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Effective PSA levels for taking prostate biopsy in the elderly – the Indian scenario

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Doi: 10.47750/pnr.2022.13.S05.339

Abstract

Background- As of now prostatic carcinoma (PCa) is the second leading site of cancer among males in almost all the major Indian cities and is among the top ten leading sites of cancer in the rest of India. The diagnosis of PCa is not direct. It passes through various stages from clinical suspicion to biopsy diagnosis. The clinical symptoms usually lead to further investigations in the form of digital rectal examination (DRE), estimations of serum prostate specific antigen (PSA) levels. These investigations, although contributory, are not diagnostic of PCa. There was a need to study as to what levels of PSA actually imply the need for biopsy. This information becomes more practically relevant in Indian scenarios where economic constraints are always present for detailed investigations of biopsy and further workup. This will also cut down the number of such unnecessary biopsies done yearly. Every consecutive trus guided biopsy sent for histopathological examination to rule out malignancy was studied for its outcome and was correlated with age and the PSA levels.

Methods-This is a retrospective study that includes all the consecutive TRUS-guided prostate biopsies sent to the department of pathology during a study period of one year. The inclusion criteria followed was that there was no previous diagnosis of PCa, suspicious cases on DRE, and or recorded PSA levels. The exclusion criteria followed was that the re-biopsy specimen, previously diagnosed cases of PCa, and biopsies which were not satisfactory for opinion. Following histopathological diagnosis, the data was studied for the association of age, PSA levels, and PCa, and results were tabulated.

Results and Conclusion- In the Indian scenario, PSA levels of 11-50 ng/dl and levels above 100 ng/dl were highly associated with PCa in patients aged 60 years and above. PSA levels between 51-99 ng/dl had the least incidence of PCa irrespective of age. Carefully categorizing high-risk patients will reduce the unnecessary prostatic biopsies done and thereby reduce the economic as well as mental stress the patient undergoes through these procedures.

Keywords- Prostate Carcinoma, PSA, Biopsy, Prostatitis

INTRODUCTION

The incidence of prostate cancer (PCa) was an estimated 396,100 new cases a year in 1990 which is expected to grow to 1.7 million new cases and 499000 new deaths by the year 2030. [1,2] This may be partly attributed to the aging global population. The prevalence of prostate cancer in India is no less compared to the western world. This may be attributed to the rapid migration of people from rural areas to urban areas, changing lifestyles and of course, increased awareness and easy access to medical facilities leading to an increase in the pickup of cases. As of now PCa is the second leading site of cancer among males in almost all the major Indian cities and is among the top ten leading sites of cancer in the rest of India. The data also shows that almost all the regions in the country are equally affected by PCa.[3]

The diagnosis of PCa is not direct. It passes through various stages from clinical suspicion to biopsy diagnosis. The clinical symptoms usually lead to further investigations in the form of digital rectal examination (DRE), estimations of serum PSA levels. These investigations, although contributory, are not diagnostic of PCa. Pretreatment levels of prostate-specific antigen (PSA), Gleason score (GS), and the clinical stage of the tumor (TS) are considered independent predictors of prostate cancer.[4] D'Amico et al proposed the first clinical classification system for PCa.[5] However, pretreatment PSA is included in all the risk stratification systems with PSA>20 ng/ml categorized as a high risk for PCa.[4,6-8]

PSA

PSA is a protein secreted by the prostate gland and was primarily used for screening for prostatic carcinoma. Globally the PSA levels vary widely. The Indian men are said to have lower age-specific levels of PSA as compared to their

counterparts in the western population.[9] However Indian men with lower urinary tract symptoms often tend to have raised PSA levels. [10]

We studied the association between age and PSA levels with the PCa in 87 consecutive trus guided prostate biopsies in our hospital.

MATERIALS AND METHODS

This is a retrospective study that includes all the consecutive TRUS-guided prostate biopsies sent to the department of pathology during a study period of three year after the institutional ethics committee clearance was taken.

The inclusion criteria followed was that there was no previous diagnosis of PCa, suspicious cases on DRE, and or recorded PSA levels. The exclusion criteria followed was that the re-biopsy specimen, previously diagnosed cases of PCa, and biopsies which were not satisfactory for opinion were not included in the study.

The prostatic biopsies were taken as per the standard protocol which included preoperative antibiotic therapy, anti-inflammatory suppositories, and appropriate anesthesia with the lidocaine gel before the procedure. Written consent was taken from the patient before the procedure. The biopsy was done using an endocavitary ultrasound probe with a 7.5MHz frequency and an 18-gauge needle with an automatic biopsy gun.

