HISTOPATHOLOGICAL ANALYSIS OF PROSTATIC LESIONS & THE ROLE OF p63 VERSUS HIGH MOLECULAR WEIGHT CYTOKERATIN IN DISTINGUISHING PROSTATIC CARCINOMA FROM BENIGN PROSTATIC LESIONS & ITS PRECURSORS

DISSERTATION

SUBMITTED FOR M.D PATHOLOGY

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CERTIFICATE

This is to certify that this dissertation entitled "**HISTOPATHOLOGICAL ANALYSIS OF PROSTATIC LESIONS AND ROLE OF p63 VERSUS HIGH MOLECULAR WEIGHT CYTOKERATIN IN DISTINGUISHING PROSTATIC CARCINOMA FROM BENIGN PROSTATIC LESIONS AND ITS PRECURSORS"** is a bonafide record work done by **Dr. R. UMA SAMUNDEESWARI** submitted as partial fulfillment for the requirements of **M.D. Degree Examination - Pathology** to be held in **April 2013.**

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This is to certify that this dissertation titled " **HISTOPATHOLOGICAL ANALYSIS OF PROSTATIC LESIONS AND THE ROLE OF p63 VERSES HMWCK IN DISTINGUISHING PROSTATIC ADENOCARCINOMA BENIGN PROSTATIC LESIONS AND ITS PRECURSORS** is the original and bonafide work done by **DR. R.Uma Samundeeswari** under my guidance and supervision at the Government Medical college, Thanjavur, during the period of her course in M.D. Pathology from April 2010-April 2013 held under the regulation of the Tamilnadu Dr M.G.R Medical university, Guindy, Chennai-600032.

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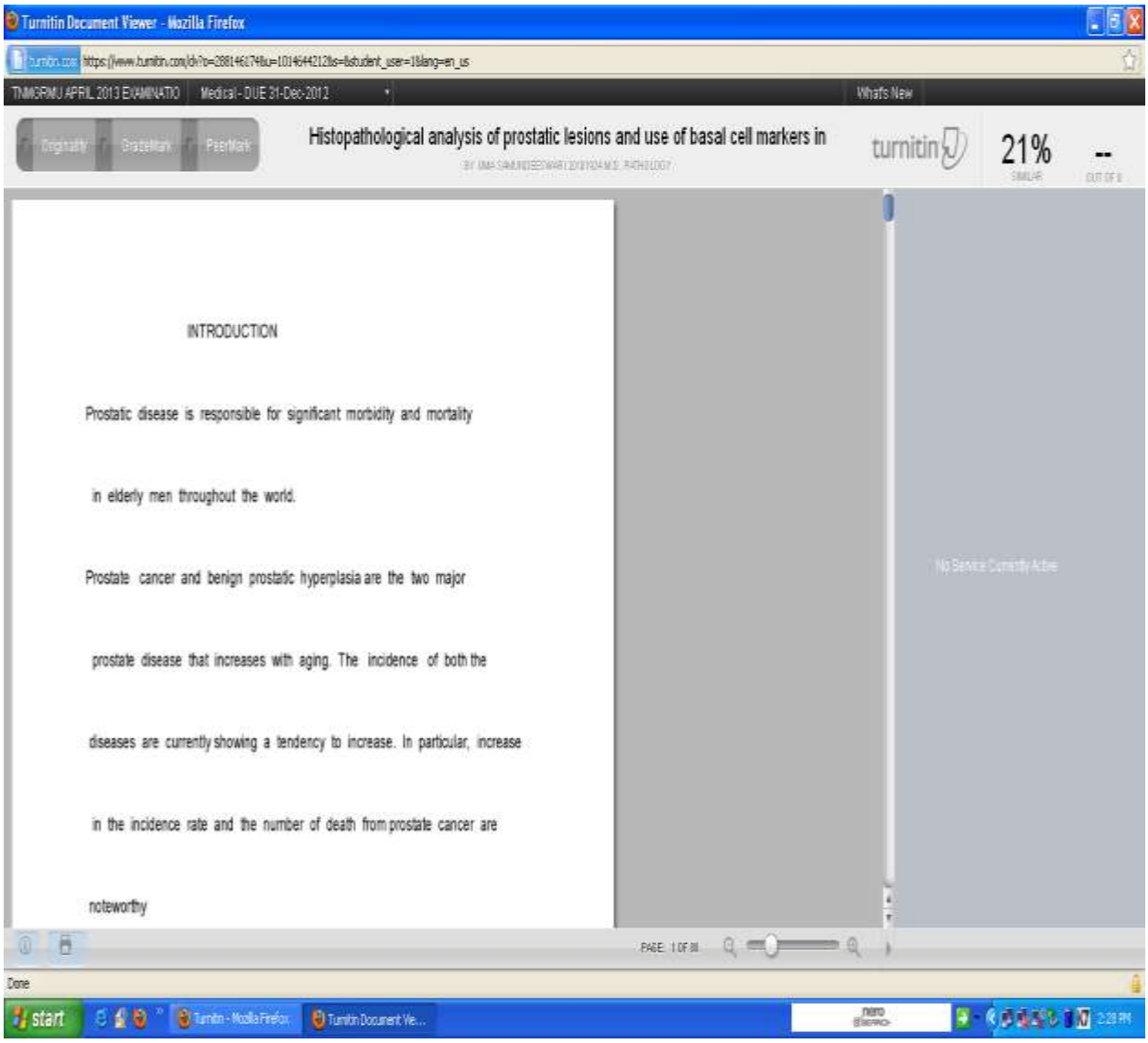
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CONTENTS

LIST OF ABBREVATIONS

1. AAH – Atypical adenomatous hyperplasia
2. AJCC – American joint committee on cancer
3. AMACR – Alpha methyl acyl co-A recemace
4. BCH – Basal cell hyperplasia
5. BPH – Benign prostatic hyperplasia
6. CZ – Central zone
7. DHT – Dihydro testosterone
8. DRE – Digital rectal examination
9. H&E – Haemotoxylin and eosin
10. HGPIN – High grade prostatic intraepithelial neoplasia
11. HMWCK – High molecular weight cytokeratin
12. LGPIN – Low grade prostatic intraepithelial neoplasia
13. N/C – Nuclear cytoplasmic ratio
14. PAP – Prostatic acid phosphatase
15. PIN – Prostatic intraepithelial neoplasia
16. PSA – Prostate specific antigen
17. PZ – Peripheral zone
18. TRUS – Transrectal ultrasound
19. TURP – Transurethral resection of prostate
20. TZ – Transition zone
21. WHO – World health organisation

INTRODUCTION

INTRODUCTION

Prostatic disease is responsible for significant morbidity and mortality in elderly men throughout the world.

Prostate cancer and benign prostatic hyperplasia are the two major prostate diseases that increases with aging. The incidence of both the diseases are currently showing a tendency to increase. In particular, increase in the incidence rate and the number of death from prostate cancer are noteworthy

It is predicted that the number of affected individual will exceed those of gastric cancer, placing it second to lung cancer by the year 2020.[53]

It is not uncommon to underdiagnose small focus of prostatic adenocarcinoma or overdiagnose benign lesions mimicking cancer. It represents a potential liability for pathologist and may cause unfortunate consequences for patients.

The diagnosis of prostatic carcinoma can usually be made on morphologic features which include major and minor criteria, like infitrative glandular growth pattern, absence of basal cells and nuclear atypia, nuclear hyperchromasia, mitotic figures (etc).

