



## ROLE OF TRANSRECTAL ULTRASOUND GUIDED BIOPSY IN PATIENTS WITH RAISED SERUM PROSTATE SPECIFIC ANTIGEN LEVELS WITH HISTOPATHOLOGICAL CORRELATION: A PROSPECTIVE STUDY IN A TERTIARY CARE CENTRE

### Radio-Diagnosis

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### ABSTRACT

**Background:** The prostate cancer is one of the commonest malignancies in men. Serum prostate specific antigen (PSA) testing and prostatic biopsy are performed routinely whenever carcinoma of prostate is suspected. The present study was undertaken to evaluate the role of Transrectal Ultrasound (TRUS) guided biopsy in patients with raised serum PSA levels with histopathological correlation. **Method:** This prospective study was conducted on total 85 male patients attending urology/nephrology OPD with urinary symptoms and a serum PSA >4ng/ml during a period of 24 months from August 2020 to August 2022. TRUS guided biopsy was performed using 12-core biopsy technique and samples were sent to the department of pathology for histopathological evaluation. **Results:** Most of the patients (76.5%) had voiding difficulties as lower urinary tract symptom. Maximum patients (58%) had focal lesion in prostate visualized on TRUS, of which 50% of lesions were hypoechoic in appearance. 46% had focal lesion in the peripheral zone of prostate, out of those lesions 54% had well defined margins. 56% of patients had hypo vascular lesions in prostate. 68% of patients had BPH and 32% patients had prostatic malignancy. Most of the patients (42.4%) had Grade 2 Prostatomegaly on DRE and 49.4% had serum PSA >50ng. However, 49.4% of patients had prostate volume between 31 to 50cc. The positive correlation was found between histopathological result Gleason's Score vs Serum PSA (ng/ml). PSA was more in adenocarcinoma compared to BPH. **Conclusion:** Thus, TRUS guided biopsy is effective, cheap, and safe method of prostate biopsy. It aids in correlating ultrasound imaging finding in benign and malignant conditions of prostate with serum PSA and histopathological findings.

### KEYWORDS

Prostate cancer; Prostate specific antigen; Transrectal Ultrasound; Histopathology; Hypoechoic; Prostatomegaly; Gleason's Score

### INTRODUCTION

Prostate cancer is the second most common cause of cancer-related deaths among men in the United States. In India, prostate cancer affects 4-5 men per 100,000 population [1]. It is a major healthcare concern as it causes significant morbidity and mortality. Although it is a common disease, it is slow to manifest clinical signs. It is estimated that 36.4% of men older than 45 years harbour latent prostate cancer. In many of these men it remains latent until death. However, it is further estimated that approximately 1% of latent disease is clinically diagnosed each year [2].

The management of prostate cancer is a complex issue because of the difficulty in accurate staging and in predicting the speed of disease progression [3]. There are multiple options for treatment including watchful waiting, hormonal treatment, radical prostatectomy (open, laparoscopic, or robotic), various forms of radiation therapy (conformal or intensity-modulated external beam and permanent interstitial or high-dose-rate brachytherapy), or combined approaches [4, 5].

As location of prostate is not favourable for direct examination, digital rectal examination and prostate specific antigen (PSA) levels were used historically to evaluate prostate cancer. This method of examination was inadequate. Introduction of ultrasound has provided a new means to evaluate prostate. A biopsy of prostate is required for confirming the diagnosis of prostate cancer in patients who have elevated levels of prostate specific antigen and abnormal findings on digital rectal examination (DRE) [6].

Currently Transrectal ultrasonography (TRUS) is the most commonly used modality of choice for imaging the prostate gland. However, before PSA testing and TRUS became widely available, most patients presented with cancer-specific symptoms owing to locally advanced disease and the cancers were diagnosed by DRE, so that the majority were diagnosed at stage T2 or more. Nowadays, most cases (>90%) are diagnosed at an asymptomatic early stage (stage T1) because the advent of widespread PSA testing and TRUS-guided biopsy has enabled early diagnosis, with nearly half of all newly diagnosed patients falling into the "favourable risk" group [7]. The TRUS-guided systematic prostate biopsy is the gold standard for diagnosis of prostate cancer. Hence the present study was undertaken to evaluate the role of Transrectal Ultrasound (TRUS) guided biopsy in patients with raised serum PSA levels with histopathological correlation.

### MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from all the patients, this prospective study was carried out in the Department of Radio diagnosis at Tertiary care centre in India during a period of 24 months from August 2020 to August 2022. Total 83 male patients of age more than 50 years attending urology OPD/ nephrology OPD with or without urinary symptoms, asymptomatic/symptomatic patients with raised serum PSA values (>4 ng/ml), with palpable mass on DRE, USG suggestive of diffusely heterogeneous appearance or suspicious prostatic lesion, excessive PSV of prostatic vessels on prostatic doppler were included in the study. While patients with bleeding diathesis, histologically proven cases of carcinoma prostate, patients on aspirin >75mg, patients with uncontrolled diabetes mellitus, uncooperative patient, patients with local painful pathologies like anal fissures/rectal fistulas and repeat biopsies were excluded from this study.

Prior to the day of biopsy, complete clinical history, clinical evaluation, necessary routine investigations and proper preparation of the patient was done. Patient was then taken up for TRUS guided prostate biopsy. The patient was positioned in a left lateral decubitus position. Local application of lignocaine jelly was used as the method of anesthesia. Prophylactic use of oral antibiotic (ciprofloxacin) started 3 days prior and 2 days after the procedure. A 12-core biopsy was performed under TRUS guidance. Patient was asked to watch out for per rectal/perineural bleed post procedure.

### Statistical Analysis

The data were analysed by using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. Z-test (Standard Normal Deviate) was used to test the significant difference of proportions. Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test. Once a t value is determined, a p-value can be found using a table of values from Student's t-distribution.

If the calculated p-value is below the threshold chosen for the statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis. p-value  $\leq 0.05$  was considered for statistically significant.

OBSERVATIONS AND RESULTS

Out of 85 patients most of the patients (52.9%) were 61-70 years old as shown in table 1. This was statistically significant, and the mean age of patients was 68.94 $\pm$ 9.85 years.

Table 1: Distribution Of Patients According To Age

| Age group in years | No. of patients | Percentage |
|--------------------|-----------------|------------|
| 41 to 50           | 06              | 7.1        |
| 51 to 60           | 05              | 5.9        |
| 61 to 70           | 45              | 52.9       |
| 71 to 80           | 20              | 23.5       |
| $\geq 81$          | 09              | 10.6       |
| Total              | 85              | 100.0      |

Most of the patients (65; 76.5%) had voiding difficulties and 20 (23.5%) patients had dysuria as the lower urinary tract symptom. Majority of the patients (58%) had focal lesion in prostate visualized on TRUS and that in significantly higher number of patients (50%) the lesions were hypoechoic in appearance. Most of the patients (46%) had focal lesion in the Peripheral zone of prostate which was statistically significant and out of those lesions' majority (54%) had well defined margins as shown in table 2.

Table 2: Distribution Of Focal Lesion On TRUS And TRUS Findings

| Parameters             |                                   | No. of patients | Percent age |
|------------------------|-----------------------------------|-----------------|-------------|
| Focal Lesion on TRUS   | Yes                               | 35              | 41.2        |
|                        | No                                | 50              | 58.8        |
| Appearance on TRUS     | Heterogeneous                     | 12              | 24.0        |
|                        | Hyperechoic                       | 13              | 26.0        |
|                        | Hypoechoic                        | 25              | 50.0        |
| Zone of focal lesion   | Focal lesion in Peripheral zone   | 23              | 46.0        |
|                        | Focal lesion in Transitional zone | 20              | 40.0        |
|                        | Focal lesion in Central zone      | 07              | 14.0        |
| Margin of focal lesion | Ill Defined                       | 23              | 46.0        |
|                        | Well Defined                      | 27              | 54.0        |

A greater number of patients (28; 56%) had hypo vascular lesions in prostate and 22 (44%) had hyper vascular lesion. Majority of the patients had BPH (68%), and 32% patients had prostatic malignancy, (Figure 1).

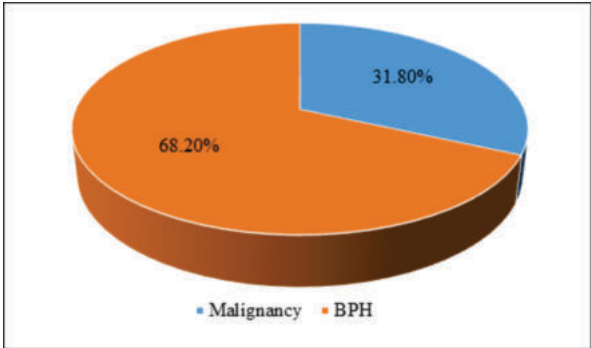


Figure 1: Distribution of histopathological result

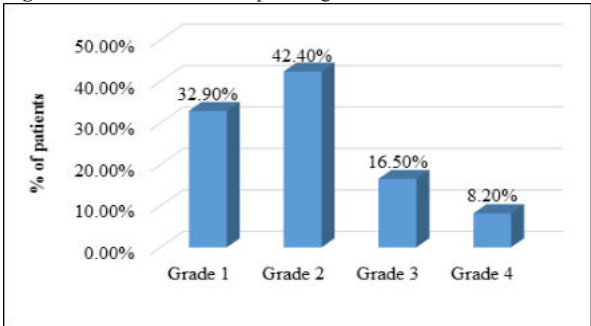


Figure 2: Distribution of Grade of Prostatomegaly on DRE

1 (1.2%) patient had post procedure per rectal bleed and another 1 (1.2%) patient had post procedure infection. We found that, most of the patients (42.4%) had Grade 2 Prostatomegaly on DRE as depicted in figure 2.

