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Histopathological And Immunohistochemical Study Of Prostatic Lesions In A Teritary Care Centre

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Abstract

Background

Prostatic disease constitute significant morbidity and mortality in elderly men throughout the world.The most important categories of the prostatic disease usually encountered are Inflammatory lesions, Benign Prostatic hyperplasia, prostatic intraepithelial neoplasia,Carcinoma etc .Carcinoma of prostate is the second most common and the sixth leading cause of cancer death in world.Early detection and accurate diagnosis of prostate cancer is prime interest in medicine to control the death rate and management of affordable markers for diagnosis is essential .Primary objective of this study is Histopathological analysis of prostatic lesions. And the Secondary objective is Study of expression of HMWCK(34βE12),α-Methylacyl CoA racemase (P504S) in prostatic carcinoma cases.

Materials and methods

This study is a Descriptive study conducted at Dept of Pathology,Govt Medical college,Trivandrum from January 2020 to December 2020 .Study samples are Prostatic specimen including prostatic biopsies, TURP & prostatectomy specimen received in the Dept of pathology, Govt medical college Trivandrum .Biopsy specimen with no glandular component are excluded. Only Prostatic specimens with Glandular component is included.111 samples were studied.Prostatic specimens received in the Department of pathology during the study period was formalin fixed,paraffin embedded and thin sections made.slides are stained using H and E stain.The blocks of those slides with prostatic adenocarcinoma were collected.Unstained sections were made from the same and IHC was done on those slides and their expressions were studied.Collected data and results are entered in Microsoft excel sheet and analysis done

Result

TURP and Trucut biopsy are the two main specimens received at pathology Dept .Benign lesions are mainly seen in TURP and malignancy is more common in Trucut. Among benign lesions, Nodular hyperplasia is the commonest.Low grade PIN is more common finding than HGPIN.Carcinoma more common in >70 years age group and Nodular hyperplasia incidence is maximum in 60-69yrs age group.

Conclusions

The present study showed that majority of cases were benign lesions(73%) of which Nodular hyperplasia contributed to 55% of cases followed by Adenocarcinoma(27%).Chronic prostatitis is more prevalent than acute prostatitis.Low grade PIN is more common than High grade PIN.In the present study peak incidence of prostatic carcinoma was seen in age group more than 70yrs.Maximum number of carcinoma shows Gleason Grade 1 followed by Gleason Grade group 5. Positive cancer specific marker AMACR along with negative basal cell marker HMWCK can increase the level of confidence in establishing a definitive diagnosis of prostatic adenocarcinoma on limited biopsy.

Keywords: *Prostate,Benign Prostatic Lesions,Prostatic Adenocarcinoma,Gleason Grading,Hmwck Amacr*

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I. INTRODUCTION

Prostatic disease constitute significant morbidity and mortality in elderly men throughout the world.The most important categories of prostatic disease usually encountered are inflammatory lesions,Benign nodular hyperplasia,prostatic intraepithelial neoplasia,carcinoma etc.Carcinoma of prostate is the second most common and the sixth leading cause of cancer death in world.TURP(transurethral resection of prostate) is one of the most often performed surgical procedure in clinics.Deterioration of quality of life caused by prostatic disease is also a problem due to its symptoms. Prostatic specimens constitute a good percentage of surgical pathology workload.Early detection and accurate diagnosis of prostate cancer is prime interest in medicine to control the death rate and management of prostate cancer.Therefore there is an increasing demand for effective and affordable markers for diagnosis is essential. Alpha-methylacyl CoA racemase (AMACR) is a peroxisomal and mitochondrial enzyme that plays an important role in bile acid biosynthesis and beta oxidation of fatty acids

Now some studies show that decreased Alpha methylCo A racemase expression in localized prostate cancer with an increased biochemical recurrence and death. Prostatic lesions on routine staining sometimes cause diagnostic deliemma between benign and malignant lesions like atypical adenomatous hyperplasia and intra epithelial neoplasia .The basal cell markers like HMWCK,P63 etc can be used in diagnostically challenging cases.Primary objective of this study is histopathological analysis of prostatic lesions and secondary objective is study of expression of HMWCK and Alpha MethylCoA Racemase in prostatic carcinoma cases

II .MATERIALS AND METHODS

***Study design* :** Descriptive study
***Study setting* :**Dept of Pathology,Govt.Medical college.Trivandrum
***Study period*:**Prospective study
One year from the date of approval (1st January 2020 to 31st to December 2020)
***Study population*:** Prostatic specimens including prostatic biopsies,TURP and prostatectomy specimens received in the Dept of Pathology.Govt medical college.Trivandrum
***Exclusion criteria*:** Biopsy specimen with no glandular component
***Inclusion criteria*:** Prostatic specimens with glandular component
Sample size:111 Cases (parent study-Histopathological spectrum of prostatic specimens including immunohistochemistry with special reference to grey zone lesions.Monika Garg,Gurman kaur,Vineeta Malhotra,Ravish)
Sample technique:Consecutive
Procedure methodology:Demographic data regarding type of specimen ,age of the patient,clinical diagnosis collected from the record of the department.

All the specimens are fixed in 10% neutral buffered formalin.After the process of cutting,bitting,tissue processing,paraffin embedded blocks are made.Section of 4-5 micrometre thickness are cut from the blocks and stained with H and E staining.The slides are analysed under optical microscope and diagnosis is made as per WHO

The following microscopic features will assess

- Histopathological diagnosis
- BPH Type
- Prostatis-acute or chronic
- PIN-high grade or low grade
- Pattern of adenocarcinoma
- Gleason scoring
- Perineural invasion

Immunohistochemistry will perform on prostatic carcinoma slides with AMACR and HMWCK.Control population keeping for IHC are benign lesions of prostate.