However , the diagnosis of prostatic carcinoma on routine biopsies (like Trucut) and TURP can be challenging when pathologist are faced with certain problems such as limited tissue samples, small foci of carcinoma or benign mimickers of prostatic cancer like atrophy, atypical adenomatous hyperplasia, basal cell hyperplasia (etc).[64]

Therefore , the application of immunohistochemistry to distinguish prostate cancer from its benign mimickers and to confirm the diagnosis become helpful and necessary, especially in equivocal cases.[64,67]

The most commonly used basal cell-specific markers in prostatic gland are high molecular weight cytokeratin (HMWCK) and newly described basal cell marker (p63). HMWCK shows cytoplasmic positivity within the basal cells whereas p63 shows nuclear positivity within the basal cells.[67]

This study mainly aims at evaluating the actual incidence of differerent prostatic lesions in this institution, as well as at evaluating and comparing the sensitivity and specificity of HMWCK and p63 in distinguishing prostatic carcinoma from benign prostatic lesions.

AIM OF THE STUDY

AIM OF THE STUDY

1. To analyse the incidence of prostatic lesions in Transurethral resection of prostate, Trucut biopsy in this institution during 2010-2012.
2. To subclassify the lesions and their prevalence.
3. To apply gleason's histological grading system for prostatic carcinoma
4. To study and compare the role of P63,HMWCK in distinguishing prostatic carcinoma from its benign lesions and its precursors.

MATERIALS AND METHODS

MATERIALS AND METHODS

This retrospective study includes 150 cases of prostatic lesions, referred from Urology department of Thanjavur Medical College, Thanjavur, during the 2 years period from Jan 2010 to March 2012.

A detailed clinical history like age, duration of complaints, nature of symptoms and haematological investigations were done in all cases.All types of prostatic specimens including TURP and Trucut biopsies were considered.

All the prostatic specimens were subjected to a careful and detailed gross examination. Fixation was done by neutral buffered 10% formalin and paraffin embedded tissue sections from these specimens were used for microscopic study.

Sections were made manually with histokinette of thickness 2 - 4 micro m. Staining was done with routine haematoxylin and eosin and every slide was examined thoroughly and looked for the presence of malignancy, prostatic intraepithelial neoplasia, metaplasia, acute and chronic inflammation and other secondary changes associated with benign nodular hyperplasia.

Immuno histochemistry with basal cell specific markers like HMWCK (34βE12) and p63 was done for 12 cases including nodular Hyperplasia of prostate, prostatic intraepithelial neoplasia, benign mimickers like basal cell hyperplasia, atrophy and prostatic adenocarcinoma.

Statistical analysis was done to compare the role of HMWCK and p63 in these cases.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The human prostate gland is one of the male accessory sex organ which include the prostate, seminal vesicle and bulbo urethral gland[82,86]

ANATOMY

It is a pyramidal fibromuscular gland which surrounds the prostatic urethra from the bladder base to the membranous urethra and is itself surrounded by a thin tough connective tissue capsule.

It lies at a low level in the lesser pubis, behind the inferior border of the symphysis pubis and pubic area below the neck of the urinary bladder and anterior to the rectal ampulla through which it can be palpated.[95]

The weight of normal adult prostate is 20 g on an average. Anatomically, prostate is divided into five lobes anterior, posterior, median and two lateral lobes. The contemporary classification of the prostate into different zones was based on the work of Mc.Neal.[10]

He divided prostate into peripheral zone (PZ), which lies mainly posteriorly [7o% of the prostate] and from which most carcinomas arise and a central zone (CZ), which lies posterior to the urethral tumour and

above the ejaculatory ducts.[25% of prostate]. There is also a periurethral and transitional zone (TZ) [5% of prostaticvolume] which is the most common location of benign prostatic hyperplasia[92]

The capsule of the prostate is made up of inner smooth muscle layer and outer collagen layer. The glandular elements are less at the apex with ill defined capsule which is a mixture of striated,smooth muscle and fibrous connective tissue. Hence the prostatic capsule is not a true capsule but a pseudocapsule.[93]

The understanding of anatomical lobes and surgical zones are essential in interpretation of prostatic biopsy specimens sent in transurethral resection of prostate [TURP] and in trucut needle biopsy.

The prostate is supplied by branches from the inferior vesical, internal pudental and middle rectal arteries. It drains into vesical and internal illiac veins.

Lymphatics from the prostate drain chiefly into internal illiac, sacral and obturator nodes. The prostate has an abundant nerve supply from the inferior hypogastric plexus.[91,95]

HISTOLOGY[91]

The Prostate is composed of glands and stroma which has fibroblast and smooth muscles. The duct and glandular system is arranged in a complete architectural pattern. The ducts consist of elongated branching tubular structures and end blindly in rounded acini. The glands are lined by three distinct epithelial cell populations.

Secretory

Basal

Neuroendocrine cell

The luminal secretory cells are cuboidal to columnar, have pale to clear cytoplasm. These stain positively with prostatic acid phosphatase, prostate - specific antigen and other enzymes. Non neoplastic secretory cells also may contain acid and neutral mucins, lipofuscin and melanin.

Basal cells are peripherally located in the gland between the secretory cells and basement membrane. These are cigar shaped with the long axis parallel to the basement membrane. The basal cells may have either a finely granular, uniform distributed chromatin pattern and show cytoplasmic staining with high molecular weight keratin or nuclear reactivity for p63.

These are thought to represent the stem cell compartment within the prostate. Neuroendocrine cells are irregularly distributed throughout the ducts and acini and are difficult to recognize without the use of special staining techniques.

HISTOCHEMICAL FEATURES[10]

Prostatic secretion is commonly present atleast focally, which is PAS positive. Neutral mucin may also be seen in prostatic adenocarcinoma.

Acid mucins are not usually found in normal or hyperplastic glands but are, found focally in prostatic adenocarcinoma.

Corpora amylacea is inspissated secretions present within the lumina of the glands. They are seen in approximately 25% of prostate glands in men aged between 20 - 40 years and very rarely in carcinoma. They are round laminated hyaline eosinophilic structures that may be calcified.

IMMUNOHISTOCHEMICAL FEATURES[4,20,37,52,57,58,64,67,80,85,89,96,100]

PSA is a diagnostic and a predictive marker in prostatic carcinoma. Since it is present in benign and malignant cells of the prostate,it cannot be regarded as a specific marker for prostatic carcinoma, which include antibodies to HMWCK ,CK5/6, p63. These markers are specific and are commonly used for the demonstration of the basal cells.

Normal basal cells of the prostate will exhibit positivity for HMWCK in most of the glands. p63 is a nuclear transcription factor, which regulates prostatic glands.The sensitivity and specificity of p63 is comparable to HMWCK for the demonstration of basal cells of the prostate. Since it is a nuclear marker, the detection of positively stained cells is easier with p63 when compared to HMWCK.

A recently discovered tumor marker for prostate cancer AMACR, P504S, AMACR-P is being used increasingly in conjunction with H&E histology and basal cell markers in work up of prostate needle biopsies.

