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Detection of prostatic cancer in patients complaining of benign prostatic hyperplasia

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Abstract

Background:
Prostate adenocarcinoma is found in surgical samples without prior diagnosis in number of the patients in whom there was no previous suspicion but they were completely incidental. These incidental tumors were of low grade; mainly grade (6) (3+3) according to Gleason scoring system; and less aggressive; and some of them associated with low and high-grade prostatic intraepithelial neoplasia (PIN).

Objectives:
To detect the percentage of incidental prostatic tumor with low and high grade PIN and their relation to clinical data.

Patients & Methods:
A cross-sectional study conducted in pathology department – Al-Yarmouk Teaching Hospital - Baghdad on a total of 80 patients, aged from 43 to 88 years, diagnosed histo-pathologically with benign prostatic hyperplasia were included and studied during the period from 2012-2017. All patients were evaluated, preoperatively; with a digital rectal examination (DRE), prostate-specific antigen (PSA) screening as indicated by American Urological Association (AUA) guidelines, and prostate biopsy when indicated (patients with an elevated PSA or an abnormal DRE). Histopathological results of tissue were analyzed and scored according to Gleason score.

Results:
The results revealed that 26 patients diagnosed incidentally as prostatic carcinoma, 12 patients with incidental PIN, and the remaining 42 patients diagnosed as benign prostatic hyperplasia. 31.3% of patients were with age range 60-79 years with variable serum PSA values and significant relation between incidental tumor and level of PSA. The commonest Gleason score was grade 6 (3+3) forming 18.8% which represent moderately differentiated prostatic adenocarcinoma while only 1.3% were with high-grade tumor score 8 (4+4).

Conclusion:
Patients with prostate cancer diagnosed through TURP and open prostatectomy samples are considered as incidental tumors, which might change the line management for both adenocarcinoma and low and high-grade PIN. In cases of benign lesion (no any tumor), TURP making the follow-up of these patients easier and decreasing the symptoms and PSA level.

Key words: Prostate, Benign prostatic hyperplasia, Incidental tumor.

INTRODUCTION:

Inflammation, hyperplastic, changes of prostate, and tumors; are the commonest pathological, processes that affect prostate gland, in men, related to, increasing age [(1)].

Prostate cancer is a disease, of the prostate, a walnut-size, gland in the male reproductive system. Most common type of prostate, cancer is prostate adenocarcinoma, which arise from, glandular elements and graded, based on its Gleason score, depends on the, population of the cells under, the microscope, ranging from two, to ten. A low Gleason score, means that the cancer, tissue is similar to normal cells, (well-differentiated tumor); and unlikely, to spread. A high Gleason score means that the cancer cells are very different from, normal cells (poorly differentiated tumor); and are likely to, spread [(2)].

Prostate, cancer and benign prostatic, hyperplasia (BPH); are two major prostate diseases that increased, with aging. The incidence of both, diseases are currently increased [(3)].

Most prostate carcinomas are currently diagnosed, by biopsies (trans-rectal biopsy) then the patient evaluated, for prostate-specific antigen (PSA), which is widely used now a day [(4)].

However, adenocarcinoma, is still found in histopathological specimen, of surgical samples for patients, without previous diagnosis which is not surprising, findings since those patients, underwent the surgery for symptomatic, BPH associated with elevated, PSA and negative, preoperative prostatic biopsies; while in incidental, finding of tumors; the tumor would, never have been detected if the surgery had, not been indicated, especially if they would not produced symptoms or the PSA, level not elevated [(5)].

Incidental prostate, cancer (clinically stage, T1) is defined as clinically, in apparent tumor that is neither, palpable nor visible by imaging, or biopsy. Prostate cancer (clinical T1a, and T1b) are diagnosed when transurethral, resection of the prostate (TURP) for benign, prostatic disease was done. T1a disease, involves only 5%, or less of the resected, prostatic tissue, whereas T1b, disease involves more, than 5% of the resected, tissue. Previously, before the PSA era, up to 27% of prostate cancers were detected, incidentally at the time of, TURP [(6)]. With frequent, PSA screening, there has been decrease in the incidence, of these lesions [(7)].