Analysis of IHC-

AMACR positive staining is easily visible on low power examination.positive is circumferential,granular,luminal to subluminal or diffuse cytoplasmic staining of acini along with malignant features on H and E section.Negative staining or weak or non circumferential staining in adjacent benign glands.HMWCK positive staining is continous intact circumferential staining in benign glands.Collected data and results enter in Microsoft excel sheet and analysis were done.

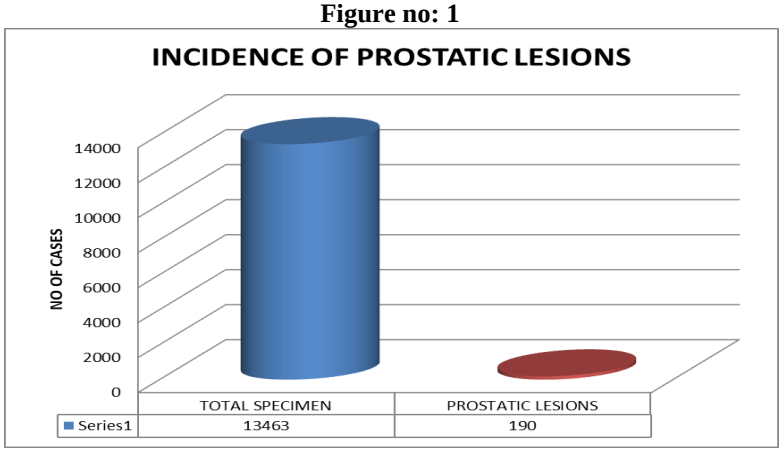
III.RESULTS

A total number of 13463 specimens received in the Dept. of pathology, during the study period of which prostate specimens constituted 190 specimens.

Table no: 1

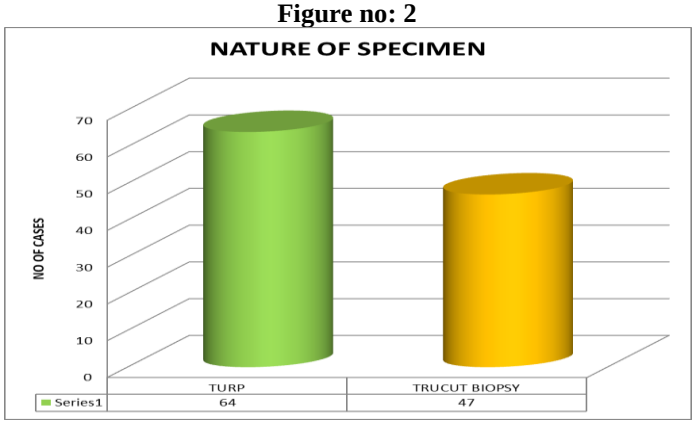
Period	Total no. of specimens	No. of prostatic specimens	Percentage
2020	13463	190	1.4%

Figure no: 1



Nature of specimen for the samples studied of which TURP(Transurethral resection of the prostate) is 64 and Trucut biopsy is 47 [Total number of specimens studied = 111]

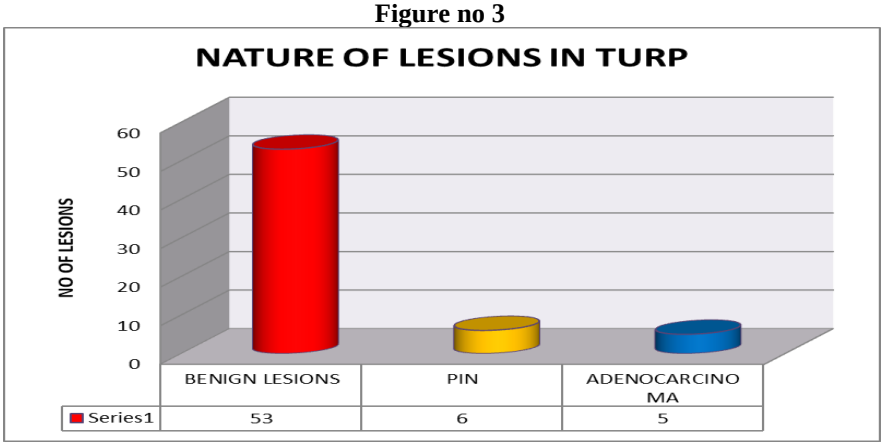
Figure no: 2



Nature of lesions in TURP

Benign Lesions = 53
Prostatic intraepithelial neoplasia = 6
Prostastic adenocarcinoma = 5