WHO Classification of prostatic hyperplasia, Tumours and Tumour like lesions.[45]

Epithelial tumors

Glandular neoplasm

Adenocarcinoma (acinar)

- Atrophic
- Pseudo hyperplastic
- Foamy
- Colloid
- Signet ring
- Oncocytic
- Lymphoepithelioma - like
- Carcinoma with spindle cell differentiation

    (carcinosarcoma, sarcomatoid carcinoma)

Prostatic intraepithelial neoplasia (PIN)

Ductal adenocarcinoma

- Cribriform
- Papillary
- Solid

Urothelial tumors

Urothelial carcinoma

Squamous tumors

Adenosquamous carcinoma

Squamous cell carcinoma

Basal cell tumors

Basal cell adenoma

Basal cell carcinoma

Neuroendocrine tumors

Endocrine differentiation within adeno carcinoma

Carcinoid tumor

Small cell carcinoma

Paraganglioma

Neuroblastoma

Prostatic stromal tumors

Stromal tumor of uncertain malignant potential

Stromal sarcoma

Mesenchymal tumors

Leiomyosarcoma

Rhabdomyosarcoma

Chondrosarcoma

Angiosarcoma

Malignant fibrous histiocytoma

Malignant peripheral nerve sheath tumor

Hemangioma

Chondroma

Leiomyoma

Grandular cell tumor

Hemangiopericytoma

Solitary fibrous tumor

Hematolymphoid tumors

Lymphoma

Leukemia

Miscellaneous tumors

Cystadenoma

Nephroblastoma (Wilms tumor)

Rhabdoid tumor

Germ cell tumors

Clear cell adenocarcinoma

Melanoma

Metastatic tumors

Tumour like lesions[17]

Benign prostatic lesions--- 1. Epithelial

2. stromal

Epithelial ----1.Benign prostatic hyperplasia

2.Basal cell hyperplasia

3.Clear cell cribriform hyperplasia

4.Atrophy

5.Post atrophic hyperplasia

6. sclerosing adenosis etc

Stromal lesions

Benign nodular hyperplasia

The term “nodular hyperplasia” proposed by Moore is a more exact designation than the common name BPH. It represents a nodular enlargement of gland caused by hyperplasia of both glandular and stromal components.[61,86] Nodular hyperplasia commonly affects the transition zone and periurethral area.[10]

Epidemiology:[54,55]

Nodular hyperplasia is extremely common disease of the aging population. It is prevalent in an age group ranging from 4^{th} decade to 9^{th} decade.

Risk factors[10]

The undisputed risk factors for nodular hyperplasia are advanced age and intact androgen supply. These will not occur in men castrated before puberty. The risk is lower in patients with androgen resistance or, deficiencies.

Etiology & pathogenesis[97]

The etiology and pathogenesis of nodular hyperplasia remain poorly understood . A number of factors, including marital status , socioeconomic status, diseases such as diabetes mellitus, hypertension and cirrhosis, have

been investigated and are not thought to be etiologically related to nodular hyperplasia. Testicular androgen production is necessary for the development of nodular hyperplasia.

The principal androgenic hormones are testosterone and dihydrotestosterone (DHT). DHT is the active metabolite of testosterone which many believe is related to the development of nodular hyperplasia.

Clinical features:[10]

Nodular hyperplasia of prostate interferes with the sphincteric function and also causes urinary outflow obstruction at the bladder neck. This leads to symtoms like increased frequency, hesitancy, urgency, decreased size of the urinary stream and force, nocturia and a sense of incomplete bladder emptying.

Gross appearance[10]

Grossly, nodular hyperplasia is composed of variable sized nodules. Cut surface of the nodules is yellow-gray, soft to firm with rubbery consistency and a bulging cut surface. Weight of the gland ranges from 40 to 400g. If there is epithelial predominance, gland shows soft spongy nodules grossly. In case of stromal predominance, trabeculations will be seen in the gland with no apparent nodularity.

Microscopic appearance[84,89,91]

Frank's classification of hyperplastic nodule

The stromal (fibrous or fibrovascular nodule)

The fibromuscular nodule

The muscular nodule

The fibro adenomatous nodule

The fibromyoadenomatous nodule

The glands of nodular hyperplasia are usually medium to large , sometimes cystic and may show architectural complexity and papillary infolding. The epithelium usually has distinct double layer of secretory and basal cells, but the basal cells are not always conspicuous. The cells are often thrown into papillary folds with some stratification, although the nuclei are usually aligned in a single row.

Secondary changes and other findings[91]

Sclerosing adenosis, cystic dilatations, corpora amylacea, calcification, acute and chronic inflammation squamous metaplasia, transitional metaplasia, infarction are at times noted.

Basal cell hyperplasia[17,18,46,51,59,63,76]

It is relatively a common lesion in hyperplastic prostates, being examined in Turp specimens uncommon in needle biopsies. Occurs in the same age group as BPH (mean 74 yrs) . Usually seen in transitionzone , recently it has been recognized that it may also affect the peripheral zone.

Classification of prostatic basal cell hyperplasia[91]

Complete

Incomplete

Atypical basal cell hyperplasia

Atrophy associated

Adenoid cystic like BCH

Microscopically[15,16,44]

BCH is usually characterized by nodular growth of nests, tubules and cords filled with proliferating, small darkly staining basal cells, with scanty cytoplasm, round spindly hyperchromatic nuclei.

May be complete or incomplete on the basis of whether central lumina are absent or present. Complete BCH is characterized by solid nests of basal cells without differentiation.[17] whereas Incomplete BCH often

shows significant central glandular differentiation with cuboidal or columnar secretory cells.

Nucleoli of basal cells are usually indistinct except in atypical basal cell hyperplasia, where it is more prominent (mean dm 1.96 micro m) nucleomegaly, pleomorphism, mitosis.

BCH may also occur in associated with atrophy in the setting of antiandrogen therapy.[46]

Post atrophic hyperplasia[16]

Post atrophic hyperplasia arises from the peripheral zone of the prostate.It consists of combination of cluster of small acini which are atrophic and those that are lined by cells with more clear and ambhophilic cytoplasm. The lobular arrangement is usually maintained.Budding of neoacini can be seen which is lined by cuboidal cells with clear cytoplasm.

Clear cell cribriform hyperplasia[46]

Occurs in transition zone. Cells comprising the cribriform glands have abundant clear cytoplasm and the nucleus is small uniform with inconspicuous nucleoli. These cells are surrounded by basal cell layer in many of the glands.

Atrophy[6,7,9,16,31,98]

It is commonly seen in the peripheral zone usually admixed with areas of nodular prostatic hyperplasia. Atrophy can also be seen in central and transition zones.Radiotherapy and antiandrogen therapy are some of the risk factors.

Various patterns like lobular , sclerotic, cystic and linear patterns are recognized.

The cytological features are common showing small, dark, shrunken cells having uniform nuclei, and lacking nuclear membrane irregularity and chromatin abnormalities ,but show high N/C ratio.

Sclerosing adenosis[15]

Incidental finding in TURP specimens The lesion is partially well circumscribed with minimal infiltrative margin at the periphery. It is composed of well formed small glands admixed with a dense cellular spindle cell stroma.

The glands are lined by clear cells with small uniform nuclei with occasional prominent nucleoli. Basal cell layer is identified in many of glands and shows striking myoepithelial cell differentiation on IHC.

Hyperplasia of mesonephric remnants[23]

These are composed of very small glands with tubular dilatation or arranged in micropapillary pattern with epithelial tufting. The lining epithelium of the glands are cuboidal.

Verumontanum mucosal gland hyperplasia[40]

It is characterized by uniform closely packed glands with corpora amylacea. Basal cells are identified and the nuclear features of malignancy is absent.

Nephrogenic adenoma[17,59]

This can be rarely seen in prostatic urethra which presents as an exophytic lesion, nodule or a flat lesion.

