

# INCIDENCE OF CHIPS POSITIVE CARCINOMA OF PROSTATE FOLLOWING TURP FOR CLINICALLY BENIGN PROSTATIC HYPERPLASIA PATIENTS WITH NORMAL SERUM PSA

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## ABSTRACT

*A cross sectional study was performed to evaluate the frequency of chips positive carcinoma of prostate following TURP for clinically benign prostatic hyperplasia patient with normal serum PSA. A total of 250 patients were initially screened & 100 patients were included into the study according to the selection & exclusion criteria. They were evaluated by using IPSS, a physical examination including DRE & neurological examination to exclude any neurological deficit & neurologically related bladder dysfunction. The prostate was next assessed by transabdominal US. Serum PSA level was then measured & at a cut off value of < 4 ng/ml were enrolled in this study. In our study only 2 patients were found having adenocarcinoma. Therefore incidence of carcinoma prostate in clinically BPH patients with normal s. PSA is low. Low incidence in present series revealed the usefulness of s.PSA screening method. To avoid unusual systemic needle biopsy for diagnostic purpose s.PSA measurement should be done.*

## Introduction

Carcinoma of the prostate is the most common form of malignancy in males as followed closely by lung cancer and the second leading cause of cancer death. It is more common in developed than developing countries.

The incidence rates show a 63 fold difference between countries, being lowest in Far East countries such as China- Shanghai (2.5 per 10<sup>5</sup>) and highest in US blacks in Detroit (158 per 10<sup>5</sup>). US blacks have a particularly high risk of prostate cancer with almost a two fold high incidence rate than that for US whites<sup>1</sup>. Prostatic cancer is extremely rare in Asians<sup>2</sup>.

The incidental carcinomas includes those cases of prostatic carcinoma that are neither suspected nor detected clinically, are diagnosed by histopathological examination of tissue harvested by TURP or millin's or transvesical prostatectomy of clinically BPH patients.

Most prostatic carcinomas arise from the peripheral zone of the gland and there is considerable scope for sampling

error at the time of the original transurethral prostatectomy, if the presence of carcinoma is unsuspected, which may lead to an inaccurate assessment of tumour volume<sup>3</sup>.

There are a number of similarities between benign prostatic hyperplasia (BPH) and cancer. Both display a parallel increase in prevalence with patient age according to autopsy studies (86.2% and 43.6%, respectively, by the ninth decade), although cancer lags by 15-20 years. Both require androgens for growth and development and both respond to antiandrogen treatment regimens. Most cancers arise in prostates with concomitant BPH (83.3%), and cancer is found incidentally in a significant number of transurethral prostatectomy (TURP) specimens (10%). The clinical incidence of cancer arising in patients with surgically treated BPH is approximately 3%. BPH may be related to a subset of prostate cancer which arises in the transition zone, perhaps in association with atypical adenomatous hyperplasia (AAH). It is important to exclude cancer in patients presenting with symptoms of bladder outlet obstruction presumably due to BPH. For such patients, digital rectal examination (DRE) and, at least in high-risk patients, serum prostate specific antigen (PSA) determination is recommended. Transrectal ultrasound (TRUS) should be employed in patients with elevated PSA levels to determine the volume of the prostate, the relative contribution of BPH to volume, and the PSA density (ratio of PSA level to volume). Biopsy should be obtained from any area suspicious for cancer. Early detection and treatment of cancer when it is localized offers the greatest chance for cure<sup>4</sup>.

The extensive pool of asymptomatic prostate disease in the population, which increased substantially with age, suggests that the frequent use of transurethral resection of the prostate in recent decades has had a large effect on prostate cancer incidence. Besides this, TURP almost always performed to relieve outflow obstruction but not as a diagnostic procedure. Before the widespread use of PSA screening, frequency of incidental carcinoma in prostate chips were more<sup>5</sup>.