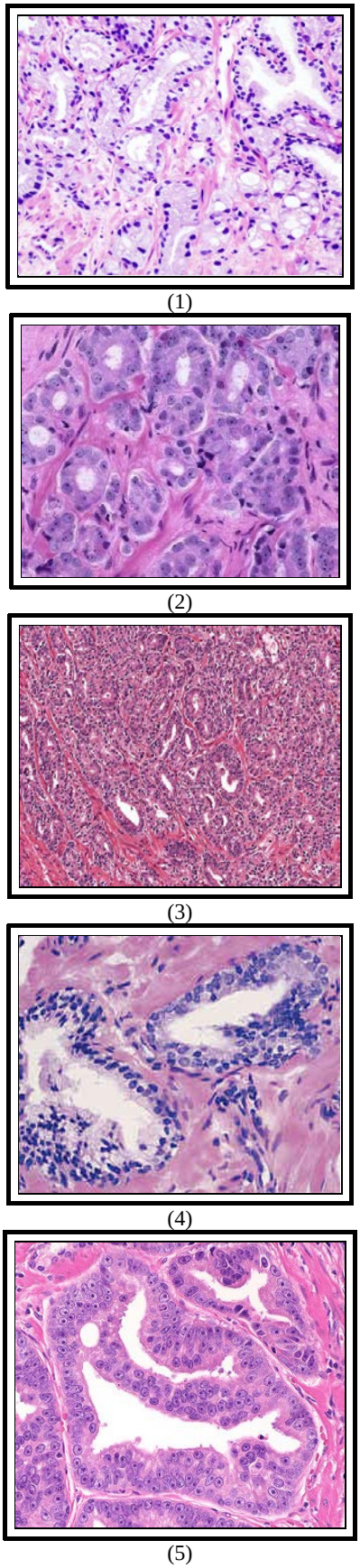
In our, screening practices, we sought, to identify the rates, of incidentally detected prostate, cancer in TURP and prostatectomy, specimens. Hence, the current study is a trial to detect the rate of incidental prostatic tumor with low and high grade PIN and their relation to clinical data in patients with BPH.

MATERIAL & METHODS:

A total of 80 patients, aged from 43 to 88 years, diagnosed histo-pathologically as having BPH were included and studied, from those registered in a department of histopathology in Al-Yarmouk Teaching Hospital-Baghdad during the period from 2012-2017. They included 26 patients diagnosed, incidentally as prostatic, carcinoma and 12 patients, diagnosed incidentally, as prostatic intraepithelial, neoplasia (PIN) and the remaining 42 patients diagnosed as benign prostatic, hyperplasia. Any known case with prostatic cancer, were excluded from this study (exclusion criteria).

All patients were evaluated, preoperatively; with a digital, rectal examination (DRE), PSA screening, as indicated by American,Urological Association (AUA) guidelines, and prostate, biopsy when indicated; which was performed,on patients with an elevated PSA or an abnormal, DRE which was done by, surgeon. Histopathological results of tissue were, analyzed and scored according to Gleason, score. These samples were represented by Formaline-fixed, paraffin, embedded tissue.

Patients were analyzed for clinical, data with special focusing, on the age, level of serum PSA, previous diagnosis, DRE, incidental, tumor, Gleason scoring, system, and the type of operation (prostatectomy or trans-urethral resection of prostate "TURP"). The blocks were sectioned at 4 micron thickness, and stained by Hematoxyllin and Eosin stain. Histopathological, examination was performed by pathologist, to confirm the diagnosis (Figure 1) and to exclude other pathology. The degree of differentiation, was assessed according to Gleason, grading system to evaluate the prognosis of men with prostate cancer.



(1) (2) (3) (4) (5)

Figure 1: The histopathological sections, for different view of prostatic adenocarcinoma. (1) and (2) well differentiated prostatic adenocarcinoma, Gleason, 3, H&E, Stain; 40X. (3) Gleason 4, prostatic adenocarcinoma, H&E Stain; 40X. (4) Low grade, PIN, H&E stain; 40X. (5) High grade PIN, H&E Stain; 40X.