Microscopically, these are characterized by closely packed small tubular structures, lined predominantly by cuboidal or columnar cells at scanty occasionally moderate to large amount of eosinophiic cytoplasm. The nuclei are round and small or pyknotic and lack nucleoli. Some have nuclei with hobnail appearances.

Stromal lesions[17]

Stromal hyperplasia

Leiomyoma

Phyllode - type atypical hyperplasia

Fibroadenoma like hyperplasia

Stromal hyperplasia

Benign stromal hyperplasia is the most common stromal lesion. It is characterized by a bland spindle cell proliferation devoid of glandular elements, these are arranged in a fascicular or whorled pattern.

Leiomyomatous nodules:

Stromal nodules with prominent smooth muscle differentiation often cellular with mild nuclear variability.

Fibroadenoma like hyperplasia:

Glands and cellular fibrovascular stroma are organized in a fashion similar to fibroadenoma of breast.

Phyllodes - type hyperplasia:

In exuberant, sometimes myxoid, stromal proliferation, usually associated with intra luminal polypoid projections like phyllodes tumour of the breast.

PRE - MALIGNANT LESIONS OF PROSTATE[8,11,12,21,26,34,35,42,78,87,90]

The two proposed histological premalignant lesions of prostate are

1. Prostatic intraepithelial neoplasia (PIN)
2. Atypical adenomatous hyperplasia (AAH).

PROSTATIC INTRAEPITHELIAL NEOPLASIA

Definition

It is a neoplastic transformation of lining epithelium of prostatic ducts and acini which is confined within the epithelium.[45]

Bostwick introduced the term PIN in 1987 which replaced the terms used earlier like duct acinar dysplasia,malignant change marked atypia and intraductal dysplasia. PIN is categorized in to low and high grade at present as apposed to the previous three grade system.

PIN - 1 is considered as low grade and PIN 2 and PIN 3 are considered as high grade.

Prostatic intraepithelial neoplasia[(10)]---Diagnostic criteria.

S.NO	FEATURES	LGPIN	HGPIN
1	Architecture	Epithelial Cell Crowding and stratification with irregular spacing.	Similar to low grade PIN withmore crowding and stratification and shows patterns – tufting, micropapillary, cribriform and flat.
2	Cytology		
a)	Nuclei	Enlarged with marked size variation.	Enlarged
b)	Chromatin	Normal	Increased density and clumping.
c)	Nucleoli	Rarely prominent.	Occasionally frequently large and prominent.
3	Basal cell layer	Intact	May show some disruption.
4	Basement membrane	Intact	Intact

There is much evidence supporting a preneoplastic role of PIN. The prevalence of PIN increases with age, peaking in the 6th decade and predating the onset of most carcinomas by more than 5 years.

PIN is much more common in prostates with carcinoma than in benign glands and is more often multifocal, more extensive and of high grade in the former. Like carcinoma, PIN is mainly identified in the peripheral zone and is often adjacent to carcinoma.[47,97]

LGPIN:[45]

In LGPIN, secretory cells of the lining epithelium proliferate and "pill up" with irregular spaces between them. The nuclei are enlarged, vary in size, have normal or slightly increased chromatin and possess small or inconspicuous nucleoli. The basal cell layer normally surrounding secretory cells of ducts and acini remains intact.

HGPIN:[93]

Characterized by cellular proliferation within medium to large glands characterized additionally by cytologic atypia.

Regardless of the architectural pattern, nuclear changes are the hallmark of high grade PIN.

Nuclei are enlarged with hyperchromasia and irregular chromatin nucleoli are large irregular, often multiple and may be focal (grade 2 PIN) or more extensive (Grade 3 PIN)

Various architectural patterns of HGPIN[77]

Tufting : Nuclei become more piled up, resulting in undulating mounds of cells.

Micropapillary pattern : show columns of atypical epithelium that typically lacks fibrovascular cores.

Cribriform pattern : Consists of complex architectural pattern such as Roman bridge and cribriform formation.

Flat pattern : shows nuclear atypia without significant architectural changes.

Histologic variants :[45]

Signet ring variant: HGPIN with signet ring cells is exceedingly rare. Histologically, cyoplasmic vacuoles displace and indent PIN cell nuclei. The vacuoles are mucin- negative by histochemical staining.

Mucinous variant :

It is a rare variant exhibiting mucin filled glands which flatten the lining epithelium.

Foamy variant :

Microscopically, foamy PIN glands are large with papillary infoldings lined by cells with bland nuclei and xanthomatous cytoplasm.

Inverted variant :

This is characterized by polarization of enlarged nuclei towards the lumen of glands with micropapillary pattern.

Small cell neuroendocrine variant :

Rare variant, where small neoplastic cells are arranged like a rosette. The small cells are chromogranin and synaptophysin positive and harbour dense core membrane - bound neuro secretory granules at the ultra structural level.

Clinical significance of PIN :[36,49]

The findings of low grade PIN should not prompt further investigation and it is not reproducibly recognized. In contrast, high grade PIN is an important diagnosis, but should be made with care. If high -

grade PIN is encounted in a needle biopsy specimen, additional levels should be considered to rule out carcinoma.

A diagnosis of high - grade PIN without concurrent carcinoma should prompt careful clinical follow - up and further biopsies especially if the serum PSA is elevated or abnormalities are noted on rectal or ultrasound examination.

ATYPICAL ADENOMATOUS HYPERPLASIA[11,26,40,39]

It is one of the most common lesions that may be confused with carcinoma. Other terms for AAH are adenosis, small gland hyperplasia, atypical adenosis and small acinar atypical hyperplasia.

It is characterized by proliferating small to medium - sized acini that usually form a well - circumscribed nodule but occasionally extend into the adjacent prostatic stroma. This has been identified in 1.5 - 19.6 % of turp and in up to 33% of radical prostatectomies.

Diagnostic criteria for AAH &difference between AAH & low grade adenocarcinoma.[11,26,39,40]

AT LOW MAGNIFICATION

AAH	LOW GRADE ADENOCA
Lobular growth	Infiltrative/Haphazard
Small crowded glands admixed with larger glands	May be pure population of small crowded glands

AT HIGH MAGNIFICATION

AAH	LOW GRADE ADENOCA
Huge ≥3microm nucleoli absent	Occasional huge nucleoli present
Small glands share cytological and nuclear features with admixed benign glands	Small glands differ from surrounding benign glands
Pale to clear cytoplasm	May have amphophilic cytoplasm
Blue tinged mucinous secretion rare	Blue tinged mucinous secretions common
Corpora amylacea common	Rare
Occasional glands with basal cells	Basal cells absent
Basal cell – specific antikeratin antibodies stain basal cells in some glands	Small glands are not immunoreactive to anti keratin antibodies.

AAH has been proposed as a precursor of prostatic adenoma in the transitional zone.

CARCINOMA OF THE PROSTATE[25,28,48,53,65,70,71,73,75]

Prostate cancer is the most common cancer in men accounting for 33% of all malignant tumors in men accounting for 9% of cancer deaths the third highest in men after lung and colorectal cancers.

Both incidence and mortality rate have increased over the last few decades all over the world, even in India.[17]

Prostatic cancer commonly occurs in the sixth to eighth decade, and it is rare before the age of 50. The incidence and mortality rates vary according to geographical location. The incidence is low in the far east and is very high in Northern European and North American populations.[47]

The etiology and pathogenesis of prostate cancer are poorly understood. Both genetic and epigenetic factors have been implicated. There is also familial association in a minority of cases. Risk factors are advancing age, race, heredity and hormonal activity. The other factors are viruses, cadmium exposure, high fat diet vit A and D deficiency .[71,91,93]

Clinical features :

Prostatic carcinoma has no specific presenting symptoms, and is usually clinically silent but locally extensive tumours cause pubic pain , rectal obstruction or bleeding.

