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General Surgery

TRIPLE PRONGED APPROACH TO DETECT EARLY PROSTATE CANCER IN GREY ZONE OF PSA 4-10 NGMS/ML

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ABSTRACT

INTRODUCTION Early detection of cancer is an important issue in the field of oncology. The prostate gland is no exception to this rule. The routine screening of the vulnerable elderly male population with the three-pronged approach: Digital rectal examination, Transrectal ultrasound and estimation of Prostate specific Antigen(PSA) in serum has led to marked increase in the frequency of prostatic biopsies. This surveillance has given rise to detection of many patients with small sized cancers, considered ideal for radical prostatectomy and favourable prognosis of disease.

AIM The study was undertaken to correlate the patients with PSA level 4 to 10 ngms/ml with Carcinoma Prostate and prostate volume by Ultrasonography.

MATERIALS AND METHODS A total of 30 patients with lower urinary tract symptoms were studied and all of them were subjected to digital rectal examination, serum prostate specific antigen and ultrasonography guided biopsy at tertiary care hospital during the study period of 18 months .

RESULTS In the study population of 30 patients with PSA level 4-10ngms/ml. CA prostate accounted for 4 out of 30 cases.13.3% of total cases are diagnosed as CA prostate

CONCLUSION Confronting patients, distressed and annoyed with symptoms of prostatism, has led clinicians to diagnose precursor lesion earlier in life. Triple assessment increases the detection rate of early prostate cancer. Prostatic Intraepitelial Neoplasia (PIN) is considered the most likely precursor of clinically significant prostate cancer. Possibility of cure is highest at the stage of PIN

KEYWORDS : Prostate Specific Antigen, Prostate cancer, Prostatic Intraepithelial Neoplasia.

INTRODUCTION

Prostate cancer is the second most common cause of cancer death in men in the western world. Its medical and social impact is comparable to that of breast cancer in women. Although it is well recognized that early treatment is a possibility for reducing the high incidence of death from prostate cancer, routine screening and even early treatment in suspected cases remains a controversial issue. It is estimated that a newborn male has a 10% chance of developing prostate cancer and a 3% chance of dying from it on the other hand. Prostate cancer is the fourth most common cancer in men with incidence and mortality rates that vary markedly among and within different countries. since the introduction of prostate specific antigen (PSA), the incidence of local regional disease has increased, whereas the incidence of metastatic disease has decreased PSA is the single test with highest positive predictive value for cancer. Most of them are confirmed by biopsy. The risk of Carcinoma (CA) prostate is directly related to PSA level. Approximate chance of cancer on biopsy is 1 in 4 for PSA level 4to 10ngms/ml. [1] The majority of men with PSA elevation (80%) have serum levels in the range of 4 to 10 nanograms/millilitre (ngms/ml). The present cancer detection rate in the initial biopsy was 52%.[2] Unlike some screening tests e.g; mammography. Screening by PSA simply requires a blood sample, which can readily be taken in general practice and is then analyzed in a biochemistry laboratory. [3] Serum PSA elevation is often the first sign of prostate pathology.

The positive predictive value (PPV) of PSA for prostate cancer detection using transrectal ultrasound (TRUS)-guided biopsy or radical retropubic prostatectomy is estimated to be 30-42% in patients with gray-zone PSA levels [4,5,6]. The availability of modalities like prostate biopsy, ultrasonography (USG) and increased number of patients with lower urinary tract symptoms (LUTS) attending our urologic out patient department made me to take up this study.

OBJECTIVES OF THE STUDY

- To study the clinical presentation of patients with carcinoma prostate
- Confirmation of carcinoma prostate with PSA level 4.0 to 10.0ngms/ml by Biopsy
- Correlation of carcinoma prostate with PSA level 4.0 to 10.0ngms/ml with prostate volume by Ultrasonography.

MATERIALS AND METHODS

The present study is a descriptive hospital-based study done in department of urology in collaboration with department of general surgery, radiodiagnosis and pathology at tertiary care hospital for a period of 18months.

METHOD OF COLLECTION OF DATA

The source of our study includes patients admitted in department of urology and also patients referred from other departments with LUTS. serum PSA level, Ultrasonography and Biopsy of the prostate were considered in detecting prostate cancer in present study.

INCLUSION CRITERIA- Patients with lower urinary tract symptoms with PSA level 4-10gms/ml, Patients with Abnormal DRE, Age more than 40 yrs.