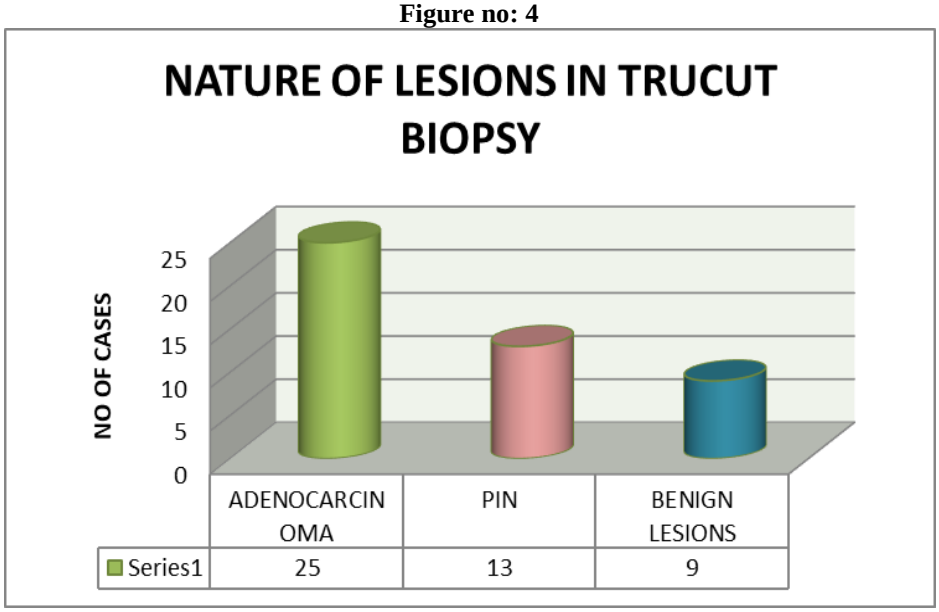
Figure no 3



Nature of lesions in Trucut biopsy

Benign Lesions = 9
Prostatic intraepithelial neoplasia =13
Prostastic adenocarcinoma=25

Figure no: 4



Frequency of benign, PIN & malignant lesions

Table no-2

Nature of specimen	Benign lesions	PIN	Prostatic adenocarcinoma
TURP	53	6	5
Trucut	9	13	25

Age incidence of prostatic lesions

Table no -3

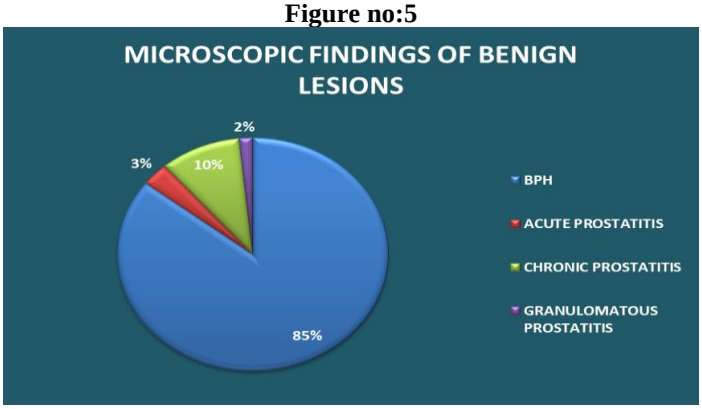
Sl. No	Age (Year)	Benign	PIN	Malignant
1	40-49	3	___	4
2	50-59	12	7	4
3	60-69	39	4	11
4	70-79	15	7	10
5	>80year	4	1	5
Total		62	19	30

Microscopic findings of benign lesions

Table no-4

Sl.No	FINDINGS	No. of cases
1	BPH	53
2	A/c prostatis	2
3	C/c prostatis	6
4	Granulomatous prostatitis	1
Total		62