Presenting symptoms of metastatic disease include bone pain and tenderness, cord compression. On rare occasions prostatic carcinoma may manifest as a paraneoplastic syndrome.[17,24,93]

Screening methods :[70]

Digital rectal examination, measurement of serum PSA, Transrectal ultra sound (TRUS). The detection rate for DRE is about 0.8 - 2.7 % Most of the carcinomas are detected by transurethral resection.[93,97]

In many patients abnormal PSA elevation may the first finding. A PSA valve above 4ng/ml is considered abnormal.

On TRUS, areas of hypoechogenicity may be detected. But in some cases, no abnormalities are seen. Directed biopsies of abnormal areas can be obtained. If no abnormalities are detected, multiple areas are systematically biopsied. Biopsies are taken in basal mid and apical portions of the gland with or without the transition zone, on both sides.[24,48]

Methods to obtain prostate tissue for detection of prostate neoplasia:

Needle core biopsy :[1,60,75]

Done using 18 gauge needle, post biopsy infection is minimal. Needle biopsy involves tissue only from peripheral zone.

Transurethral resection of prostate :

In TURP, the tissues are removed mainly from periurethral zone, transitional zone, anterior fibromuscular stroma and bladder neck.

If adenocarcinoma is found in TURP samples they indicate that tumour has arisen from the peripheral zone which is the common site for prostatic adenocarcinoma and it has invaded the transition zone which means the tumour is larger at an advanced stage. .

Prostatic enucleation [suprapubic prostatectomy]

In patient with massive BPH this procedure is applied. The specimen usually consists exclusively of transitional zone and periurethral tissue with grossly visible nodules.

Radical prostatectomy:

a)Retropubic prostatectomy allow staging, lymphnode biopsies with frozen section evaluation prior to removal of prostate.

b) perineal prostatatectomy

Prostatic carcinomas can be divided into two major categories

1) Adenocarcinoma of peripheral ducts and acini

2) Carcinoma of large ducts

Most prostatic carcinomas arise in the peripheral zone. Grossly the tumour may be difficult to see, but usually can be identified as gray or yellowish, poorly delineated, firm area. Microscopically, prostaticadenoca exhibit a wide spectrum of appearances ranging from anaplastic tumours to highly differentiated neoplasm, which will be very difficult to differentiate from normal and benign glands.[17,48]

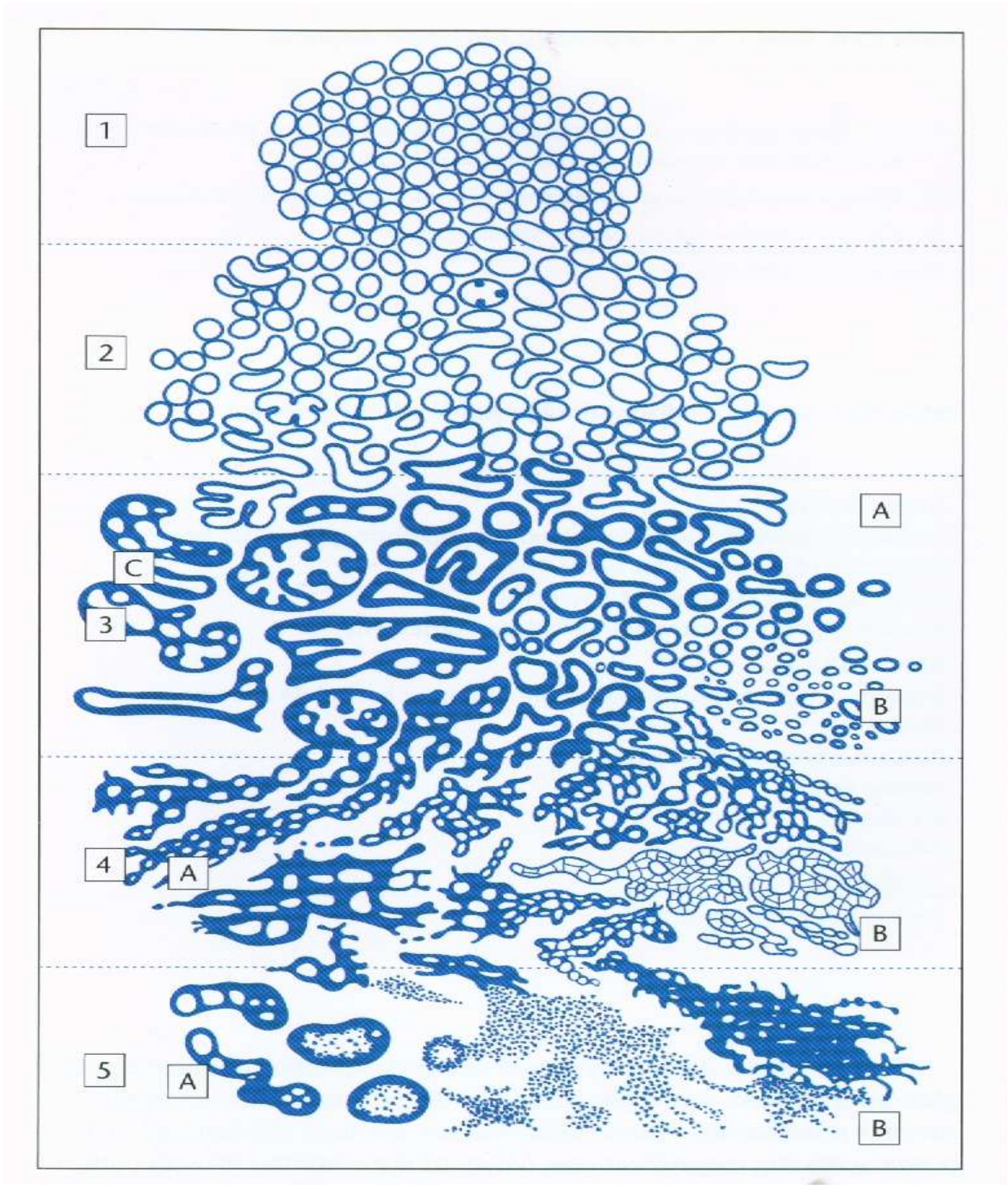
Histological grading

Brode et al is the pioneer who introduced the first grading system in 1925 in an attempt to estimate the malignant potential of cancer. It was based on degree of glandular differentiation, cell morphology, mitotic activity and degree of invasiveness.

Later in 1966 it was Donald f gleason, Who created a gleason grading system[27,32,38,62,79] which later recommended by a WHO consensus conference. He utilized glandular differentiation and growth pattern in relation to stroma to identify tumor grades. Gleason grading system defines five histological pattern or grades with decreasing differentiation.

In 2005, international society of urological pathology consensus conference on gleason grading of prostatic carcinoma gave the modified gleason grading system.

GLEASON'S GRADING SYSTEM : [45,46,79,91,93]



[Adapted from – Benign mimickers of prostatic adeno carcinoma, The Journal of modern Pathology (2004),Vol 17]

This is the most powerful prognostic indicator of prostate carcinoma.[86]

1. Single separate, uniform glands closely packed with definite edges.

2. Single separate, less uniform glands loosely packed with irregular edges.

3A. Single separate variable glands, scattered.