PSA is a glycoprotein. MW is 33,000 and acts as a serine protease and found exclusively in the epithelial cells of the prostate. PSA is measured in the serum. PSA used as a tumor marker have occurred since 1980s and widely used as a clinical marker of prostate cancer by 1988<sup>6</sup>. In pre PSA period TURP was a usual procedure for symptomatic relieve in case of obstructive features due to BPH and it had a great role for higher prevalence rate of incidental carcinoma. Now-a-days incidental findings of prostatic carcinoma decreased markedly due to strict and purposive screening by PSA as well as DRE and Trans abdominal ultrasound. Considering cut off value 4 ng/mL of PSA we can exclude suspicious cases. By judging this cut off value surgeons can avoid inadvertent operative procedure in case of BPH patients. In our country there is no study on actual prevalence rate of incidental carcinoma in patients with PSA value less than 4ng/mL. So this study is a little endeavor to elucidate the prevalence rate of incidental carcinoma of BPH patients having PSA level d"4ng/mL.

**Materials and Methods**

This cross sectional and interventional study was conducted from July 2007 to December 2008 in the Department of Urology, Sir Salimullah Medical College and Mitford Hospital, Dhaka. Study populations were suffering from BPH who attended the Urology OPD, SSMC and Mitford Hospital with LUTS. Purposive sampling technique was used with a sample size of 100. Inclusion criteria were IPSS >20, Posts void residual volume > 100, Peak urine flow rate (Q<sub>max</sub>) <10ml/sec, Serum PSA normal (d"4ng/mL), DRE-Prostate is enlarged, no suspicious nodules, USG-no hypoechoic nodules. Exclusion criteria were clinically palpable suspicious nodules, Serum PSA >4ng/mL. The initial evaluation consisted of the IPSS, a physical examination including DRE and neurological examination to exclude any neurological deficit and neurologically related bladder dysfunction. The prostate was next assessed by Transabdominal USG. Prostate volume, echopattern, and post void residue (PVR) of urine also measured. Serum PSA level was then measured. Uroflowmetry was done in relevant cases. After proper evaluation the selected patients were undergone TURP. All prostatic chips were embedded. The paraffin embedded blocks were sectioned at 4 microns. Samples were taken randomly for histopathological examination. All the data were checked and edited after collection. Then the data were entered into the computer and analyzed with the help of SPSS-14(SPSS incorporation, Chicago, IL, USA) window version 14 software programmed. After processing of all available information, statistical analysis was done.

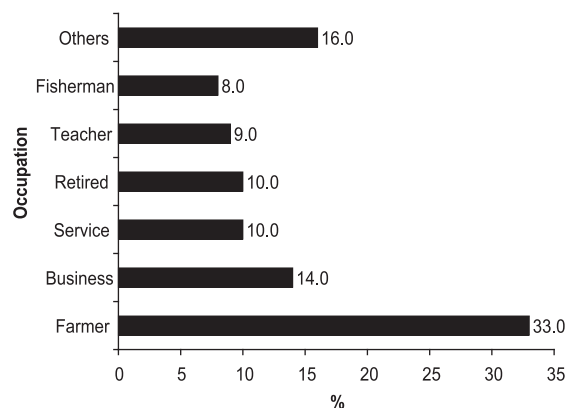
**Result and observations**

**Table I**  
*Incidence of enlarged prostate among different age group (n=100)*

Age (in year)	Frequency	Percent
>60	23	23.0
60-70	68	68.0
>70	9	9.0
Total	100	100.0

Mean ± SD (Range) = 65.67 ± 6.26 (50-80)

Table shows the age distribution of the patients. The average age of the patients was 65.67 years. The youngest patient was 50 years old and the oldest was 80 years. This highest incidence of BEP was noted in 60 to 70 years age group.