Figure no:5

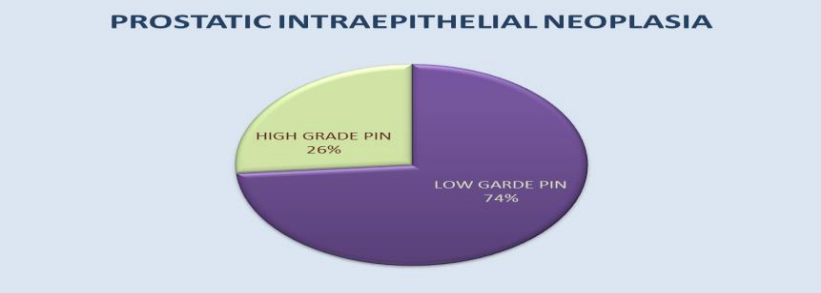


Prostatic intraepithelial neoplasia

Table no-5

Sl.No	PIN	No.
1	Low grade PIN	14
2	High grade PIN	5
Total		19

Figure no:6



Gleason grading system for carcinoma

Table no-6

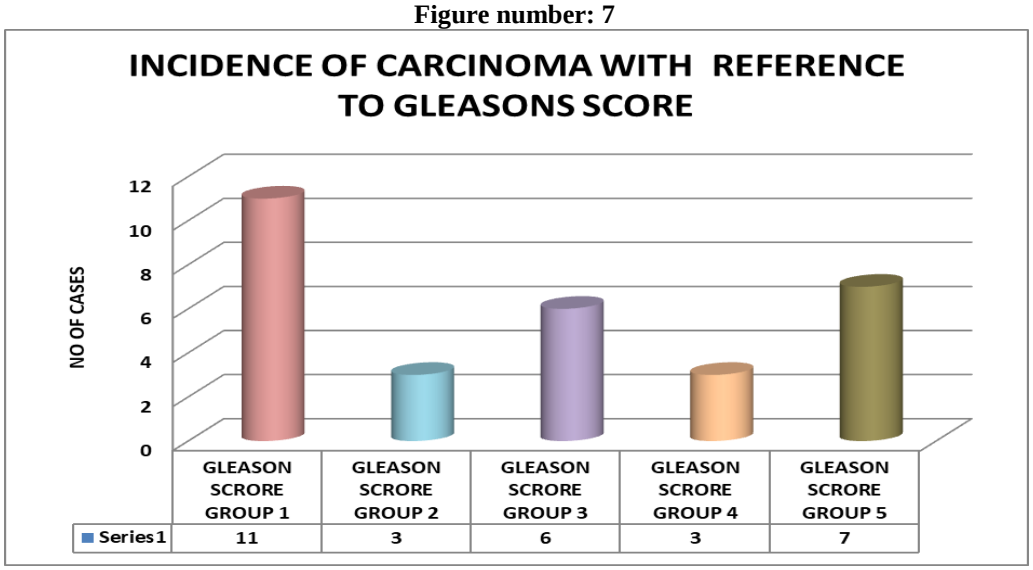
Sl.No	Biopsy No	Histopathological diagnosis	Gleason grade	Gleason score
1	118/2020	Prostatic adenocarcinoma	4	4+4=8
2	565/20	prostatic adenocarcinoma	5	4+5=9
3	1328/20	Prostatic adenocarcinoma	1	3+3=6
4	1353/20	Prostatic adenocarcinoma	5	5+5=10
5	1608/20	Prostatic adenocarcinoma	1	3+3=6
6	2456/20	Prostatic adenocarcinoma	3	4+3=7
7	2457/20	Prostatic adenocarcinoma	3	4+3=7
8	2458/20	prostatic adenocarcinoma	3	4+3=7
9	2487/20	Prostatic adenocarcinoma	2	3+4=7
10	3030/20	Prostatic adenocarcinoma	1	3+3=6
11	3144/20	Prostatic adenocarcinoma	1	3+3=6
12	3395/20	Prostatic adenocarcinoma	2	3+4=7
13	3971/20	Prostatic adenocarcinoma	1	3+3=6
14	4462/20	Prostatic adenocarcinoma	1	3+3=6
15	4541/20	Prostatic adenocarcinoma	1	3+3=6
16	4775/20	Prostatic adenocarcinoma	3	4+3=7
17	6417/20	Prostatic adenocarcinoma	1	3+3=6
18	6451/20	Prostatic adenocarcinoma	2	3+4=7
19	6617/20	Prostatic adenocarcinoma	4	4+4=8
20	6827/20	Prostatic adenocarcinoma	4	4+4=8
21	7035/20	Prostatic adenocarcinoma	5	5+4=9
22	7079/20	Prostatic adenocarcinoma	5	5+4=9
23	7199/20	Prostatic adenocarcinoma	5	5+4=9
24	7526/20	Prostatic adenocarcinoma	1	3+3=6
25	7616/20	Prostatic adenocarcinoma	3	4+3=7
26	7892/20	Prostatic adenocarcinoma	2	5+4=9
27	7994/20	Prostatic adenocarcinoma	1	3+3=6
28	8016/20	Prostatic adenocarcinoma	5	4+5=9
29	8128/20	Prostatic adenocarcinoma	1	3+3=6
30	8936/20	Prostatic adenocarcinoma	3	4+3=7

Incidence of Carcinoma with Reference to Gleason score

Table no 7

Gleason score group	No. of Carcinoma cases
1	11
2	3
3	6
4	3
5	7
TOTAL	30

Figure number: 7

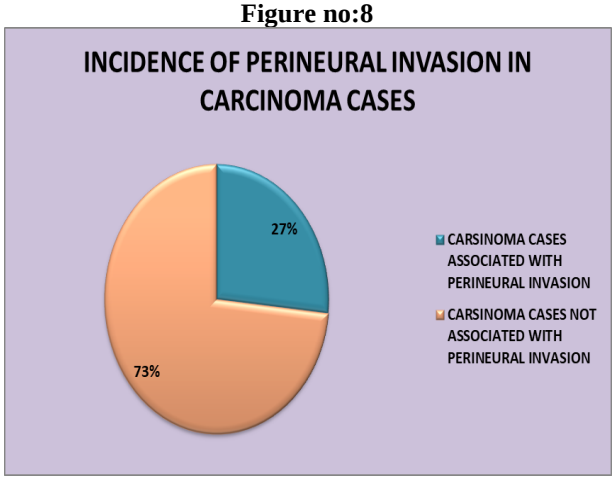


Incidence of perineural invasion in Carcinoma cases

Table no:8

Sl.No	Gleason score group	No. of cases
1	Carcinoma cases associated with perineural invasion	8
2	Carcinoma cases not associated with perineural invasion	22
	TOTAL	30

Figure no:8

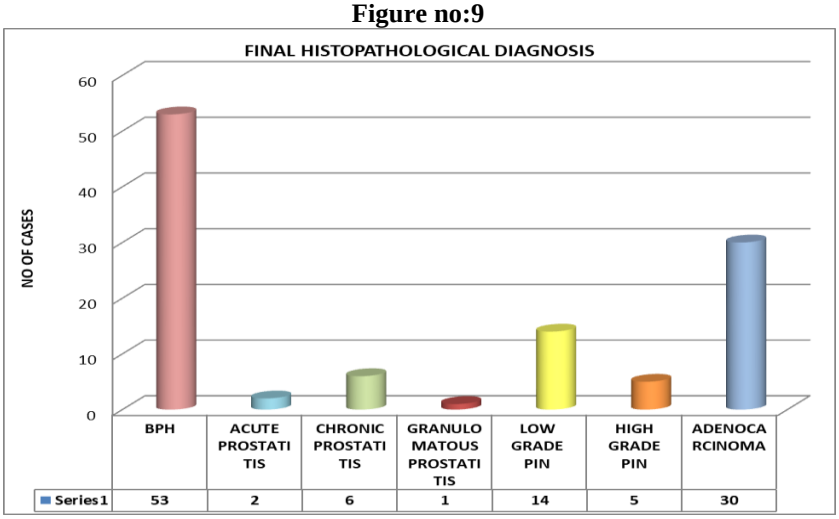


Final Histopathological Diagnosis

Table no:9

Sl.No	Diagnosis	No. of cases
1	Benign Nodular Hyperplasia of Prostate	53
2	Acute prostatitis	2
3	Chronic prostatitis	6
4	Granulomatous prostatitis	1
5	Low grade prostatic intraepithelial neoplasia	14
6	High grade prostatic intraepithelial neoplasia	5
7	prostatic adenocarcinoma	30
	TOTAL	111

Figure no:9



Immunohistochemistry

Total No. of Cases selected = 30

To study immunohistochemical reaction of prostatic adenocarcinoma towards AMACR & HMWCK

Evaluation of IHC

AMACR positive staining is early visible on Low power examination.

