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Histopathological Study of Prostatic Needle Biopsies for Diagnosing Prostatic Lesions in Kashmir Valley.

KEYWORDS: Prostatic disorders, Gleason's score, Histopathology, Adenocarcinoma.

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ABSTRACT *The present study was conducted in the department of Pathology, Government Medical College Srinagar, in collaboration with the department of Surgery. This study was conducted on 60 patients presenting with abnormal digital rectal examination or elevated serum prostatic specific antigen (>4ng/ml) or both. Out of 60 patients studied 15% of the patients were diagnosed with adenocarcinoma and rest of the patients were diagnosed of different prostrate complications.*

Out of the 09 patients diagnosed as adenocarcinoma, including the one confirmed by immune-histochemical analysis, majority of the patients viz. 6 (60%) were having a Gleason's score of 6-7 (intermediate grade) and 4 patients (40%) were having a Gleason's score of 8 (high grade). Mean Gleason's score was 7.

Introduction:
Prostatic cancer among adult males is the most common neoplasm in most developed countries. It has been estimated that over 200,000 men in United States are diagnosed annually with prostate cancer and 300,000 men still die from this disease each year (Troyer et al). The age-standardised incidence of prostate cancer in the European Union is 65/100,000 and the EU, s mortality rate is 26/100,000 per year (Kataja et al). In South Korea the incidence rate of this disease increased from 0.41/100,000 during 1985-1989 to 3.38/100,000 during 1995-1999; the crude incidence rate among Korean men estimated to be 10.09/100,000. Prostate cancer incidence is increasing in India- Currently it ranks 5th in incidence and 4th in mortality for men in Mumbai (Yeol BB et al). The incidence is increasing by 1% every year. Above 50 years, the age-specific incidence rate increases three or four –fold for every 10 year increase in age (Cheon J et al). These trends have been related to diet i.e. high consumption of meat, dairy products and fats (Whiltemore et al and Kolomel et al) as determined by improved diagnostic techniques (Meltlin C et al, Engelbrecht et al).

The frequency and extent of symptoms can be quantified by using a questionnaire, and changes during therapy can thus be documented. The International Prostate Symptom Score (IPSS) is the most commonly used Questionnaires. On the basis of this score, the symptoms can be classed as mild (IPSS score 0–7), moderate (IPSS score 8–19), or severe (IPSS score 20–35).

Physical examination including general physical examination, neurological examination and the digitorectal examination (DRE). The digitorectal examination provides information on the size, pain, and consistency of the prostate.

Needle biopsy of the prostate plays a central role in the evaluation of prostate cancer. The morphological diagnosis of carcinoma relies on a combination of architectural and cytologic findings.

Patients and Methods:
A total of sixty patients presenting with elevated serum prostatic specific antigen (PSA) of >4ng/ml or abnormal digital rectal examination (DRE) were selected for the study.

History and Clinical Examination:-
A detailed history of every patient with particular reference to age, presenting complaints of obstructive voiding such as hesitancy, poor flow, intermittent stream, dribbling, sensation of poor bladder emptying, episodes of retention and irritative symptoms like frequency, nocturia, urgency, urge incontinence and abnormality on DRE were recorded. All patients underwent thorough general physical examination, abdominal examination including genito-urinary examination.

Lab. Investigations:-
Baseline investigations like HB, TLC, DLC, platelet count, coagulogram, KFT and urine examination were done on all patients.

PSA determination :-
In all investigated individuals the level of PSA was determined in identical way. PSA was estimated in venous blood by electrochemiluminescence method. The biopsy was performed with "Tru-cut" needle using transrectal or transperineal approach with previous preparing of patient (purgation and antibiotic protection). The indications for biopsy were: An abnormal DRE suspicious of malignancy and/or high serum PSA values.

Histopathological analysis:-
Histomorphological analysis of obtained material was done on standard hematoxylin-eosin (HE) preparations. Gleason,s grading was done in the adenocarcinoma patients.

The data obtained was analyzed statistically using standard statistical methods.