**Fig.-1: Occupation of the patients**

**Table II**  
*Prostatic findings by digital rectal examination (n=100)*

	Frequency	Percent	Enlarged
• Slightly enlarged	13	13.0	
• Moderately enlarged	68	68.0	
• Hugely enlarged	19	19.0	
Upper limit			
• Can be reached	77	77.0	
• Can not be reached	23	23.0	
Tenderness			
• Tender	12	12.0	
• Not tender	88	88.0	

On per rectal digital examination prostate gland was found to be enlarged in all cases. Of them 68.0% had moderate enlargement, 19.0% had huge enlargement and 13.0% had mild enlargement. Upper limit of prostate gland can be reached at 77.0% patients. Out of all patients 12.0% had tenderness of DRE and 88.0% non tender.

**Table III**

*Transabdominal ultrasonographic findings (n=100)*

Ultrasonographic findings	Frequency	Percent
Volume of prostate (in gm)		
• <40	73	73.0
• 40-60	17	17.0
• >60	10	10.0
Echo pattern		
• Homogenous	100	100.0
• Non homogenous	0	.0

Out of all patients maximum 73.0% patients had prostatic volume less than 40 gram, 17.0% had 40 to 60 gram and 10.0% had more than 60 gram. Echo pattern is homogenous in 100% cases.

**Table IV**

*Distribution of the respondents by serum PSA (ng/ml) level (n=100)*

Serum PSA level	Frequency	Percent
<2.00	5	5.0
2.01-3.00	7	7.0
>3.01	88	88.0
Total	100	100.0
Mean ± SD (Range)	3.47 ± 0.64	0.6-3.9

Out of all patients 5.0% patients' serum PSA level were less than or equal to 2 ng/ml, 7.0% patients were between more than 2 to 3 ng/ml and 88.0% patients serum PSA level were more than 3 ng/ml. Mean (± SD) PSA was 3.47 (± 0.64) and the minimum and maximum values were 0.6 and 3.9 respectively.

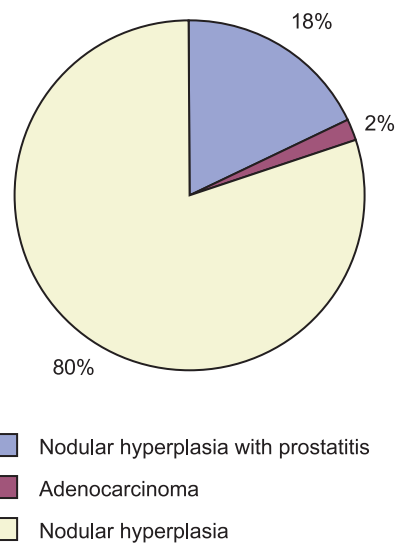
**Table V**

*Distribution of the respondents by histological findings (n=100)*

Histological findings	Frequency	Percent
Nodular hyperplasia (no evidence of malignancy)	80	80.0
Nodular hyperplasia with prostatitis	18	18.0
Prostatic intraepithelial neoplasia	0	0.0
Adenocarcinoma	2	2.0

Histopathological examination of the specimens showed 80.0% had nodular hyperplasia, 18.0% nodular hyperplasia with prostatitis and 2.0% had adenocarcinoma. No patient had got prostatic intraepithelial neoplasia.

The two patients having adonocarcinoma of prostate are found with Gleasons score- 7 (4+3) and 7 (3+4).



**Fig.-2: Histopathological findings**

**Discussion**

Benign prostatic hyperplasia is a growing global health burden. As expected male lifetime is increasing rapidly, more men will need treatment. Transurethral resection of the prostate (TURP) has been the gold standard for active treatment since the 1970s<sup>7</sup>. A large number of investigators have shown that examination of every fragments of TURPs or serial sectioning in retropubic prostatectomy specimens can detect many prostatic carcinoma which are mostly undetected in conventional procedure of sampling the prostatic tissue for routine histology. Inadequate sampling rather than inaccurate

pathological evaluation is the most frequent problem in the diagnosis of prostatic cancer. Small lesion whether localized by rectal examination or radiography are not always easy to punctate and while, needle biopsies from clinically suspicious cases can be thoroughly examined pathologically, they commonly lack neoplastic foci. In contrast TURP provide much tissue that extensive pathological evaluation is not usually done in routine histology practice. Gross inspection and palpation for carcinoma in prostatectomy specimens have been unrewarding for most pathologists and random sampling is preferred technique. Since the majority of prostatic tissue removed for benign condition is an important consideration while histopathological examination.

