

# Correlation of Serum Prostate Specific Antigen (PSA) with Incidentally Detected Prostatic Cancer in Patients Undergoing TURP for Clinically Benign Prostatomegaly: A Single Centre Study

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## ABSTRACT

**Objective:** The aim of this study is to estimate the incidence of prostatic cancer in patients undergoing transurethral resection of prostate for clinically benign prostatomegaly and its correlation with serum PSA.

**Materials and Methods:** It is retrospective observational study. All the patients with symptomatic prostatomegaly undergoing transurethral resection of prostate from Dec 2017 to Jan 2022 were included in this study.

**Results:** A total of 141 patients who underwent transurethral resection of prostate were included in this study. The average age of patients was  $64.07 \pm 7.58$  years. Mean symptom score was  $20.71 \pm 3.54$ . 123 patients (87.23%) presented with acute retention of urine with failed catheter free trial. 24 patients (17.02%) had PSA value between 4-10 ng/ml while as 117 patients (82.98%) of the study population had PSA between 0-4 ng/ml. The mean PSA value was  $3.66 \pm 2.68$  ng/ml and the mean PSA density was  $0.653 \pm 0.054$ . Only 3 (2.13%) had adenocarcinoma of prostate detected on histopathological examination of TURP chips. Out of 3 patients diagnosed as carcinoma prostate, 1 had gleasons grade 6 and 2 had gleasons grade 7.

**Conclusion:** Incidental detection of Ca Prostate in patients undergoing TURP for clinically benign prostatomegaly is low and was found to be 2.13 % in our study. Our study also provides evidence that  $PSA > 4$  ng/ml (Range 4-10 ng/ml) is a risk factor for occult prostate cancer and suggests screening in these patients.

**Keywords:** Adenocarcinoma prostate; Incidentally detected prostatic cancer; Serum prostate specific antigen; Transurethral resection of prostate

## INTRODUCTION

Among all the malignancies occurring in the humans prostate cancer is one of the most prevalent and least understood. It is presenting clinically in 8% of men. On autopsy, up to 60% of 70 years old and 80% of 80 years old are found to have latent prostate cancer [1]. Pathological evidence suggests that malignant changes of prostatic epithelium begin early in life but do not become clinically relevant until decades later. Some patients live out their lives with a prostatic cancer that do not bother much to the patients for decades without treatment, while in other cases, the cancer spreads very aggressively, responds poorly to the therapy and results death within few years. Prior to PSA era, up

to 27% of prostate cancer were detected incidentally at the time of TURP [2]. Incidence of Prostate cancer arising exclusively from the transitional zone is uncommon and ranges between 2-7% of all prostate cancers [3,4]. Several recent studies have reported that cancer arising from the transitional zone have a more favourable prognosis than tumor that arise in one peripheral zone [3,5]. In the post PSA era, incidental prostate cancer on TURP remains common, occurring in 4.1-16.7% of TURP specimens [6,7]. The disease is becoming an increasingly significant health problem worldwide. Its incidence has increased and is expected to continue to do so through the next century. Incidence and mortality rate have been rising over the last three decades [8]. Such growing importance of disease was

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addressed by researchers and scientists who believe that these trends for Ca Prostate are more artefactual than real, being due to population ageing, and increase in number of incidentally diagnosed prostatic cancers. Aim of this study was to detect incidence of prostate cancer in patients undergoing TURP for BPH.

## MATERIALS AND METHODS

All the patients with BPH with up to 75 years of age during the period from Dec 2017 to Jan 2022 undergoing TURP were taken for study. All patient having PSA level >10 ng/ml and having radiotherapy and radical prostatectomy as appropriate treatment options were excluded from the study. Detailed history was taken as per the prepared proforma and then completes clinical examination and follow-up was done. All data based on prepared questionnaire regarding age, clinical presentation, DRE findings, prostate size PSA value, TURP, histopathologic outcome and follow up were recorded and analysed. Informed consent was taken.

## RESULTS

During the study total 187 BPH patients were admitted at SKIMS Srinagar for surgery out of which 45 patients (10 patients were unfit for surgery, 12 patients were diagnosed having Ca prostate in Biopsy, 23 patients were having PSA >10 ng/ml) excluded from study. Finally 141 patients who were operated as TURP were included in the study. In our study Mean age of presentation is  $64.07 \pm 7.58$  years and most patients (n=110) presents in their 5th and 6th decade of life. Symptoms graded on IPSS score and 55.31% patients (n=78) presented with symptom score between 20-35 and graded as severe symptoms. While 49 (34.75%) patients presented with moderate symptoms (score between 8-19) and only 14 (9.92%) patients presented with mild symptoms (score between 0-7). Mean