Analysis of data was carried out using the available, statistical package of SPSS-24 (Statistical, Packages for Social Sciences-version 24). Data were presented in simple, measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). The significance of difference of quantitative data was tested using Students-t-test for difference, between two independent means or ANOVA test for difference among more, than two independent means. The significance of difference of different, percentages (qualitative data) were tested using Pearson Chi-square test (χ^2-test) with application of Yate's correction or Fisher, Exact test whenever applicable. Statistical, significance was considered whenever the P value was equal or less than 0.05.

RESULTS:

A clinic-pathological, assessment revealed that the commonest, age group for development of prostatic, changes and their related presentation was at, age between 60-79 years (31.3%) while patients age 80 years and above represent (8.8%) as shown in table 1.

Table 1: The number, and percentage of the age of the patients.

Age (years)	No	%
40---49	6	7.5
50---59	17	21.3
60---69	25	31.3
70---79	25	31.3
=>80	7	8.8
Mean±SD (Range)	66.2±10.3 (43-88)	

The level of, the serum PSA in our patients was around 3 ng/dl represent 21.3% while higher than 7 ng/dl, represent 16.3% as shown in table 2.

Table 2: The level of serum PSA (ng/dl).

PSA (Units)	No	%
1.0---	8	10.0
2.0---	15	18.8
3.0---	17	21.3
4.0---	11	13.8
5.0---	6	7.5
6.0---	10	12.5
=>7.0	13	16.3
Mean±SD(Range)	4.5±2.9 (1-19)	

Sixty-one patients were diagnosed to have BPH account for (76.3%) while the remaining 19 patients were diagnosed to have BPH with chronic prostatitis (23.7 %) as shown in figure 2.

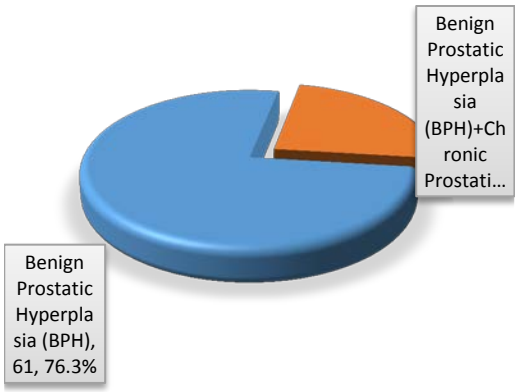


Figure 2: The histopathological diagnosis of the patients.

Twenty-six patients (32.5%) were diagnosed, previously as BPH and found to have incidental prostatic adenocarcinoma, while the others (12) (15%) patients were diagnosed to have incidental prostatic, adenocarcinoma with low and high-grade PIN. Forty-two (52.5%) patients were negative for adenocarcinoma as shown in table 3.

Table 3: The incidental prostatic adenocarcinoma with low, and high grade, PIN.

Incidental tumor	No	%
Incidental+LGP+High Grade PIN (HGP)	4	5.0
Incidental+Low Grde PIN (LGP)	8	10.0
Incidental	26	32.5
Not	42	52.5

The, commonest Gleason score was grade 6 (3+3) forming 18.8% which represent moderately, differentiated prostatic adenocarcinoma while high-grade tumor score 8 (4+4) represent 1.3% as shown, in table 4.

Table 4: The number and percentage of different Gleason score.

Gleason Score	No	%
3+3	15	18.8
3+4	10	12.5
4+4	1	1.3
No	54	67.5

Sixty-four patients (80%) were underwent, tran urethral resection of prostate (TURP) and sixteen (20%) were underwent open, prostatectomy as shown in figure 3.

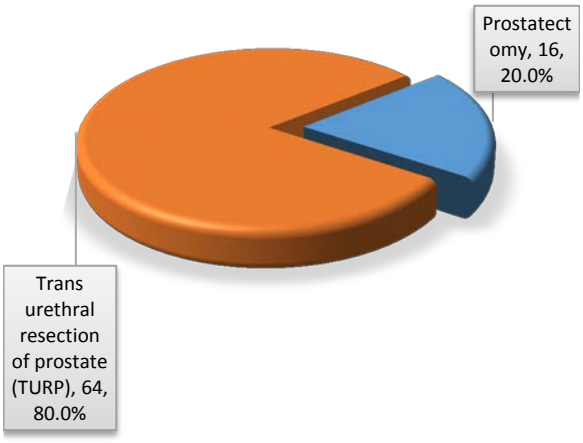


Figure 3: The number, and percentage of the type of operation.