On receiving the specimen proper label verification of the patient details was done with the requisition form. The specimen was fixed in 10% formalin overnight. The clinical details such as the age, the volume of the prostate by ultrasound, PSA levels, and clinical suspicion were recorded. The gross measurements of the biopsy strands and numbers were noted. The average lengths of the strands were recorded. Following processing using the standard technique, the hematoxylin-eosin-stained histopathology sections were assessed by a team of senior pathologists.

The cases were categorized into the following categories: 1) inflammatory lesions 2) hyperplasia 3) hyperplasia associated with additional changes 4) PIN 5) malignancy. The data was studied for the association of age, PSA levels, and PCa, and results were tabulated.

RESULTS

A total of 87 consecutive cases of trus guided biopsies of the prostate were included in the study for three years. Of the total cases, about 52% of the cases belonged to the age group of 71-80 years. Next in frequency was the age group of 61-70 years which comprised about 38%. The remaining age groups had very low incidences for undergoing prostatic biopsies in our study population (Fig 1).

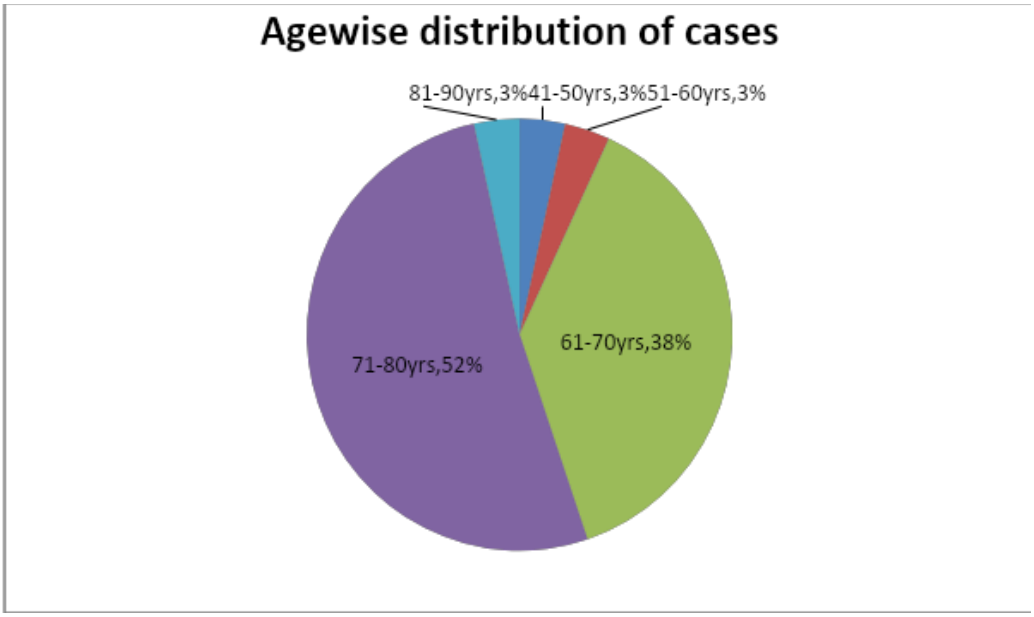

Figure 1- Age-wise distribution of cases

Age-wise distribution of the PSA levels of all the cases included in the study

We segregated the cases according to their age groups and PSA levels. The cases were divided into four groups according to the PSA levels recorded. The distribution is shown in figure 2.