The average age of the patients of present series was 65.67 years. The youngest patient was 50 years old and the oldest was 80 years. This highest incidence of BPH was noted in 60 to 70 years age group.

Similar observation was made in Shaikh et al (2000)<sup>8</sup>. The average age of patients treated with TURP in their study was 66 years (range 54-80 years) and maximum patients were belonged to 61 to 70 years age range

Histopathological examination of the specimens of TURP chips showed 80.0% nodular hyperplasia, 18.0% nodular hyperplasia with prostatitis and 2.0% adenocarcinoma. No patient had got prostatic intraepithelial neoplasia. Histopathological diagnosis of some previous studies in Bangladesh showed frequency of incidental carcinoma of prostate ranged from 4.0 to 10.6% (Khan 1983; Hossain 1984; Islam 1985 ) and much higher from the rate of present series. The two chips positive patients of our study had Gleasons score of 4 (2+2) and 5 (3+2).

In review of 108 cases in which suprapubic operation was performed for benign hyperplasia of the prostate, Treiger et al found malignancy in 12.6% of the cases.

Of the 75 cases of apparently benign prostatic obstruction analyzed by Myer's in 1991<sup>9</sup> in which there was no clinical evidence of carcinoma and which were operated either by the suprapubic route or by transurethral resection, 29.4% revealed malignancy.

Labess (1952) found malignant tissue in 9.2% of a consecutive series of 98 cases clinically diagnosed as benign enlargement.

Boring CC and Squires TS (1992)<sup>10</sup> found carcinoma in 23 or 46% of a consecutive series of 50 prostate obtained from men over 50 years.

In a pathological study of 490 prostates which were diagnosed non-malignant, both macroscopically and microscopically in postmortem examination, Kahler (1939) by further examination of these glands found 54 (11.0%) cases of carcinoma.

A total of 14 such patients were identified and the outcome of TURP was analyzed by Radhakrishnan et al (2004)<sup>11</sup>. Three patients were found to have cancer in the resected specimen.

All of the above study shows higher frequency rate of incidental carcinoma. Jones et al (2009)<sup>12</sup> showed a comparison between pre-PSA era (1986–1987) and the PSA era (1994–2000), excluding patients with known CaP. A total of 228 men without a known history of prostate cancer underwent TURP during the pre-PSA era time frame and 501 underwent the procedure during the PSA era time frame. Malignancy diagnosed at the time of TURP decreased from 14.9 to 5.2% of patients in the pre-PSA and PSA eras, respectively. In our study we have excluded all patients having serum PSA level more than 4ng/mL. Mean ( $\pm$  SD) PSA was 3.47 ( $\pm$  0.64) and the minimum and maximum values were 0.6 and 3.9 respectively This was the reason behind low incidence rate of carcinoma in our study. Histopathological examination of the specimens showed 80.0% had nodular hyperplasia, 18.0% nodular hyperplasia with prostatitis and 2.0% had adenocarcinoma with confidence level of -0.74 to 4.74.

These two patients are advised for staging evaluation and were treated accordingly.

### Conclusion

Before the widespread use of PSA screening, frequency of incidental carcinoma in prostate was more as revealed by various studies described elsewhere in this paper. Actually TURP is almost always performed to relieve out-flow obstruction but not as a diagnostic procedure. In this study along with digital rectal examination and transabdominal ultrasound we have used PSA as a screening method at a cut off value of 4ng/mL and patients having below this level were enrolled here only. Lower rate of incidental carcinoma of prostate in the present series revealed the usefulness to follow the preoperative screening methods that is DRE, USG & PSA. To avoid unusual systemic needle biopsy and TURP for diagnostic purpose PSA should be done.

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