcinoma regardless of the finding on digital-rectal examination.[8,9]

The optimal tumor marker for prostate cancer would be effective for early detection, staging, and monitoring patients after definitive treatment. Unfortunately, such a "super" marker does not exist at this time. However, prostate-specific antigen (PSA) has current utility in the diagnosis and staging of prostate cancer.[10]

The study was performed by Fournier G et al on 100 consecutive male patients with mean age 68±10.8 years, comprising of 80 patients with benign disease (80%) and 20 prostate carcinoma patients (20%), who had histopathologically proven prostate cancer. Patients with total PSA between 2-25 ng/ml were included in the study. Thirty normal healthy males with mean age 55±10 years, served as control. Serum total PSA were analyzed using Chemiluminescence immunoassay method. The mean total PSA in normal healthy control subjects was 1.72±1.06 ng/ml. It was increased significantly in diseased condition. Its mean concentration in carcinoma patients was 12.6±5.3 ng/ml and in benign patients it was 6.3±4.6 ng/ml. The most dramatic organic manifestation of andropause in terms of a decrease in quality of life is benign prostate hypertrophy (BPH), in its ultimate consequences a life-threatening condition due to obstruction of the urethra and, finally, uremia.[11]

There is much evidence to suggest that benign prostatic hypertrophy is an endocrine disease. In the adult male, testicular androgens regulate development, growth and functional maintenance of the prostate gland. Androgens regulate prostate specific antigen (PSA) secretion by acinar epithelial cells.[12]

Stamey et al (1989)[13] reported a mean serum PSA of 563 ng/ml in 35 untreated prostate cancer patients. The PSA values beyond upper limit of gray zone i.e.,10 ng/ml were reported as 7% and 14% by Barak et al (1989)[14] and Partin et al (1990)[15] Similarly, The study conducted by Wodrum D.L. et al (1998)[16] reported only 3% of BPH patients to have PSA greater than 10 ng/ml .

Prostate specific antigen (PSA), a useful tumor marker is a single chain glycoprotein consisting of 93% amino acids and 7% carbohydrates. In healthy males, the prostate epithelium synthesizes and secretes PSA and efficiently prevents the escape of the protease into the circulation.

In the study conducted by Malati T. et al (2006),[4] mean serum PSA concentration was very high (408 ng/ml) due to advanced malignancy in majority of untreated 267 patients diagnosed as adenocarcinoma patients. Similarly, Stamey et al[23] reported a mean serum PSA of 563 ng/ml in 35 untreated prostate cancer patients. The PSA values beyond upper limit of gray zone i.e. 10 ng/ml were reported as 14% and 7% by Barak et al (1989)[14] and Partin et al (1990) [15] respectively However, according to study conducted by Wodrum et al (1998) [16] only 3% of BPH patients were reported to have PSA greater than 10 ng/ml. According to Rosaria Alba et al19 the mean serum PSA level was 14.34±11.85 ng/ml, varying from 3.80 to 57.20 ng/ml in BPH patients which were significantly higher than those of healthy donors. Our results were in accordance with previous studies (Malati T. et al,[4] Stamey et al,[13] Barak et al,[14] Partin et al[15] and Rosaria Alba et al[1]).

SUMMARY AND CONCLUSION

In Group A and B maximum patients i.e. 25 (43.86%) , 26 (46.61%) were from age group 66-75 years. The mean age of Group A was 66.02±10.05 years whereas in Group B the mean age was 68.38±8.49 years.

The mean PSA in Group B was 19.21±11.95 ng/ml, which was comparatively higher than Group A. In Group A it was 6.32±2.12 ng/ml. This mean difference of PSA between two groups was found to be statistically significant ($p<0.0001$).