Results:
A total of 60 patients were selected for the present study. The age of all the patients was, in the range of 40-80 years with a mean age of 65 years. Out of all the patients, 09 patients were diagnosed with adenocarcinoma who were having either irritative (11.1%) or obstructive (88.9%)

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symptoms. Most of the patients diagnosed with adenocarcinoma were in the age group of 61-70 years (55.8%). None of the patients diagnosed with adenocarcinoma was below 50 years of age. The preoperative serum PSA level in 77.8% patients was greater than 20 which is summarized in Table I. digital rectal examination conducted on such patients showed single nodule in 33.3% patients; multiple nodule in 55.6% patients and grade III prostratomegaly in 11.1% patients. However, grade 0, grade I, grade II and grade IV prostratomegaly were not observed in any of the adenocarcinoma patients. Gleason's score of 5 to 10 was found in adenocarcinoma patients. Mean Gleason's score was 7 (Table II). Histomorphological analysis of adenocarcinoma patients showed hypertrophy, basal cell hyperplasia, intraepithelial neoplasia and gross degenerative changes (Figure I and II).

The present study revealed that no level of PSA was associated with a 100% positive predictive value and negative biopsy can occur virtually at any PSA level.

Table I. PSA in patients with Adenocarcinoma(N=09)

PSA(ng/ml)	N	%
<4	01	11.1
4 to 10	0	0
10.1 to 20	01	11.1
>20	07	77.8
Median 200 (Range 3.15 to 4240), 95% CI, p= 0.0001		

Table II. Gleason's Score of the Adenocarcinoma Patients (N=9)

Gleason's Score	N	%
2 to 4	nil	0
5 to 7	5	55.5
8 to 10	4	44.5
Mean Gleason's Score-7		

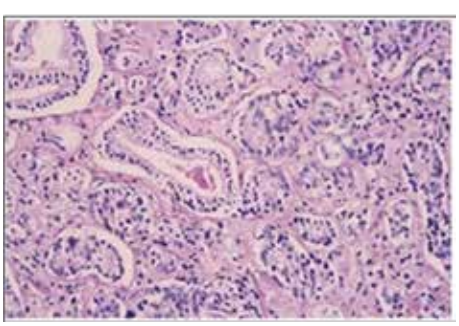

Figure I: Prostatic Adenocarcinoma (Gleason's pattern 7)—40x

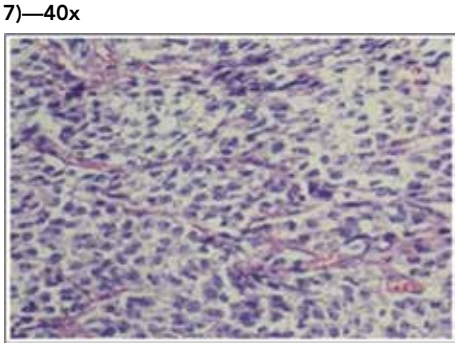

Figure II: Prostatic Adenocarcinoma (Gleason's pattern 5)—40x

Discussion:

Prostate cancer incidence is increasing in India- Currently it ranks 5th in incidence and 4th in mortality for men in Mumbai [9]. The incidence is increasing by 1% every year. There is an even more frequent anatomic form of prostate cancer in which the microscopic focus of cancer is discovered as an incidental finding either at postmortem examination or in surgical specimen removed for other reasons (e.g. nodular hyperplasia). Approximately 90% of these lesions do not cause trouble in the lifetime of the prostate [1]. In approximately 70% of patients, carcinoma of prostate arises in the peripheral zone of the gland, classically in a posterior location. Histologically, most lesions are adenocarcinoma that produce well-defined readily demonstrable gland pattern [2].

Out of 30 patients with BHP, most of them 28 (93%) were in the age group of 50-70 years, mean age being 62.4 years. These findings were consistent with the study conducted by Ishtiaq *et al* [12]. Patients with BHP 11(36.6%) had serum PSA of less than 4ng/ml, 9(30%) had serum PSA in the range of 4-10ng/m and 10 (33.3%) patients had serum PSA more than 10ng/ml. Mean serum PSA was 8.9ng/ml. These results were comparable with the other studies [3; 8;10;9; 11; 20).