Positive is circumferential, granular, luminal to subluminal or diffuse cytoplasmic staining in malignant glands

HMWCK positive staining is intact circumferential staining in benign glands,but discontinuous staining in malignant lesions.

The result of following cases after being treated with AMACR & HMWCK Immunostains

Table no:10

Sl.No	Biopsy No	Histopathological diagnosis	AMACR	HMWCK
1	118/2020	Prostatic adenocarcinoma	positive	negative
2	565/2020	Prostatic adenocarcinoma	positive	negative
3	1328/2020	Prostatic adenocarcinoma	positive	negative
4	1353/2020	Prostatic adenocarcinoma	positive	negative
5	1608/2020	Prostatic adenocarcinoma	positive	negative
6	2456/2020	Prostatic adenocarcinoma	positive	negative
7	2457/2020	Prostatic adenocarcinoma	positive	negative
8	2458/2020	Prostatic adenocarcinoma	negative	negative
9	2487/2020	Prostatic adenocarcinoma	positive	negative
10	3030/2020	Prostatic adenocarcinoma	positive	negative
11	3144/2020	Prostatic adenocarcinoma	positive	negative
12	3395/2020	Prostatic adenocarcinoma	positive	negative
13	3971/2020	Prostatic adenocarcinoma	positive	negative
14	4462/2020	Prostatic adenocarcinoma	negative	negative
15	4541/2020	Prostatic adenocarcinoma	positive	negative
16	4775/2020	Prostatic adenocarcinoma	positive	negative
17	6417/2020	Prostatic adenocarcinoma	positive	negative
18	6451/2020	Prostatic adenocarcinoma	positive	negative
19	6617/2020	Prostatic adenocarcinoma	positive	negative
20	6827/2020	Prostatic adenocarcinoam	positive	negative
21	7035/2020	Prostatic adenocarcinoma	positive	negative
22	7079/2020	Prostatic adenocarcinoma	positive	negative
23	7199/2020	Prostatic adenocarcinoma	positive	negative
24	7526/2020	Prostatic adenocarcinoma	negative	negative
25	7616/2020	Prostatic adenocarcinoma	positive	negative
26	7892/2020	Prostatic adenocarcinoma	positive	negative
27	7994/2020	Prostatic adenocarcinoma	positive	negative
28	8016/2020	Prostatic adenocarcinoma	positive	negative
29	8128/2020	Prostatic adenocarcinoma	positive	negative
30	8936/2020	Prostatic adenocarcinoma	positive	negative

Percentage of carcinoma cases positive for AMACR is 90%.Percentage of carcinoma case negative for HMWCK is 100%.Positive cancer specific marker AMACR along with negative basal cell marker can increase the level of confidence in establishing a definitive diagnosis of prostatic adenocarcinoma in a limited biopsy sample.

Figure No:11- Nodular Hyperplasia 4x

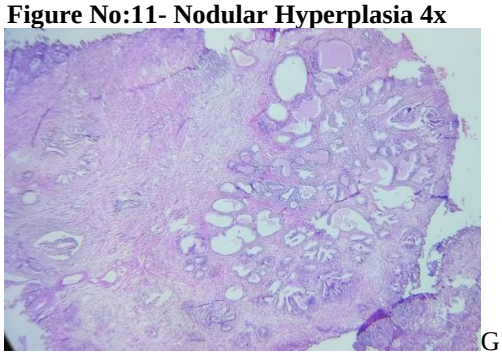
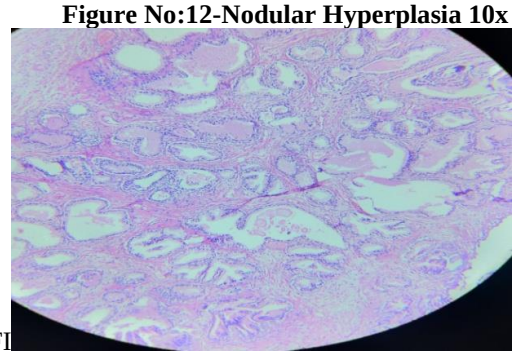