3B . Single separate, very small glands than 3A, scattered.

3C. Sharply,smooth, circumscribed rounded masses of papillary or loose cribriform tumor.

4A. Fused glands, raggedly infiltrating

4B. Same as 4A with large pale cells (hypernephroid)

5A. Almost solid, rounded masses, necrosis (comedocarcinoma)

5B. Anaplastic, poorlydifferentiated with ill defined cords & sheets of cells.

WHO histopathplogical grading (45)

G_x-----Grade cannot be assessed.

G_1----Well differentiated tumour (Gleason score 2-4)

G_2------Moderately differentiated tumour(Gleason score 5-6)

G_{3-4}---Poorly differentiated tumour(Gleason score 7-10)

Gleason score:

Primary grade is assigned to the dominant pattern and secondary to the sub dominant pattern. The two numeric grades are added to obtain the combined gleason score. In tumors with one pattern , the number is doubled.

Stout criteria for prostatic adenocarcinoma[91,93]

1. Glandular pattern - small irregular glands without any particular relation to the adjacent stroma or normal glands.
2. Arrangement of glandular epithelium - lack of basal cells in cancer.
3. Cellular details - large, deeply staining prominent nucleoli.

Criteria for diagnosis of prostatic adenocarcinoma[17,47,93]

Major criteria

Architectural- Infiltrative small glands or glands with cribriform pattern.

Basal cells are absent and the glands are lined by single cell layer.

Features of nuclear atypia like nuclear and nucleolar enlargement are seen.

Minor criteria

Intraluminal crystalloids

Intraluminal wispsy blue mucin.

Mitotic figures.

Adjacent high grade PIN

Amphophilic cytoplasm

Pink amorphous secretions.

Specific features of carcinoma

Glomerulations

Perineural invasion

Collagenous micronodules

Prognostive factors [84]

Category I

Surgical margins

Serum PSA

Pathologic stage

Gleason grade

Category II

Volume of cancer in radical prostatectomy

Volume of cancer in needle biopsies histologic subtype

DNA ploidy

Category III

Androgen receptors

Apoptosis

Lymphnode micro metastasis

MIB - 1

Mitotic figures

Nuclear chromatin texture

Nuclear roundness

PCNA

Perineural invasion

PSA derivatives

Benign mimickers of prostatic adenocarcinoma[15,18,23,41,46,51,59,63,76]

In small biopsy specimens, the diagnosis of prostatic adenocarcinoma is becoming difficult because of the presence of numerous benign lesions which can mimic prostatic adenocarcinoma on histopathological examination. The mimickers of prostatic carcinoma can be classified according to their growth patterns so that it can be compared to the patterns in gleason's gading system. There are four major growth pattern that can be described in a sample from prostate.

1. Small gland
2. Large gland
3. Fused gland
4. Solid

Benign mimickers in relation to major growth pattern of prostatic adenocarcinoma.

The lesions showing small gland pattern are

Cowper's gland

Seminal vesicle

Basal cell hyperplasia

Nephrogenic metaplasia

Mucinous metaplasia

Atrophy

Post atrophic hyperplasia

Atypical adenomatous hyperplasia

Verumontanum mucosal gland hyperplasia

Sclerosing adenosis

Mesonephric gland hyperplasia

Benign nodular hyperplasia

Large gland pattern is seen in

Adenoid cystic like basal cell hyperplasia

Reactive atypia

Cribriform hyperplasia

Fused gland pattern is seen with

Malakoplakia

Paraganglioma

Xanthogranulomatous lesions

Solid pattern is seen in

Granulomatous prostatitis

Prostatitis with crush artifacts.

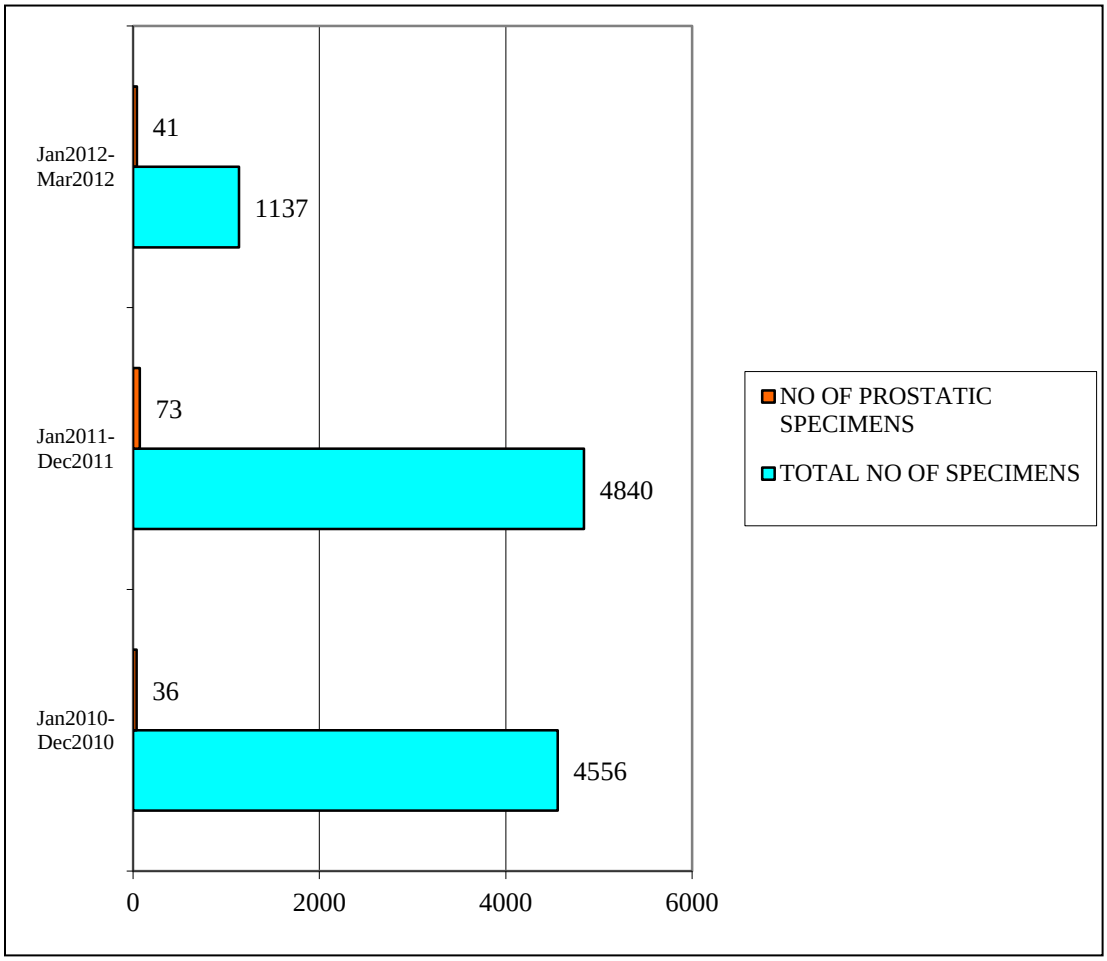
In general, recognition of this differential diagnosis coupled with careful routine microscopy will lead to correct diagnosis. In some instances, however ancillary immunohistochemical studies aimed at identifying prostatic basal cells (34βE12, CK 5/6 , p63), prostatic secretory cells (PSA, PAP, CD 57) neuroendocrine cells (chromogranin, synaptophysin) and inflammatory cells (LCA, CD 68) may be required to resolve a diagnostic dilemma.