symptom score is  $20.71 \pm 3.54$ . Total 123 patients (87.23%) presented with Urinary Retention out of which 103 patients (73.04%) were having Acute and 20 patients (14.18%) were having Chronic retention and were relieved on Foley's catheterization and remain persistently or intermittently on catheter until surgery. total 37 patients (26.24%) presented with other complications out of which 17 patients (12.05%) were having hematuria, 15 patients (10.63%) were having bladder stone, 5 patients (3.54%) were presented with Chronic Renal Failure and 4 patients (2.8%) were presented with recurrent UTI which were conservatively managed prior to surgery. Maximum patients i.e. 83 (58.87%) had prostate size between 51 to 80 gms. Mean prostate size is  $59.71 \pm 14.40$  gms (Table 1). In this study, 15 patients i.e. 10.63% of study population were found having upper tract abnormalities like Hydronephrosis and Hydroureteronephrosis. Patients are categorized into two groups based on their PSA value. 24 patients (17.02%) of the study population having PSA value between 4-10 ng/ml and 117 patients (82.98%) of the study population having PSA value between 0-4 ng/ml. Mean PSA value is  $3.66 \pm 2.68$  ng/ml. 18 patients (12.76%) of study population having PSA density below 0.15 and 123 patients (87.23%) of the study population having PSA density equal or above 0.15 while mean PSA density is  $0.653 \pm 0.054$ . We found that 3 patients (2.13%) of the study population were diagnosed having incidental Ca Prostate by histopathological report and patients which were diagnosed as incidental prostate cancer have PSA value more than 4 ng/ml and all 117 patients having PSA value less than 4 ng/ml and 21 patients having PSA value more than 4 ng/ml were diagnosed as BPH after histopathology confirmation (Table 2). Out of 3 patients diagnosed as Ca Prostate 1 had gleasons grade 6 and 2 had gleasons grade 7. During follow up period out of 3 patients diagnosed as Ca Prostate 2 patients were treated with Androgen Deprivation Therapy (B/L orchidectomy) and 1 patient opted for Active Surveillance.

S. No.	Prostate weight in gms	No of patients	Percentage
1	21-30	4	2.83%
2	31-50	37	26.24%
3	51-80	83	58.87%
4	>80	17	12.06%

**Table 1:** Showing size of prostate.

PSA Value (ng/ml)	Outcome	No. of patients	Percentage
0-4	BPH	117	82.97%
	Ca Prostate	0	0%
4-10	BPH	21	14.89%
	Ca Prostate	3	2.12%

**Table 2:** Showing histological outcome.

## DISCUSSION

Incidental prostate cancer is defined as a symptom-free cancer unexpectedly discovered upon microscopic examination of resected tissue. In past few decades knowledge about prostate cancer has increased in the society. Serum PSA assays and other screening examinations for prostate cancer are now widely available. Incidence of incidentally detected cancer in prostate was up 27% prior to the PSA era. After PSA testing became widely available, the incidence of incidentally detected carcinoma prostate in TURP specimens without prior diagnosis has now reduced to 5-13%. Although this incidence vary across the globe since various factors can influence the detection of this malignancy in TURP chips. In our study 41% patients (n=58) presented with mean age of presentation is  $64.07 \pm 7.58$  years which is similar to the study of Ganesh, et al. [9]. Whereas several other studies like Yoo, et al. [10], Antunes, et al. [11] and Di Silvero, et al. [12] shows mean age of incidental prostate cancer quite higher i.e. 71, 68 and 69 years respectively but our study is consistent with increasing trend of incidental prostatic cancer due to early diagnosis in our country. In our study 90% of the patients (n=127) presented with moderate to severe symptoms with mean IPSS of  $20.71 \pm 3.54$  which is similar to study of Wei Huang, et al. [13] and study of M. Hosseini, et al. [14]. In our study 73.04% patients (n=103) were presented with AUR which were primarily relieved with catheterization and eventually with surgery (TURP) and 14.18% patients (n=20) presented with chronic retention. In the older literature, the risk of recurrent AUR was cited as 56% to 64% within 1 week of the first episode and 76% to 83% in men with diagnosed BPH. Breum L, Klarskov P, Munck LK, et al. [15], have also supported these findings. In our study 10.63% patients (n=15) were having stone disease. In a large autopsy study the prevalence of bladder stones was 8 times higher in men with a histologic diagnosis of BPH (3.4%) compared with controls (0.4%) but no increased incidence of ureteral or kidney stones were found Grosse H. Frequency1990 [16]. In our study 12.05% patients (n=17) were presented to our hospital with moderate to gross hematuria which is similar to the study of Mebust WK, et al. [17] which shows in BPH patients who have been indicated to surgery, 12% showed macroscopic hematuria. One of the reason may be upregulation of vascular endothelial growth factor (VEGF) and increase in the density of microvessel density as told by Foley SJ, Bailey DM2000 [18], Pareek G, Shevchuk M, Armenakas NA, et al. [19], DiPaola RS2001 [20]. In our study 3.54% patients (n=5) were presented with Chronic Renal Failure which is similar to The Agency for Health Care Policy and Research BPH guidelines [21]. As per data available of patients who underwent upper tract imaging before TURP, 7.6% of 6102 patients in 25 series had evidence of hydronephrosis, of whom one third had features of renal failure. According to the data available the incidence of end stage renal disease in patients with benign prostatomegaly is rare and is less than 1%. Several guidelines like Homma Y, Gotoh M, Yokoyama O, et al. [22] recommend that as an initial work up measurement of serum creatinine is essential. In our study 2.8% patients (n=4) were presented with UTI, which is slightly higher for unknown reason compared to