Figure No:12-Nodular Hyperplasia 10x



G FI

Figure No:13-Nodular Hyperplasia 40x

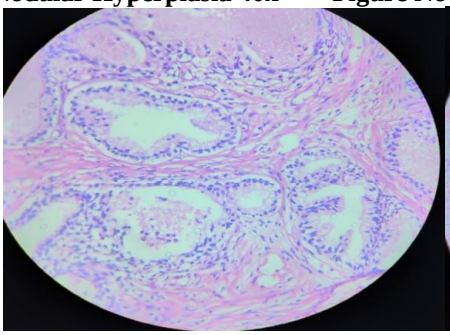


Figure No 14 Stromal Overgrowth In Nodular Hyperplasia

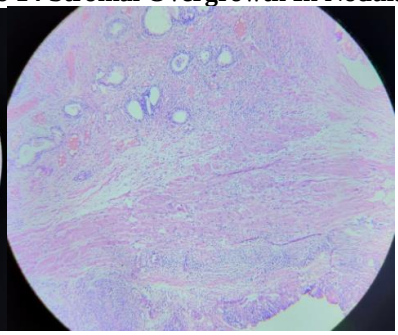


Figure No:15-Chronic Prostatitis

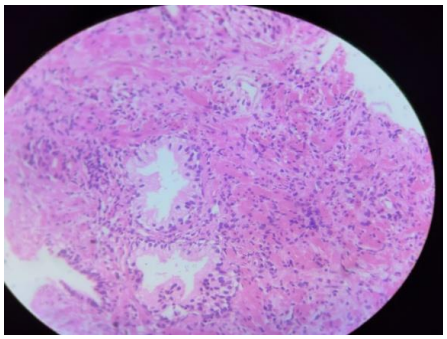


Figure No:16- Granulomatous Prostatitis

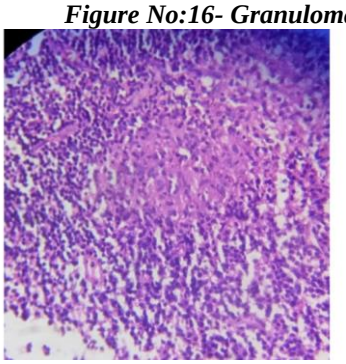


Figure No:17-Low Grade Pin

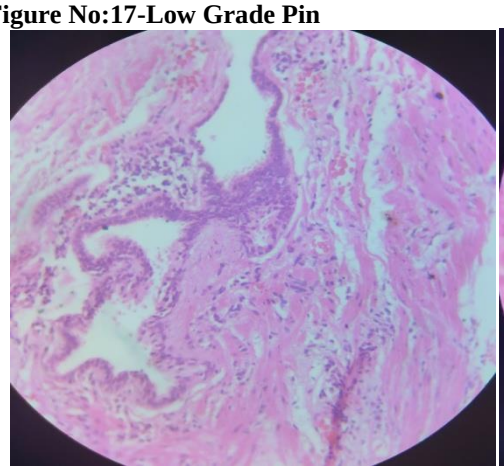


Figure No:18-High Grade Pin

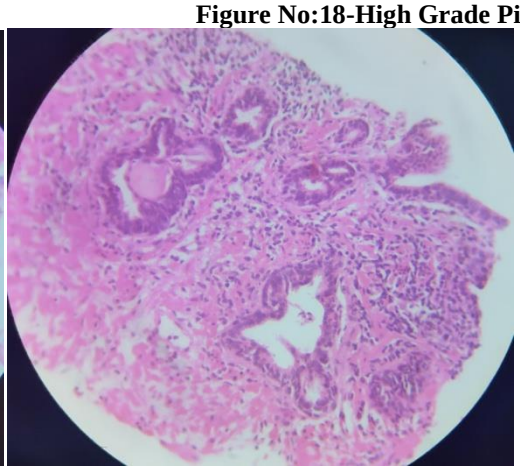


Figure No:19-Prostatic Adenocarcinoma 4x **Figure No:20-Gleason Pattern 3**

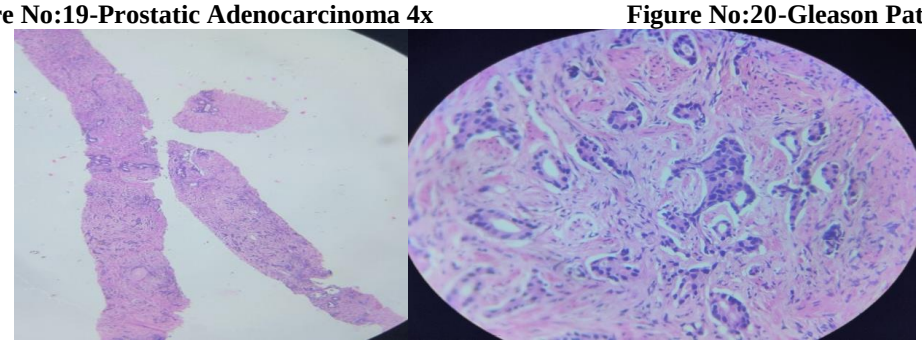


Figure No:21- Gleason Pattern 4 Cribriform Pattern **Figure No:22-Gleason Pattern 4 Fused Glands**