The new marker methyl acyl - COA racemase (P50 4s) appears to be of valve in supporting a diagnosis of adenocarcinoma, especially when one is dealing with small foci.

It is important to always be aware of the potential of false - positive cancer diagnosis, when looking at prostatic biopsies and to utilize appropriate consultation and ancillary studies to arrive at a confident and correct diagnosis.[44]

OBSERVATIONS AND RESULTS

CHART 1 : INCIDENCE OF PROSTATIC LESIONS COMPARED TO ALL CASES



OBSERVATION AND RESULTS

The present study deals with the evaluation of various histopathological lesions in Prostatic specimens and the role of basal cell markers in differentiating carcinoma and benign lesions.

TABLE 1:

INCIDENCE OF PROSTATIC LESIONS COMPARED TO ALL CASES

PERIOD	TOTAL NO OF SPECIMENS	NO OF PROSTATIC SPECIMENS	PERCENTAGE
Jan2010- Dec2010	4556	36	0.34%
Jan2011-Dec2011	4840	73	0.69%
Jan2012-Mar2012	1137	41	0.39%
Total	10,533	150	1.42%

A total of 10533 surgical specimens received in the department of pathology, Thanjavur Medical College, Thanjavur during the study period, of which prostatic specimens constituted 150 cases (1.42%) cases. (chart 1)

CHART 2 : FREQUENCY OF BENIGN, MALIGNANT LESIONS COMPARED TO

TOTAL PROSTATIC LESIONS

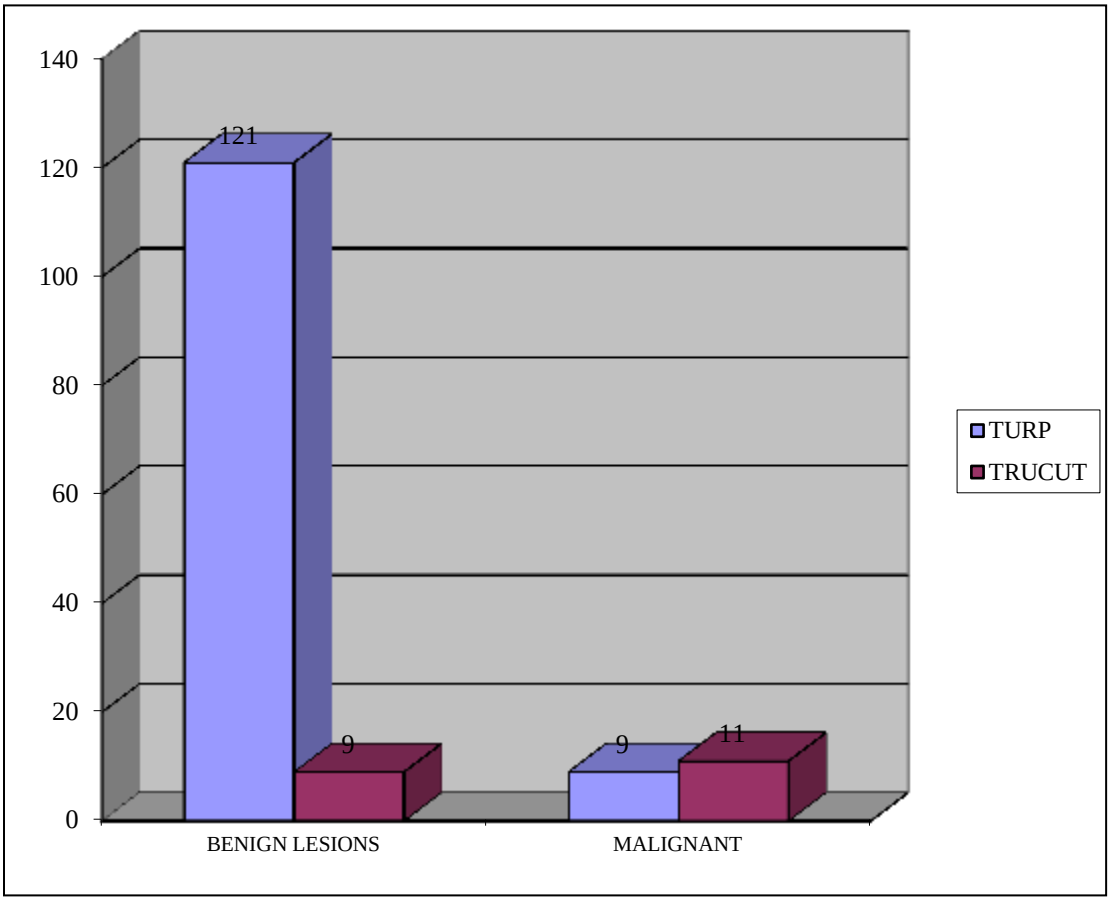


TABLE 2:

FREQUENCY OF BENIGN AND MALIGNANT LESIONS

GROSS	BENIGN LESIONS	MALIGNANT	TOTAL
TURP	121	9	130
TRUCUT	9	11	20
TOTAL	130 (86.67%)	20 (13.33%)	150 (100%)

PROSTATIC LESIONS:

Out of 150 prostatic specimen received, 130 were benign lesions and prostatic malignancy was diagnosed in 20 cases. Incidence of benign lesions was 86.67% and malignant lesions was 13.33% in this study. (chart 2)

Nature of prostatic specimen:

Among the benign lesions, 121 cases were reported in TURP specimen and 9 cases in Trucut biopsy. Malignant lesions were diagnosed in 9 TURP samples and 11 in Trucut biopsy samples.