EXCLUSION CRITERIA- Post radical prostatectomy patients, Post biopsy patients within 4weeks of procedure, Diagnosed prostate cancer from Transurethral Resection of prostate (TURP) chips and advanced prostate cancer patients.

Patients with raised/raising PSA level were counselled about the probability of detecting prostate cancer by biopsy. Written/informed consent was obtained in local vernacular in each patient included in our study. Routine investigations including Hb gms%, Complete blood count, Urine analysis, Blood urea and serum creatinine, ECG, chest x-ray. Specific investigations including Serum PSA level, USG, Biopsy and Histopathological examination are done. Symptom's assessment tool for patients suffering from prostatism. The components for basic diagnostic workup were- History, physical exam and DRE or other evaluation to rule out prostate cancer.

The International Prostate Symptom Score (I-PSS) is based on the answers to seven questions concerning urinary symptoms and one question concerning quality of life. Each question concerning urinary symptoms allows the patient to choose one out of six answers indicating increasing severity of the particular symptom. The answers are assigned points from 0 to 5. The total score can therefore range from 0 to 35 (asymptomatic to very symptomatic).

The questions refer to the following urinary symptoms: Incomplete emptying, Frequency, Intermittency, Urgency, Weak Stream, Straining, Nocturia, Question eight refers to the patient's perceived quality of life. Mild (symptom score less than or equal to 7), Moderate (symptom score range 8-19), Severe (symptom score range 20-35)

We use a range of tests to diagnose prostate cancer; common procedures include:

Digital rectal examination (DRE)- This is a quick and safe procedure during which a doctor or nurse inserts a lubricated, gloved finger into the rectum and feels for abnormal lumps or hard irregular areas, through the wall of patient's rectum. The prostate gland should feel soft, smooth and even.

Prostate-specific antigen (PSA) test- A simple, painless test that measures the levels of PSA in a blood sample. PSA is a substance produced by the prostate that is present in higher-than-normal levels in the blood of men with prostate cancer. Normal PSA levels are between 0 and 4 ngs/mL. PSA often rises as part of the natural ageing process and an increase in PSA does not necessarily indicate that prostate cancer is present. High PSA levels may also be found in men who have infection or inflammation of the prostate (prostatitis), or who have a non-cancerous condition called BPH (benign prostatic hyperplasia). If PSA levels are high, we recommend the patients to have a transrectal ultrasound, to rule out prostate cancer.

Transrectal ultrasound- A painless procedure in which an instrument is inserted into the rectum and sound waves bounce off the prostate, producing a picture of the prostate which can be used to help identify abnormal areas requiring a biopsy. If the results of the transrectal ultrasound are normal, you may be able to wait and repeat the PSA test a few months later and then have a biopsy if needed.

Biopsy- In this procedure a sample of cells, tissue or fluid is removed from the prostate and viewed under a microscope, to check for signs of the disease.

There are two types of biopsies - Transrectal biopsy: a needle is inserted through the rectum into the prostate and a sample of prostate tissue is removed.

Transperineal biopsy: a needle is inserted through the skin between the scrotum and rectum into the prostate and a sample of prostate tissue is removed. Both biopsy procedures are short and patient can usually go home the same day. A biopsy is the only way to confirm or diagnose the presence of prostate cancer. If patient is diagnosed to have prostate cancer, we want to carry out some further tests to find out if the cancer has spread to other parts of body.

Sextant biopsy- Six directed biopsies in different areas of the prostate, usually under ultrasound guidance. The core biopsies provide more information about the size and location of the tumor than a single biopsy could. Cores are taken from the right and left sides of the prostate near the apex, near the base, and from the central portion of the prostate.

OBSERVATION AND RESULTS-

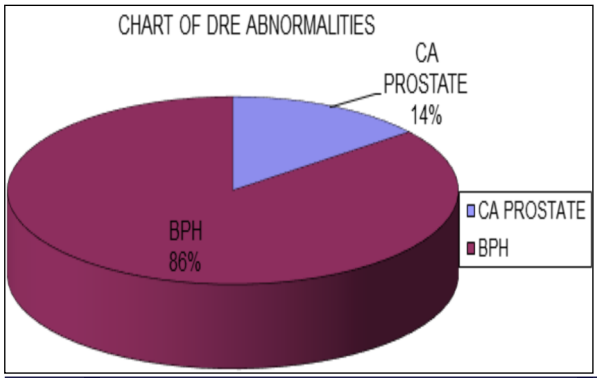
In the present study, obliteration of median groove, hardness with nodularity emerged as the most effective predictor of prostate cancer on digital rectal examination (DRE). Mobility restriction and rectal mucosal involvement were seen in few cases. In Prostate Intraepithileal Neoplasia (PIN), firm prostate was the predominant finding. In carcinoma of prostate USG showed prostate was hypoechoic and varying echogenicity.