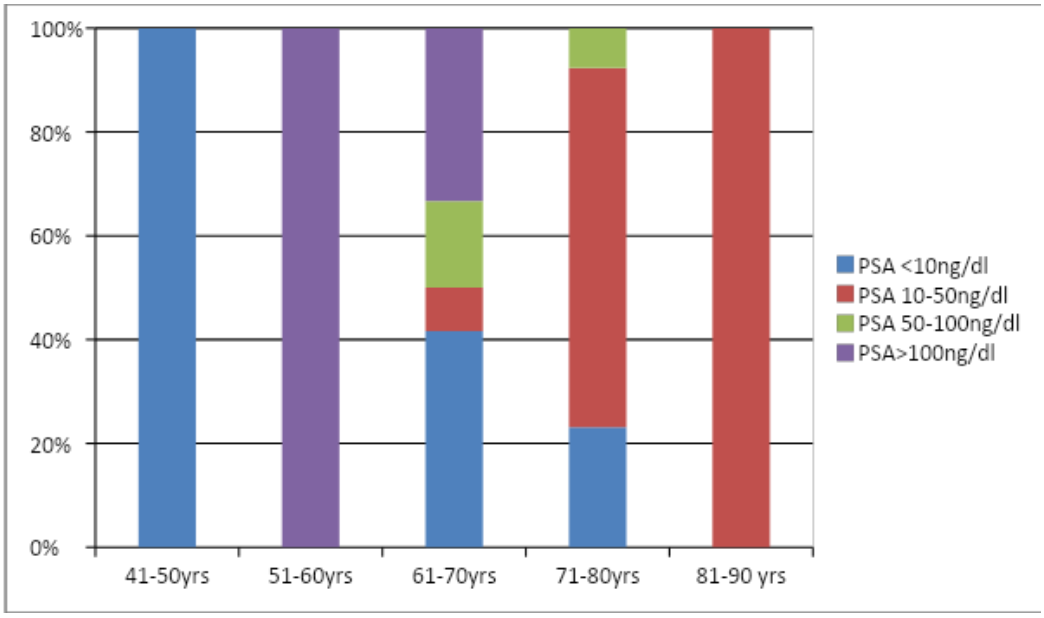

Figure 2-Age Wise distribution of PSA levels in the studied cases.

PSA levels were low in the 41-50yr age group. In older age groups (51-80yr) the levels showed marked variation.
We found that the age groups with the highest variability of PSA levels were the same as the ones with the highest incidence of prostatic biopsies. The least value of PSA was recorded to be 4ng/dl in the 78 yr old patient which turned out to be benign prostatic tissue. The highest recorded value was 920ng/dl in a 65 yr old patient which was diagnosed with carcinoma.

The spectrum of diagnosis of the trup biopsies

Following processing, the histopathology sections were assessed by a team of senior pathologists. Based on strict morphological features and IHC (wherever needed) the cases were grouped into the following categories:

1) Inflammatory lesions
2) Hyperplasia
3) Hyperplasia associated with additional changes
4) PIN
5) Malignancy

Following diagnosis and necessary workup, we found that the malignancy (PCa) comprised the most common condition. Prostatic intraepithelial lesion (PIN) comprised 10% of the lesions. Two cases in which the diagnosis was dicy, IHC was done with basal cell markers. The results of IHC were positive and the cases were diagnosed as hyperplastic lesions.So, combined the PCa and PIN comprised more than half of the total cases. The detailed numbers of all lesions are given in figure 3 and table 1.

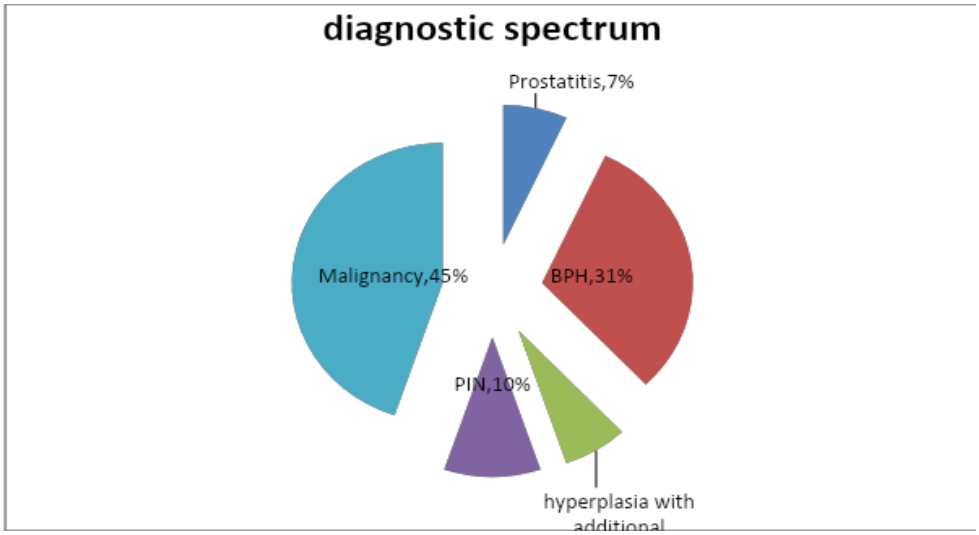

Figure 3- diagnostic spectrum of the cases.

Age group	Inflammatory	Hyperplasia	Hyperplasia with additional features	PIN	malignancy
41-50		3			
51-60				3	
61-70	6	12			18
71-80		12	6	6	18
81-90					3
Total (%)	6(7)	27(31)	6(7)	9(10)	39(45)

Table 1- Age-wise distribution of cases.