The incidental prostatic adenocarcinoma was noted more in, patients age more than 60 years but however there, was no significant relation between age, and finding of incidental prostatic adenocarcinoma as, shown in table (P= 0.747) .
There was significant higher serum level of, PSA (more than 4 ng/dl) and incidental prostatic adenocarcinoma (P=0.050) as shown in table 6 and figure 4.

Table 5: The correlation, between the mean age, and incidental prostatic adenocarcinoma.

Age (years)	Incidental tumor							
	Incidental+LGP+HGP		Incidental+LGP		Incidental		Not	
	No	%	No	%	No	%	No	%
40---49	1	25.0	-	-	3	11.5	2	4.8
50---59	1	25.0	2	25.0	4	15.4	10	23.8
60---69	2	50.0	4	50.0	8	30.8	11	26.2
70---79	-	-	2	25.0	8	30.8	15	35.7
=>80	-	-	-	-	3	11.5	4	9.5
P value			0.747					
Mean±SD (Range)	57.5±7.9 (47-65)		64.5±7.8 (54-78)		67.3±11.2 (43-88)		66.6±10.1 (44-87)	
P value			0.330					

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

#Significant difference between four independent means using ANOVA test at 0.05 level.

Table 6: The serum level of PSA by incidental prostatic adenocarcinoma.

PSA (Units)	Incidental tumor							
	Incidental+LGP+HGP		Incidental+LGP		Incidental		Not	
	No	%	No	%	No	%	No	%
1.0---	1	25.0	1	12.5	1	3.8	5	11.9
2.0---	1	25.0	-	-	4	15.4	10	23.8
3.0---	-	-	1	12.5	3	11.5	13	31.0
4.0---	-	-	2	25.0	7	26.9	2	4.8
5.0---	1	25.0	-	-	1	3.8	4	9.5
6.0---	-	-	1	12.5	7	26.9	2	4.8
=>7.0	1	25.0	3	37.5	3	11.5	6	14.3
P value			0.050					
Mean±SD (Range)	5.1±4.2 (1.9-11)		5.4±2.5 (1.9-9)		5.2±3.5 (1.2-19)		3.9±2.3 (1-11)	
P value			0.218					

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

#Significant difference between four independent means using ANOVA test at 0.05 level.

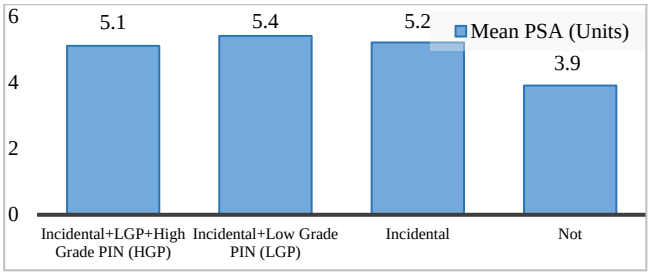


Figure 4: The serum level, of PSA by incidental prostatic adenocarcinoma.

The, commonest Gleason scoring for the collected, cases was (3+3) which represent moderately differentiated prostatic adenocarcinoma (57.7%) as shown, in table 7.

Table 7: The Gleason scoring, in incidental, prostatic adenocarcinoma.

Gleason Score	Incidental tumor							
	Incidental+LGP+HGP		Incidental+LGP		Incidental		Not	
	No	%	No	%	No	%	No	%
3+3	-	-	-	-	15	57.7	-	-
3+4	-	-	-	-	10	38.5	-	-
4+4	-	-	-	-	1	3.8	-	-
No	4	100	8	100	-	-	42	100

Six patients with incidental tumor an LGP (75%) were operated upon by TURP while the rest two cases (25%) were operated upon by open, prostatectomy compared to 17 patients with incidental (65.4%) operated by TURP as shown in table 8.

Table 8: The correlation, between type of operation and incidental, tumor.