A higher number of patients (49.4%) had serum PSA  $> 50$  ng. It was statistically significant. Also, a greater number of patients (49.4%) had prostate volume between 31 to 50 cc. It was statistically significant as shown in table 3.

Figure 3: Distribution Of SERUM PSA Group Ng Ml And Volume Of Prostate (in cc)

| Parameters                 |                  | No. of patients | Percentage |
|----------------------------|------------------|-----------------|------------|
| SERUM PSA group (ng/ml)    | PSA 1 (4 to 10)  | 11              | 12.9       |
|                            | PSA 2 (11 to 20) | 08              | 9.4        |
|                            | PSA 3 (21 to 30) | 06              | 7.1        |
|                            | PSA 4 (31 to 40) | 07              | 8.2        |
|                            | PSA 5 (41 to 50) | 11              | 12.9       |
|                            | PSA 6 ( $> 50$ ) | 42              | 49.4       |
| Volume of Prostate (in CC) | 21 to 30         | 12              | 14.1       |
|                            | 31 to 50         | 42              | 49.4       |
|                            | 51 to 80         | 26              | 30.6       |
|                            | $> 80$           | 05              | 5.9        |

The value of Pearson Correlation Coefficient (r) was .509\*\*. The Positive correlation was found between Gleason's Score vs Serum PSA (ng/ml). The P-Value was  $< 0.0001$ . The result was statistically significant.

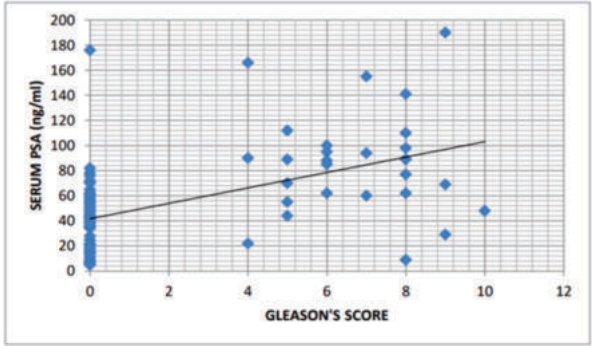


Figure 3: Correlation of Serum PSA (ng/ml) with Gleason's Score

Positive correlation was found between histopathological result Vs Serum PSA (ng/ml). It was statistically significant as shown in table 3.

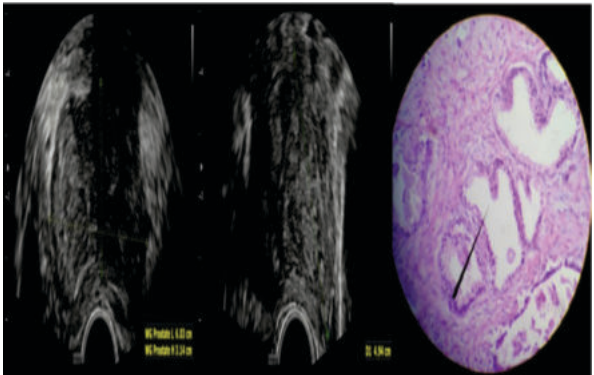
Table 4: Correlation Of Mean Serum PSA (ng ml) And Histopathological Result

| Histopathological Result | Serum PSA (ng ml) |           |        | P value    |
|--------------------------|-------------------|-----------|--------|------------|
|                          | Mean $\pm$ SD     | Range     | Median |            |
| Malignancy (n=27)        | 85.51 $\pm$ 42.36 | 9.0-190.0 | 88.0   | $< 0.0001$ |
| BPH (n=58)               | 40.37 $\pm$ 28.90 | 5.0-176.0 | 41.0   |            |

REPRESENTATIVE CASES

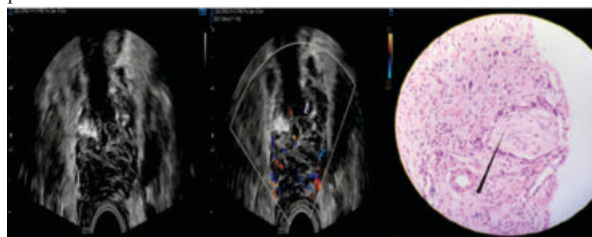
CASE 1: Benign hyperplasia of prostate

On TRUS, prostate measures approximately 45 cc with a small hyperechoic suspicious lesion in the left lobe of prostate with PSA measuring 12 ng. On the histopathology, it was diagnosed as Benign hyperplasia of prostate.