Proportion of cases- 30 Patients with PSA level 4-10ngms/ml were included in the study. CA prostate accounted for 4 out of 30 cases.13.3% of total cases are diagnosed as CA prostate. 1 case was PIN, 3 were high grade adenocarcinoma prostate. 26 cases were BPH. Patients with PSA level 4-10ngms/ml with LUTS proven to be CA Prostate in present study were aged more than 60yrs.

Digital rectal examination- The abnormality on DRE was a significant finding in the study group.14 cases presented with abnormality on DRE, 2 Cases proved to be CA prostate,12 were BPH. All presented with lower urinary tract symptoms

Abnormalities on DRE include a discrete nodule, focal induration, a diffusely hard prostate and, in some cases, asymmetry as depicted in **Table 1**.

Table 1.



symptoms at presentation- Patients presented with symptoms of Prostatism like obstructive symptoms & irritative symptoms. One patient had history of hematuria. Observations are as depicted in **Table 2** and **Table 3.**

Table 2

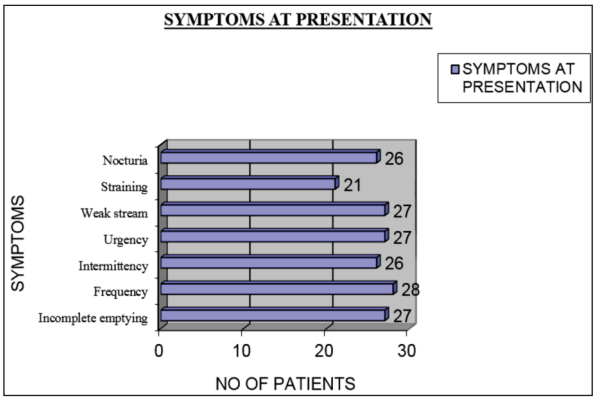
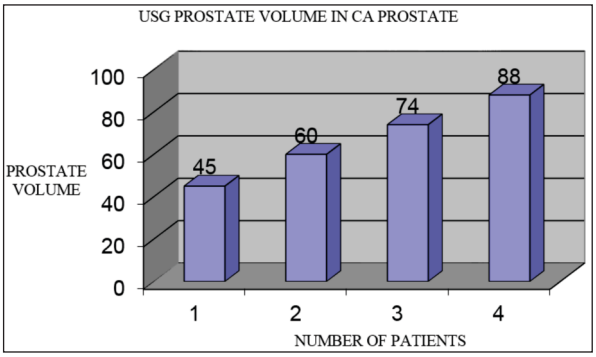


Table 3.

Sl.no	Symptom score	No of patients	% of patients
1	Mild(1-7)	3	10
2	Moderate(8-19)	17	57
3	Severe(20-35)	10	33

prostate volume by ultrasonography- Prostate volume is measured by either transabdominal or transrectal USG in patients with LUTS with PSA level4-10ngms/ml. Cases proven to be CA Prostate has the following prostate volume as in **Table 4**.

Table 4.



prostate biopsy- Patients underwent prostatic biopsy for the diagnosis. Histopathological examination of the prostatic tissue obtained by Transrectal/ Transperineal/ TURP procedure gave diagnosis of CA prostate or BPH.

DISCUSSION

CA prostate accounted for 4 out of 30 cases.13.3% of total cases are diagnosed as CA prostate. 1 case was PIN, 3 were high grade adenocarcinoma prostate. 26 cases were BPH. Kesarwani.RC et al in his study at M. L. N. Medical College and Associated SRN Hospital, Allahabad. [7] A total of 70 patients with symptoms of prostate enlargement were studied and all of them were subjected to digital rectal examination, serum prostate specific antigen, serum acid phosphatase and Ultrasonography. Prostatic tissue. It was found that 50 cases (71.4 %) were of BPH, 15 (21.4 %) were Prostatic carcinoma and the remaining 5 (7.1%) cases were PIN.