In our study, out of 30 patients with BHP, obstructive symptoms were present in 14 patients (46.6%) and irritative symptoms were present in 16 patients (53.3%) whereas in patients with adenocarcinoma, majority (89%) were having obstructive symptoms. Our results were not comparable with the study conducted by Borislav *et al* [6].

In our study DRE revealed single nodule in 16 patients (53.3%) ,multiple nodules in 9 patients (30%), grade II prostatomegaly in 2 patients (6.6%), grade III prostatomegaly in 2 patients (6.6%) and grade IV prostatomegaly in 1 patient (3.3%) of BHP patients and single nodule in 3 (33.3%) patients, multiple nodules in 5 (55.5%) and grade III prostatomegaly in 1 (11.1%) of adenocarcinoma patients. The overall sensitivity and specificity were 70.2% and 62% respectively. These results were comparable with the studies conducted by different researchers [13; 22].

Out of the 9 patients diagnosed as adenocarcinoma,5 (55.5%) were having a Gleason's score of 6-7 (intermediate grade) and 4 patients (44.5%) were having a Gleason's score of 8 (high grade). Mean Gleason's score was 7. Most of these patients 7 (77.7%) were in the age group of 70-80 years, mean age being 71.3 years. These results were nearly comparable with the study conducted by Mathias *et al*[15].

Almost all patients (89%) with adenocarcinoma had raised serum PSA of more than 10ng/ml, only one patient (11%) was having a serum PSA of less than 4ng/ml. Mean serum PSA was 703.95ng/ml. Median PSA was 200ng/ml (range 3.15-4240ng/ml). This study revealed a statistically significant correlation between serum PSA and adenocarcinoma. These findings were consistent with the earlier study [5].

In the present study the positive predictive value for increasing PSA levels was 8.3% for PSA <4ng/ml, 16.6% for PSA >4ng/ml, 24.2% for PSA >10ng/ml and 83.3% for PSA >100 ng/ml. These results were not comparable with the study of Berman et al [5].

In our study the detection rate of prostate cancer in pa-

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tients with serum PSA between 3 and 4ng/ml was 14%. These findings were consistent with the study conducted by Aus et al [4].

This study revealed a PSA value of >4ng/ml in men of 50 years age or older was associated with 20% chance of detecting prostate cancer on the initial diagnostic biopsy. These interpretations were not comparable with the study conducted by Catalona *et al* [7] and this may be due to smaller number of patients in our study.

In the present study 22 patients presented with acute urinary retention and had raised PSA values. Out of these only 6 (22%) were positive for adenocarcinoma, which raised the false positive rate of PSA as a method for detecting carcinoma. It was concluded that acute urinary retention is associated with raised PSA levels. These findings were comparable with the earlier studies [8; 16].

In the present study there was a statistically significant correlation between serum PSA and prostatomegaly. With increase in prostate size, serum PSA was also increasing, and there was also statistically significant correlation between serum PSA and histological inflammation in the prostate. These interpretations were comparable with the earlier studies [11; 17].

In the present study Immunohistochemistry for 34BETAE12 anti high molecular weight cytokeratin antibody (which stains basal cells) was done on a total of 7 cases where the histological diagnosis was PIN in 4 cases, basal cell hyperplasia in 2 and atypical suspicious of malignancy in 1 case. All the cases with PIN and basal cell hyperplasia showed positive staining with 34betaE12 while as the case with atypical glands suspicious of malignancy showed negative staining. Thus 34betaE12 staining showed adenocarcinoma in one case (15%), HGPIN in 4 (57%) cases and benign proliferations in 2 (28%) cases, therefore, confirming the diagnosis in histologicaly suspicious cases.These findings were comparable with the study conducted by Katia *et al* [14].

This study revealed that no level of PSA was associated with a 100% positive predictive value and negative biopsy can occur virtually at any PSA level.

The present study also revealed that although morphological evaluation remains the gold standard, 34betaE12 can be an extremely useful adjunct in substantiating the diagnosis of malignancy in needle biopsies containing atypical foci and direct the clinician about the need for re-biopsy.

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