the study of McConnell JD, et al. [23] which suggests the incidence of UTIs in the placebo-treated patients was only 0.1/100 patient-years in the MTOPs study. In older surgical series like Holtgrewe HL, et al. 1989 [24], UTI constitute the main indication for surgical intervention. In our study Mean prostate size is  $59.71 \pm 14.40$  gms. With the age the size of prostate tends to increase. This fact has been scrutinized in various longitudinal and cross-sectional study groups, starting with the original autopsy study supervised by Berry and colleagues [25]. It is well postulated that the source of the size enlargement of the prostate is the periurethral glands or transition zone that expands and compresses the peripheral zone of the prostate to give raise the symptoms. In our study 82.98% patients (n=117) were having PSA below 4 ng/ml and 17.02% patients (n=24) were having PSA between 4 ng/ml to 10 ng/ml while 87.23% patients (n=123) had PSA density below 0.15 and 12.76% patients (n=18) were having PSA density above or equal to 0.15. There is no such study found related to incidence of PSA or PSA density range in BPH patients undergoing TURP. In our study of 141 BPH patients who have undergone TURP without any prior suspicion of malignancy incidental Prostatic cancer were found to be in 2.13% of cases (n=3). One patient had T1a and Gleason grade <7 while 2 patients had T1b and Gleason grade  $3 \pm 4$  prostate cancer. The above incidence rate is in range with incidental Prostate cancer in modern era and close to study of Antunes et al in which they found 1.8% patients (n=3) diagnosed having incidental Prostate cancer in 168 TURP patients who were clinically benign with mean age of 68 years. When compared with several previous studies like Ziguener, et al. [26] suggested that incidental detection of Ca Prostate has decreased by more than 50 % in the PSA era. In their study, incidental prostate cancer was diagnosed in 314 (13%) of 2422 patients. However, the rate of incidental prostate cancer in patients with both negative age-specific PSA levels and negative DRE findings was 6.4%. The rate of incidental cancer in their study was only 5.2%. A study from Cleveland clinic by Jones, et al. [27] reported that incidental prostatic cancer among patients who are undergoing TURP between the pre-PSA and the PSA era has decreased in frequency from 14.9% to 5.2% with clinically significant drop in stage T1b. They also suggested that men considering surgical or medical management of clinically benign prostatomegaly be informed that it should be infrequent that they harbour clinically significant undetected malignancy. According to various studies worldwide in addition to DRE findings, a combination of volume of transition zone and serum PSA can be used as useful predictive factors of incidental prostate cancer. We have seen that in our study the age of the patient was a positive predictor for incidence of occult Ca Prostate whereas DRE findings had no correlation with presence of incidental Ca Prostate, also shown by Yoo, et al. [28]. In the study by Melchior and colleagues reported that the rate of incidental prostate cancer was found to be 5.4 %. They concluded that there is currently no possibility to reliably predict the absence of aggressive prostate cancer after TURP, and thus recommendations are to observe instead of further therapy. The low incidence rate in found in our study is may be due to narrow range of inclusion criteria, small sample size in

comparison to other studies and decreased rate of surgical management of BPH due to increased use of medical therapy as well as an increased use of ablative therapies, which do not always provide tissue for pathologic analysis in patients who ultimately require surgical management of their BPH. Also in our study the 3 patients which were diagnosed incidental carcinoma prostate have their PSA above 4 ng/ml which suggest that PSA>4 ng/ml is a risk factor for occult prostate cancer but we need more data to significantly correlate PSA value in predicting incidental Ca Prostate in BPH patients undergoing TURP. Only 1 patient had T1a and Gleason grade<7, opted for surveillance strategy due to older age and low grade lesion. Two patients had T1b and Gleason grade 3 ± 4 prostate cancers and underwent Androgen Deprivation Therapy in the form of B/L orchidectomy. This detection rate is comparable with several other recently published series and it is consistent with the overall incidental prostate cancer in the PSA era.

## CONCLUSION

Based on our study and considering the facts published in various studies, we conclude that incidentally detected Prostatic Cancer in patients who are undergoing transurethral resection of prostate for clinically diagnosed benign prostaticomegaly is low and were found to be 2.13 % in our study. Positive predictor for the incidental detection of ca prostate is the age. Our study also provide evidence that value of serum PSA more than 4 ng/ml (Range 4-10 ng/ml) is a important risk factor for occult prostate cancer and suggest screening in these patients.

## DISCLOSURE

Approval of the research protocol by an Institutional Reviewer Board: N/A (As this is a retrospective observational study approval from IRB was not needed although permission from the department was taken.

Informed Consent: Taken from the patients

Registry and the Registration No. of the study/trial (Registration number in a public trials registry: N/A

Animal Studies: N/A

Conflict of Interest: The authors declare no conflict of interest.

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