REFERENCES

1. Hammerer P, Huland H. Status of PSA determination for early detection of prostate carcinoma. S Afr Med J 2001,Aug;91(8):679-84.
2. Candas B, Cusan L, Gomez JL, Diamond P,et al. Evaluation of prostatic specific antigen and digital rectal examination as screening tests for prostate cancer. Ann Urol 2004;38(5):207-24.
3. Heyns CF , Leucona MF, Van der Merwe A. Prostate cancer among different racial groups in the Western Cape : Presenting features and management. S Afr Med J 2001;101(4):267-270.
4. Malati T, Rajani Kumari PV, Murthy LN, Ch. Ram Reddy, Surya Prakash B. Prostate specific antigen in patients of benign prostate hypertrophic and carcinoma prostate. Ind J Clin Bio 2006;21 (1): 34-40
5. Kramer BS, Brown ML, Prorok PC, Potosky A and Gohagan JK. Prostate cancer screening: what we know and what we need toknow. Ann Intern Med 1993; 119(9): 914-23.
6. Hammerer P, Huland H. Value of determining prostate-specific antigen for early detection or prostatic carcinoma. J Urolo 1995 Jul;34(4):283-89.
7. Lucia MS, Torkko KC. Inflammation as a target for prostate cancer chemoprevention: pathological and laboratory rationale. J Urol 2004;171(2 Pt 2):S30–S34. [PubMed]
8. Heyns CF, Naudé AM, Visser AJ. Early diagnosis of prostate cancer in the Western Cape. Pathologe 2005 ;26(6):469-72.
9. Saito Y, Rinsho N. The usefulness of prostate-specific antigen assays for the early detection and follow up of the prostate cancer. Jap J Clin Med 1998;56(8):1989-93.
10. Lee CT, Oesterling JE. Diagnostic markers of prostate cancer: utility of prostate-specific antigen in diagnosis and staging. Semin Surg Oncol 1995;11(1):23-35.
11. Fournier G, Valeri A, Mangin P, Cussenot O. Prostate cancer: Diagnosis and staging. Prostate Cancer Prostatic Dis 2006;9(1):6-13.
12. Brawer MK, Chetner MP, Beatie J, Screening for prostatic carcinoma with prostate specific antigen. J Urol 1992;147(3 Pt 2):841-5.
13. Stamey TA, Kabalin JN and Ferrori M. Prostate specific antigen in the diagnosis and treatment of adenocarcinoma of the prostate. J Urol 1989;141(5):1076-1083.
14. Barak M, Yoel M, Aharon L and Nachran G. Evaluation of prostate specific antigen as marker for adenocarcinoma of the prostate. J Lab Clin Med 1989;113 (5):598-603.
15. Partin AW, Carter BH, Chan DW, Jonathan Estein JI, Oesterling JE, Rock RC, Weber JP and Walch PC. Prostate specific antigen in the staging of localized prostate cancer: Influence of tumor differentiation, tumor volume and benign hyperplasia. J Urol 1990;143(4):747-52.
16. Wodrum DL, Brawer MK, Partin AW, Catalona WJ and Southwick PC. Interpretation of free prostate specific antigen clinical research studies for the detection of prostate cancer. J Urol 1998;159:5-12.
17. Elsberger B, Lankston L, McMillan DC, Underwood MA, Edwards J. Presence of tumoural C- reactive protein correlates with progressive prostate cancer. Prostate Cancer Prostatic Dis 2011;14:122–28.
18. McCall P, Catlow J, McArdle PA, McMillan DC, Edwards J. Tumoral C-reactive protein and nuclear factor kappa-B expression are associated with clinical outcome in patients with prostate cancer. Cancer Biomark 2011-2012;10:91–99.
19. Rosaria Alba Merendino1, Francesco Salvo2,Antonella Saija3, Giuseppe Di Pasquale4. Malondialdehyde in benign prostate hypertrophy: a useful marker?. Mediators of Inflammation 2003;12(2):127-28.
20. Turbidimetric immunoassay for ultrasensitive determination of C-reactive protein. Quantia CRP-US. Kit supplied by Tulip Diagnostics (P) Ltd, Verna, Goa, India.