Almost all the cases of malignancy were between the age group of 61-80 years. So also, were the cases of hyperplasia. Thus, age alone remains an unimportant criterion for suspicion of malignancy of prostate.

Diagnostic Spectrum of cases and the corresponding PSA levels

On analyzing the data after the diagnosis, we found that the PSA levels were lowest (Category PSA < 10ng/dl) for the benign lesions. Although higher PSA levels were indicative of malignancy, PSA levels between 10-50 ng/dl had the highest incidence of PCa in the study population followed by PSA levels above 100 ng/dl. A detailed comparison is presented in table 2.

PSA levels(ng/dl)	Inflammatory	Hyperplasia	BPH with associated findings	PIN	PCa
<10	3	21	0	3	0
10-50	3	6	6	3	18
50-100	0	3	0	0	6
>100	0	0	0	0	15

Table 2-Diagnostic spectrum and the corresponding PSA levels

DISCUSSION

The diseases of prostate contribute to significant morbidity and mortality withPCa is the second common malignancy amongst men. TRUS guided biopsy of the prostate is the most common and reliable method to sample prostate in suspicious PCa patients. DRE and PSA are the clinical methods that hint at the PCa as the probable diagnosis. PSA is the most common marker for screening for PCa. Marked variations in the PSA readings is noted owing to its elevation in cases of chronic prostatitis. Though widely accepted as a consistent marker and for screening for PCa, there was a need to study as to what levels of PSA actually imply the need for biopsy. This information becomes more practically relevant in Indian scenarios where economic constraints are always present for detailed investigations of biopsy and further workup. This will also cut down the number of such unnecessary biopsies done yearly. Every consecutive trus guided biopsy sent for histopathological examination to rule out malignancy was studied for its outcome and was correlated with age and the PSA levels

Age-wise distribution of cases: The age at diagnosis for prostate cancer is said to be elderly. The mean age at diagnosis is 67.5-75 yrs and is reported to be declining in recent years.[11,12] The reason for the decline in the mean age has been attributed to the increased number of biopsies in younger patients and a reduced number of biopsies being done on elderly men.[12] The mean age for PCa in our study was 70 yrs. Agarwal et al found the mean age of the cases to be 61 yrs.[13]On studying the age-wise distribution of the cases, we found that the mean age range for both the conditions benign and malignancy was the same i.e. 61-80 years. OlivérÁrpád Vida et al.in their study was also of the same opinion.[14] We found that the age of the patient alone does not imply any probability of being diagnosed with PCa.

The number of linear bits of biopsy received: The biopsy was received as multiple linear bits, the number of which ranged from four to eight. There was no consensus about the number of bits as was also found in the literature.[14]

PSA levels and the associated prostate biopsies: The indications for trus guided prostatic biopsies have been the strong suspicion of malignancy based on elevated PSA levels. PSA is the most widely used cancer serum marker for prostate in today's world.[15] It is said that the mortality associated with prostatic carcinoma has decreased along with metastasis rate with the increased screening with PSA and associated increased number of needle core biopsies. There are studies like the European Randomized Study of Screening for Prostate Cancer (ERSPC) which have demonstrated a 21% reduction in mortality due to PCa in favor of the screening programs.[16] However, data suggests that there are no mortality benefits from screening for PCa.[17] This is true for Asian countries like India where there are more financial hurdles to such screening programs.

Also, it is reported that the PSA levels for the Asian population are lower than those for western counterparts.[18]It is to be noted that age-specific cut-off values have been established for various Asian populations.[19]The detailed study of these cut-offs shows that the cut-offs are higher for the Asian populations than their western counterparts.[20]

On studying the PSA values in the different age groups, we found that the values were less than 10 ng/dl in the younger population (41-50yrs) and were benign. Marked variation in the levels was noted in the age group 61-70 years.

PSA AND PCA

We found that PSA levels less than 10 ng/dl were associated with benign conditions irrespective of age. PSA levels 11-50 ng/dl were associated with PCa in the age group of 60 years and above.
PSA levels 50-100 ng/dl had a minimum incidence of PCa irrespective of age. PSA above 100ng/dl were all associated with PCa irrespective of age.

LIMITATIONS OF THE STUDY

Long duration studies can be done to further confirm the association between PCa, PSA levels, and age of the patient.

CONCLUSION

In the Indian scenario, PSA levels of 11-50 ng/dl and levels above 100 ng/dl were highly associated with PCa in patients aged 60 years and above. PSA levels between 51-99 ng/dl had the least incidence of PCa irrespective of age.

Source of funding mentioned- Nil

Conflicts of interest disclosed-Nil

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