Digital rectal examination- The abnormality on DRE was a significant finding in the study population.14 cases presented with abnormality on DRE.2 Cases proved to be CA prostate,12 were BPH. All presented with lower urinary tract symptoms. Abnormalities on DRE include a discrete nodule, focal induration, a diffusely hard prostate and, in some cases, asymmetry. Lefevre et al in his study, one of the largest studies reported to date was supported by Hybritech, Inc., the manufacturer of one of the leading PSA assays. The study reported the results of screening with both PSA and digital rectal examination in 17,157 white men and 804 black men. [8] Partin et al observed that DRE tends to understage the disease. [9] Patients presented with symptoms of Prostatism like obstructive symptoms & irritative symptoms.

prostate volume by ultrasonography- Prostate volume is measured by either transabdominal or transrectal USG in patients with LUTS with PSA level4-10ngms/ml. In the study group, CA prostate patients USG showed prostate as hypoechoic and with varying echogenecity. Similarly, PIN was hypoechoic. Kesarwani.RC et al in his study, in carcinoma of prostate, on USG, prostate was hypoechoic (53.3%), Isoechoic (13.1%) and with varying echogenecity in the rest of 33.3% cases. Similarly, PIN was hypoechoic in 60% and isoechoic in the remaining 40% cases. In the study by Ronnett. [10] Hypoechoic prostate on USG was the feature suggestive of carcinoma prostate and PIN, consistent with Lee et al (1986). [11] The finding of isoechoic cancer was around 30-40% in recent American studies.

prostate biopsy- Patients underwent prostatic biopsy for the diagnosis. Histopathological examination of the prostatic tissue obtained by Transrectal/ Transperineal/ TURP procedure gave Diagnosis of Ca prostate or BPH. Histopathological examination of transrectal tru-cut needle biopsy, TURP or enucleated specimens of prostate were made and classified histologically as benign lesions, viz. BPH with or without prostatitis and atypical adenomatous hyperplasia. Premalignant lesions (PIN) were distributed according to McNeal (1986) and carcinoma prostate was graded according to Gleasons (1977) microscopic grading system. Slides were reviewed for area of atypical hyperplasia and foci of PIN. Slides of each suspected block were prepared from different planes for haematoxylin and eosin staining Volume of Cancer in Needle Biopsy Specimen- This assessment may be useful to differentiate organ-confined cancer from one, which has extended beyond the prostate. There are four different ways of assessing the volume of cancer: (1) percentage of biopsy cores involved; (2) percentage of cancer area in each biopsy specimen; (3) millimeters of adenocarcinoma in the entire biopsy; (4) millimeters of adenocarcinoma per core. The most commonly used method is to calculate the percentage of cancer area in all biopsy fragments. Negative Biopsy In Suspected Case of Prostatic Carcinoma. USG guided sextant biopsy is now a standard procedure in patients suspected to harbor prostatic cancer. However, the clinician is often faced with a problem of negative needle biopsy in patients having persistent elevated PSA or abnormal rectal digital examination. Indications for Repeat Biopsies are Presence of high grade PIN, Small atypical acinar proliferation suspicious but not diagnostic of cancer, persistent PSA elevation and abnormal findings on rectal examination or TRUS. The interval at which a biopsy should be repeated may be debatable but studies have recommended an interval of 3 months following the first biopsy. [12] Official clinical guideline of the The American Academy of Family Physicians recommends counseling men between the ages of 50 and 65 about the known risks and uncertain benefits of screening for prostate cancer. This certainly seems a prudent course to follow. Men deserve sufficient information to allow them to make an informed, personal decision. [13]

CONCLUSION

The purpose of the study is to identify disease in patients with LUTS at a stage where treatment will alter the natural history of the condition. All cases of CA prostate are aged more than 60 yrs. DRE Abnormalities is a significant finding, Prostate volume by ultrasonography in CA Prostate patients is highly variable. No significant cut off value of USG prostate volume in CA Prostate patients was able to establish based on present study. The stage shift in prostate cancers detected by screening is at least in part due to the bias toward detection of biologically indolent tumors, which are associated with a good prognosis, rather than detection of aggressive tumors with a poor prognosis, which generally are detected after the onset of symptoms. The next principle of screening is that a cost-effective, acceptable screening test with reasonable sensitivity and specificity must exist to allow detection in the asymptomatic phase. PSA screening does reasonably well in fulfilling this standard, although the percentage of cases detected (sensitivity) by PSA screening is not as high as one might expect. The use of triple assessment- Digital Rectal Examination, Ultrasound-guided biopsy and serum prostate specific antigen testing was found to be a better approach to detect prostate cancer early. The treatment is better and prognosis is good.

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Conflict of Interest: The authors declare they have no conflict of interest

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