### Case 2: Adenocarcinoma of prostate

On TRUS, prostate measures approximately 55cc with a diffuse heterogeneous echotexture with PSA measuring 76ng. On the histopathology, it was diagnosed as Adenocarcinoma of prostate with perineural invasion and Gleason score of 4+4=8.



### DISCUSSION

The incidence of carcinoma of prostate in Indian population is less as compared to the Western population. However, this malignancy is being increasingly detected in India especially in the urban population [8]. In the present study 85 cases of prostatomegaly who underwent TRUS guided biopsies were studied, and their serum PSA levels were correlated with the histopathology reports. Out of 85 patients most of the patients were between 61-70 years of age [45 (52.9%)] which was statistically significant ( $p < .00001$ ), ( $z = 6.733$ ) which is comparable with the previous studies [9, 10]. Maximum patients had voiding difficulties in lower urinary tract symptoms [65 (76.5%)]. It was statistically significant ( $p < .00001$ ), ( $z = 6.9027$ ). This is concordant with the study done by McAninch JW [11].

The majority of the patients had focal lesion on TRUS [50 (58.8%)] which was statistically significant ( $p = .02144$ ), ( $z = 2.3009$ ). A significantly higher number of patients had hypoechoic lesion [25 (50.0%)], ( $p = .00714$ ), ( $z = 2.6926$ ). Approximately 26% of the patients had hyperechoic lesions. These findings are in accordance with the study conducted by Reddy V et al [12] and Ndiaye M et al [13]. Most of the patients had lesion in peripheral zone [23 (46.0%)] which was statistically significant ( $p = .00128$ ), ( $z = 3.219$ ). The lesions in the peripheral zone were predominantly found to be benign. Most of the patients had well defined margin [27 (54.0%)] which was not statistically significant ( $p = .42372$ ), ( $z = 0.8$ ). Similar findings are reported in study conducted by Lee HY et al [14]. However, a greater number of patients had hypovascular lesion [28 (56.0%)] but it was not statistically significant ( $p = .23014$ ), ( $z = 1.2$ ) which is comparable with the other studies done by Sauvain JL et al [15] and Sen J et al [16].

Out of 85, 11 (12.9%) patients had PSA between 4 to 10ng, 8 (9.4%) patients had PSA between 11 to 20ng, 6 (7.1%) patients had PSA between 21 to 30ng, 7 (8.2%) patients had PSA between 31 to 40ng, 11 (12.9%) patients had PSA between 41 to 50ng and 42 (49.4%) patients had PSA between ( $>50$ ). Maximum patients had BPH [58 (68.2%)] and it was not statistically significant ( $p = .87288$ ), ( $z = 0.1639$ ). In malignancy group, the mean Serum PSA (ng ml) was  $85.5185 \pm 42.3669$  and in BPH group, it was  $40.3793 \pm 28.9069$ . Distribution of mean Serum PSA (ng ml) with Gleason's score was statistically significant ( $p < 0.0001$ ). However, PSA was more in Adenocarcinoma [ $85.5185 \pm 42.3669$ ] compared to BPH [ $40.3793 \pm 28.9069$ ] but this was statistically significant ( $p < 0.0001$ ). These findings are correlated with the study conducted by Shekhar S et al [17], Khant VS et al [18] and Okuja M et al [19].

In the current study, most of the patients had Grade 2 Prostatomegaly [36 (42.4%)]. It was statistically significant ( $p < .00001$ ), ( $z = 5.1167$ ). Also, study showed that a greater number of patients had volume of prostate between 31 to 50 cc [42 (49.4%)]. It was statistically significant ( $p < .00001$ ), ( $z = 6.3449$ ). This is in concordant with the study done by Roehrborn CG et al [20]. There was a significant number of the patients had post procedural complication i.e., per rectal bleed [1 (1.2%)], ( $p < .00001$ ), ( $z = 12.7316$ ) and infection [1 (1.2%)], ( $p < .00001$ ), ( $z = 12.7316$ ) which is comparable with the earlier studies [21, 22].

### Limitations

In spite of every sincere effort present study has lacunae. It was a single center study conducted in small sample size. The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out.

### CONCLUSION

TRUS guided biopsy is effective, cheap, and safe method of prostate

biopsy. It aids in correlating ultrasound imaging finding in benign and malignant conditions of prostate with serum PSA and histopathological findings. Use of TRUS should be done for differentiating benign and malignant lesion based on imaging findings. There is significant co-relation between the serum PSA levels and Gleason's Score.

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