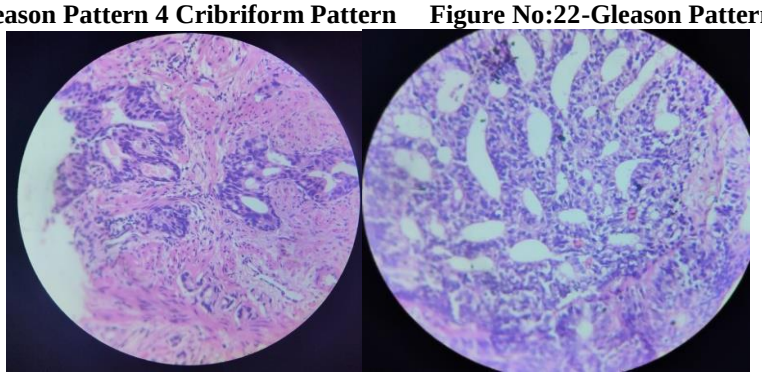


Figure No 23 Gleason Pattern 5 (Sheets) **Figure No 24 Perineural Invasion**

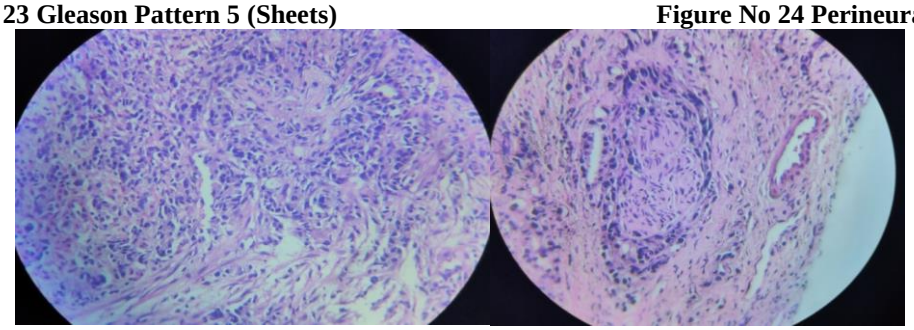


Figure No:25-Strong Positivity Of Amacr Expression In Adenocarcinoma

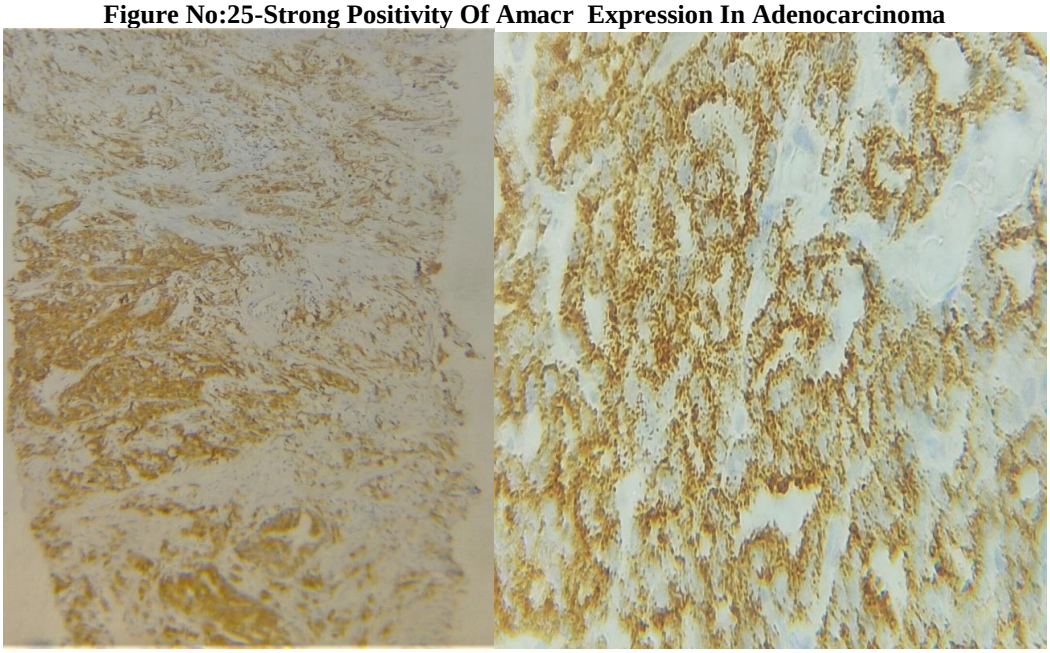
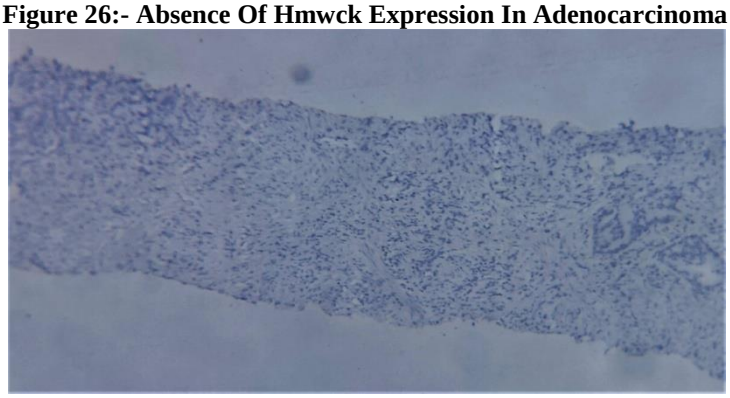


Figure 26:- Absence Of Hmwck Expression In Adenocarcinoma



IV. DISCUSSION

Benign Nodular Hyperplasia & Carcinoma of Prostate are increasingly frequent with advancing age. The various histologic appearances of BPH & prostatic adenocarcinoma are well known and have been described and illustrated extensively in the literatures

This study was undertaken to evaluate the various histological lesions in the prostatic specimens & evaluate the role of IHC in Carcinoma cases. In this study 111 prostatic lesions were analysed

Histopathological diagnosis

The present study showed that majority of cases 73% were benign lesions of which Nodular Hyperplasia contributed to 55% of cases followed by 27% of adenocarcinoma

Charles et al(1) showed that 62.8% cases of benign lesions followed by carcinoma prostate (29.3%) and 1 % prostatic intraepithelial neoplasia

Table No:11

Diagnosis	Charles et al(1)	Sushma bhat et al(2)	Present study
BPH	62.8%	89.58%	55%
Ca prostate	29.3%	8.34%	27%
PIN	1%	2%	17%
TOTAL NO OF CASES	304	96	111

Benign Nodular Hyperplasia

In the present study the incidence of benign lesions was 73%
Nodular Hyperplasia alone noted in 55%, account for majority of cases
Maximum incidence of cases noted in the 6^{th} & 7^{th} decade .