Operation	Incidental tumor							
	Incidental+LGP +HGP		Incidental+LGP		Incidental		Not	
	No	%	No	%	No	%	No	%
Prostatectomy	-	-	2	25.0	9	34.6	5	11.9
TURP	4	100	6	75.0	17	65.4	37	88.1
P value				0.097				

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

DISCUSSION:

Our, study collect patients diagnosed previously with benign prostatic, hyperplasia and presented with obstructive, symptoms later on, then; after TURP, or open prostatectomy, it was, found that 26 cases of the patients (32.5%) had incidental tumor, in stage T1a and 12 cases (15%) had low and high grade, PIN with incidental tumor in stage, T1b. Other studies showed that the rate of an incidental, prostate cancer of 1.4% (T1b) [8] and up to 27% of, prostate cancer was diagnosed at the time of TURP [6]. Ploussard showed that the rate, of incidental tumor of prostate was 23.9% which was slightly lower than our result [9].

Recently, Jones *et, al.* reported a decrease in the incidental prostate cancer from 14.9%, to 5.2% in over 700 patients [10].

Meyer *et al.* study, showed 6.16% of high grade PIN and 2.06% of low grade PIN were significantly associated with incidental prostatic tumor [11] while Micheal found, that the incidence, of high grade PIN approximately 9% with a range of 4% to 16% [12]. The reason for this variability in incidence may be due the site of tumor, transitional zone tumor may be detected earlier than tumor arise in the peripheral zone especially in TURP specimens.

In, addition, relatively the small amount of tissue removed, by TURP or transrectal biopsy could, potentially result in missing of, prostate cancer.

The, age of about one-third of the patients (31.35%) in our study was between 60-69 years, this is because these symptoms related to, increase age. Other, study showed, that median, age was 71 years which was near the age group of our results [8]. American Cancer, Society estimate that the, average of patients age at the time of diagnosis was about 66 years [13].

However, our study showed that there was no significant relation, between age and incidental tumor (P=0.747). In our study, we found that commonest Gleason, score was grade "6" (3+3) which represent 18.8% "moderately differentiated, prostatic adenocarcinoma" while high-grade tumor score "8" (4+4) represent 1.3% only.

Six patients had Gleason grade (3+3) pT1a disease and one patient, had Gleason, grade (3+4) pT1b disease. [14] Voigt *et al.* found an incidental prostate cancer rate of 11.1% in their study to identify any risk factors for these lesions, 3.4% of the patients in their clinical, coarse had, clinically relevant, prostate cancer "pT1b or Gleason grade (7–10) disease" [15]. While others found, that incidental prostate tumor had Gleason score of 6 [14]. In our, findings, these tumors were of low grade and less aggressive may be due to regular follow up of patients with BPH and early detection of cancer.

The current study showed a significant relation between serum, level of PSA (more than 4 ng/dl) and incidental prostatic adenocarcinoma (P=0.050). Monda, proposes that the PSA level generally increases with, malignant changes [16]; other study, revealed that PSA values of 6.6 ng/dl was found in incidental prostate, cancer but there was no, significant relation between, PSA value and incidental tumor [17]. The possible explanation for this variability in PSA, values that not associated with cancer may be due to increase its levels with, BPH prostatitis and catheterization.

Patients with obstructive symptoms and increased PSA value, may benefit from the surgery [18,19]. High, PSA values are usually associated, with increased risk of urinary, retention and patients with increasing PSA, who may have a transitional zone tumor are better sampled, with TUR (more informative biopsies) rather than transrectal biopsies [20].

Patients with incidental tumor, seventy-five percent of them operated by, TURP while 25% by open prostatectomy but there was, no significant relation between type of operation, and incidental, tumor. TUR of the prostate is not currently, considered as a diagnostic tool for prostate, cancer except in special cases. A TURP is considered, sufficient and, informative when at least one-third of the gland had been removed [9]. TURP can be used, for a small proportion of, patients with large prostates and, continuously increasing PSA after full diagnostic investigations [21].

Lee *et al.* found, that in most cases, TRUP did not provide enough additional information to be warranted for many, patients pursuing treatment for TURP-diagnosed, incidental prostate cancer [22]. Capitanio *et al.* found that no,relation between finding of incidental tumor and type of operation (TURP or prostatectomy) which is similar to our result [23].

In conclusion, patients with prostate cancer found in TURP and open prostatectomy samples should be considered as incidental, tumors which will change the lines of patient management for both, adenocarcinoma and low and, high grade PIN. In cases of, benign lesion (no any tumor), TURP making the follow-up of these patients easier, and decreasing the symptoms and PSA level.

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