Table No:12

Sl. No	Study	40-49 yrs	50-59yrs	60-69 yrs	70-79 yrs
1	E George etal(3)	2-3%	13.6%	40.4%	23.4%
2	Anjorin et al(4)	7.82%	25.97%	32.67%	16.94
3	Present study	4.8%	19.3%	45.1%	30.6%

Youngest patient age : 41 yr
Oldest patient age : 88 yrs

Prostatitis

Table No:13

Sl. No	Diagnosis	No of cases
1	C/c Prostatitis	6
2	A/c Prostatitis	2

Prostatic Intraepithelial Neoplasia

In the present study, 19 cases showed PIN 73% are low grade and 26% are high grade PIN.
No of cases of PIN associated with Benign Nodular Hyperplasia

Table No:14

Sl. No	Diagnosis	No of cases
1	Low grade PIN associated with BPH	5
2	High grade PIN associated with BPH	1

PIN in younger men are usually low grade,
High grade PIN noted more commonly in elder men

Prostatic Carcinoma is the second most frequently cancer among men and major cause of cancer related mortality. The no. of cases continuously increased over the past decades due to increased life expectancy, life style changes, diet changes and obesity

Comparison of Incidence of Prostatic Carcinoma

Table No:15

Sl. No	Study	Prevalence of Carcinoma among prostatic lesions
1	Avinash et al(5)	25.6%
2	Present study	27%

In our study, the prevalence of carcinoma prostate was 27% which is in close correlation with other studies.

Table No:16

Age incidence of prostatic Carcinoma in different studies

Sl. No	Study	40-49 yrs	50-59yrs	60-69 yrs	70-79 yrs
1	Bhakt Deshmukh et al(6)	-	16.66%	16.66%	66.6%
2	Kusumam et al(7)	-	27.2%	8.9%	64.3%
3	Present study	-	13.3%	36.3%	50%

In the present study, peak incidence of prostatic Carcinoma was seen in age group more than 70 yrs. Many studies shows a higher incidence of prostatic Carcinoma in this age group.

Frequency distribution of Gleason grade

TABLE NO 17

Sl. No	Study	Grade group	2	3	4	5
1	Present study	36%	10	20	10	23%
2	Nazima Hyder et al(8)	12.77%	10.64	8.51	8.5	53.9

In the present study, 30 cases of adenocarcinoma prostate were seen, corresponds to 27% all cases. All these 30 malignant cases were graded using Gleason scoring system. Most of which showed grade group I followed by grade group 5.

Analysis of incidence of perineural invasion in carcinoma cases

Table no 18

Sl.No	Study	Percentage of carcinoma cases positive for perineural invasion
1	Peter strom et al (9)	16%
2	Hassan niroomand et al (70)	25.7%
3	Present study	27%

The finding of perineural invasion at biopsy has created excitement as a potential preoperative predictor of extraprostatic tumor extension

Analysis of immunohistochemical expression of AMACR and HMWCK in prostatic adenocarcinoma

Table no:19

Sl.No	Study	% of carcinoma cases positive for AMACR	% of carcinoma cases negative for HMWCK
1	Goswami et al(10)	96%	94%
2	Present study	90%	100%

HMWCK and AMACR immunohistochemistry represents a potential novel adjuvant method for facilitating the pathological diagnosis of prostatic adenocarcinoma in prostate needle biopsy

Analysis of incidence of high grade PIN among prostate lesions

Table no:20

Sl: no	Study	% of high grade PIN in prostate biopsy specimen
1	Michael k brawer(11)	9%
2	Present study	4.5%

A diagnosis of high grade PIN is of clinical significance because it is widely accepted as a precursor to prostatic adenocarcinoma

Analysis of incidence of Granulomatous prostatitis among prostate lesions

Table no: 21

Sl.No	Study	% of granulomatous prostatitis cases
1	Rajeshwari kumbhar et al(12)	1.4%
2	Present study	0.9%

Non specific granulomatous prostatitis is the most common granulomatous inflammatory condition of the prostate accounting for more than half of the cases with prostatic granulomatous inflammation.

V.CONCLUSION

In the present prospective study,comprising of 111 cases of prostatic lesions,Histopathological analysis and role of IHC are studied during the period from January 2020 to December 2020.Following are the main observations

1. Prostatic specimens constituted around 1.4 % of total number of surgical specimens received during the same period
2. Out of cases studied,the commonest pathology encountered was benign lesions constituting 73% and malignant lesions were 27 %.
3. Among the Benign lesions ,Nodular hyperplasia is the most common observed pathology of prostatic lesions(55%).
4. The age incidence of Nodular hyperplasia is between 41 years and 88 years
5. The incidence of low grade PIN(74%) and high grade PIN (26%), among PIN lesions
6. Among the benign lesions,10% cases were diagnosed as nodular hyperplasia associated with prostatitis
7. Among the malignant neoplasm of the prostate,Adenocarcinoma is the commonest.
   Incidence of carcinoma is 27 % and peak age group affected is more than 70 years old
8. Gleason grade 1 seen in maximum number of cases
9. With regard to IHC,30 cases of prostatic adenocarcinoma were selected and tested with HMWCK and AMACR,it is found out that both are sensitive in identifiying histopathologically proven carcinoma

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