CHART 3 : INCIDENCE OF PROSTATIC CARCINOMA

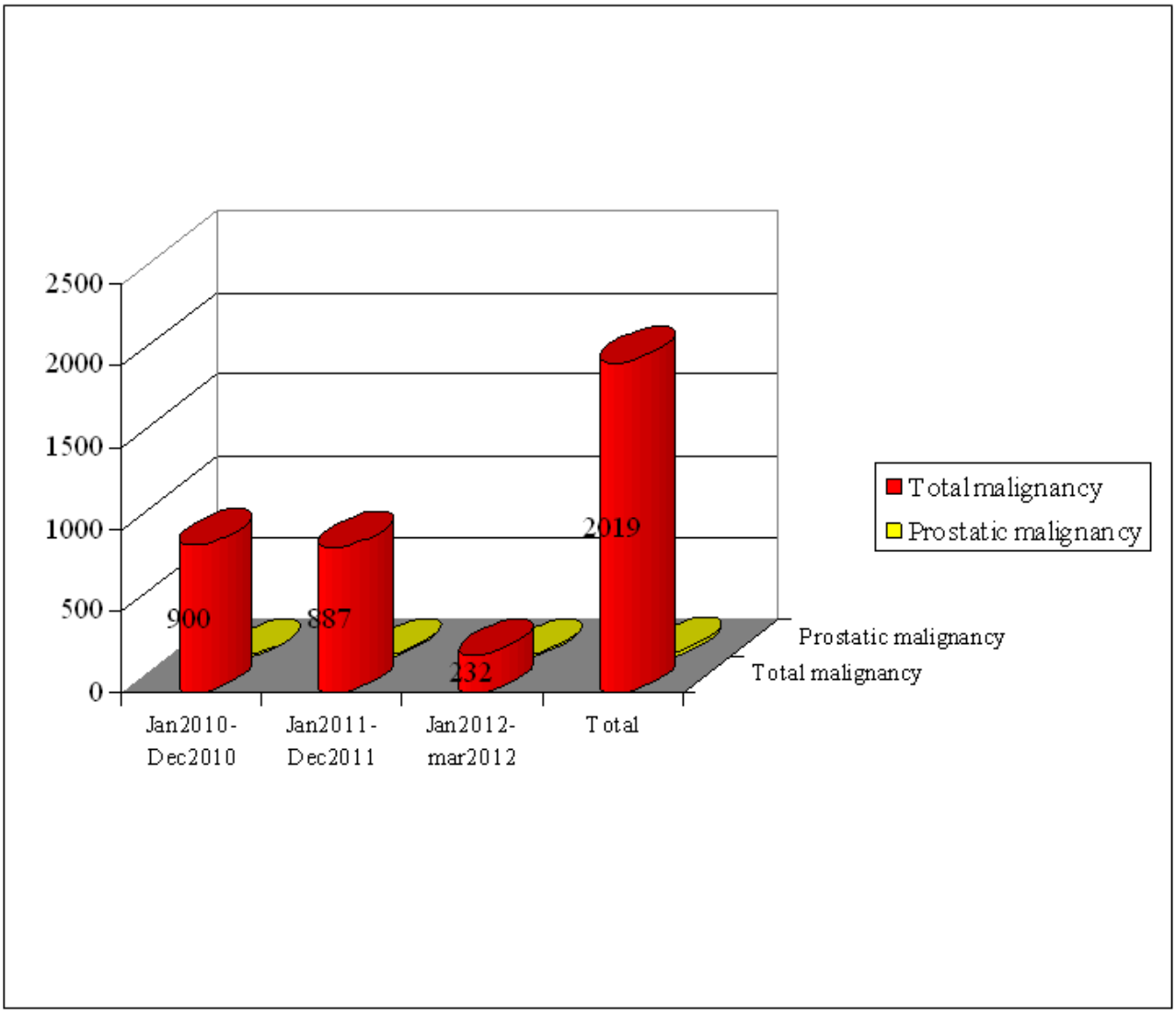


TABLE 3:

INCIDENCE OF PROSTATIC CARCINOMA

Period	Total no: specimens	Total neoplasm	Total malignancy	Prostatic malignancy	Percentage
Jan2010-Dec2010	4556	1520	900	2	0.22%
Jan2011-Dec2011	4840	1380	887	9	1.02%
Jan2012-mar2012	1654	403	232	9	1.02%
Total	11050	3303	2019	20	2.26%

Out of 11050 total specimens, received during study period, total malignancies were 2019 and out of these, prostatic malignancy constituted 2.26%. (chart 3)

CHART 4: AGE INCIDENCE OF VARIOUS PROSTATIC LESIONS

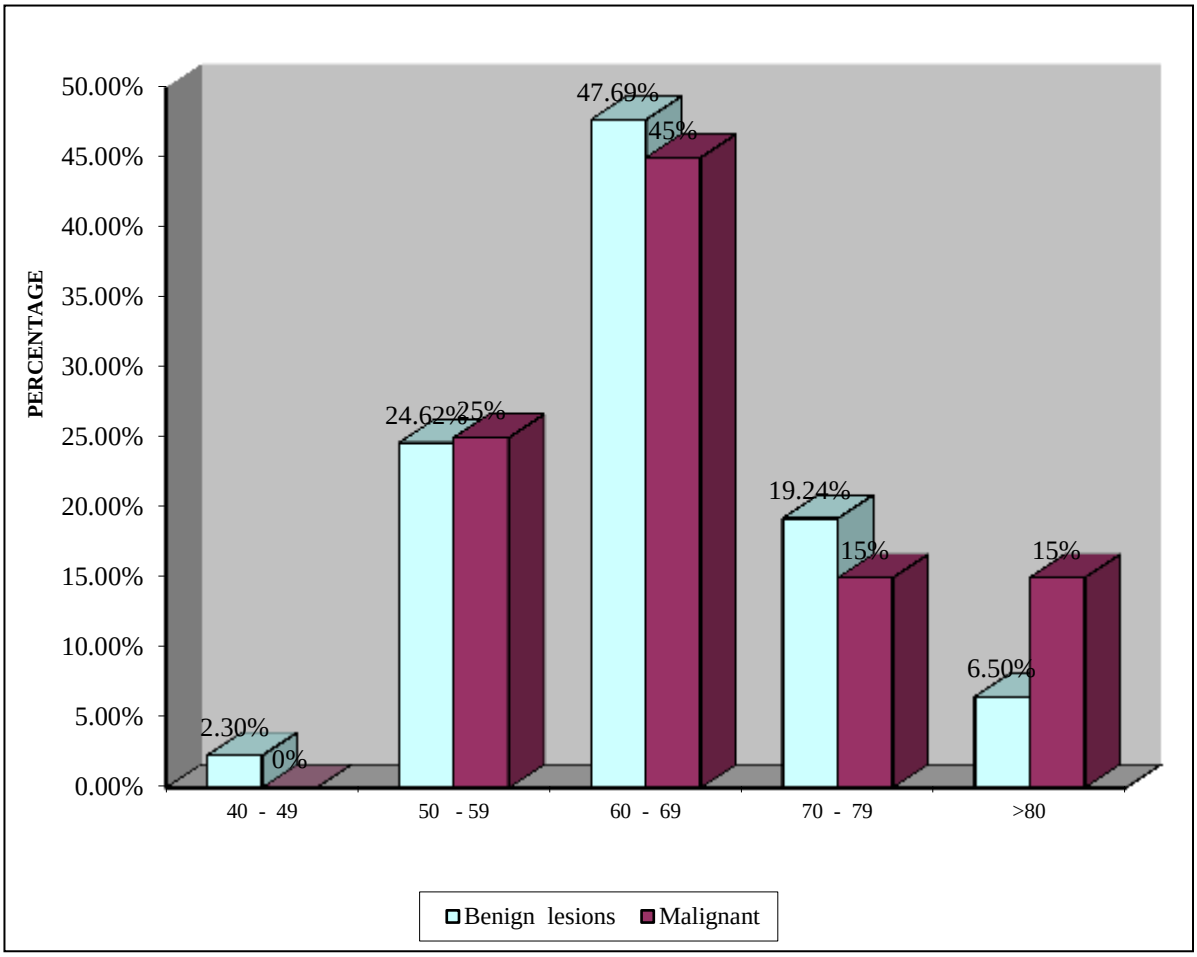


TABLE 4:

AGE INCIDENCE OF VARIOUS PROSTATIC LESIONS

S.No	Age (Years)	Benign lesions	Malignant	Total
1	40 - 49	3 (2.3%)	(0%)	3 (2%)
2	50 - 59	32 (24.62%)	5 (25%)	37 (24.67%)
3	60 - 69	62 (47.69%)	9 (45%)	7 (47.33%)
4	70 - 79	25 (19.24%)	3 (15%)	28 (18.67%)
5	>80	8 (6.5%)	3 (15%)	11 (7.33%)
	TOTAL	130 (100%)	20 (100%)	150 (100%)

Among 130 benign lesions, majority of the benign cases belonged to the age group of 60 - 69 years. Youngest case was 42 years and oldest was 83 years. (chart 4)

Among 20 malignant lesions, majority of the cases were seen in age group of 60-69 years. Youngest person was 55 years and the oldest person was 81 years old in this category.

TABLE 5:

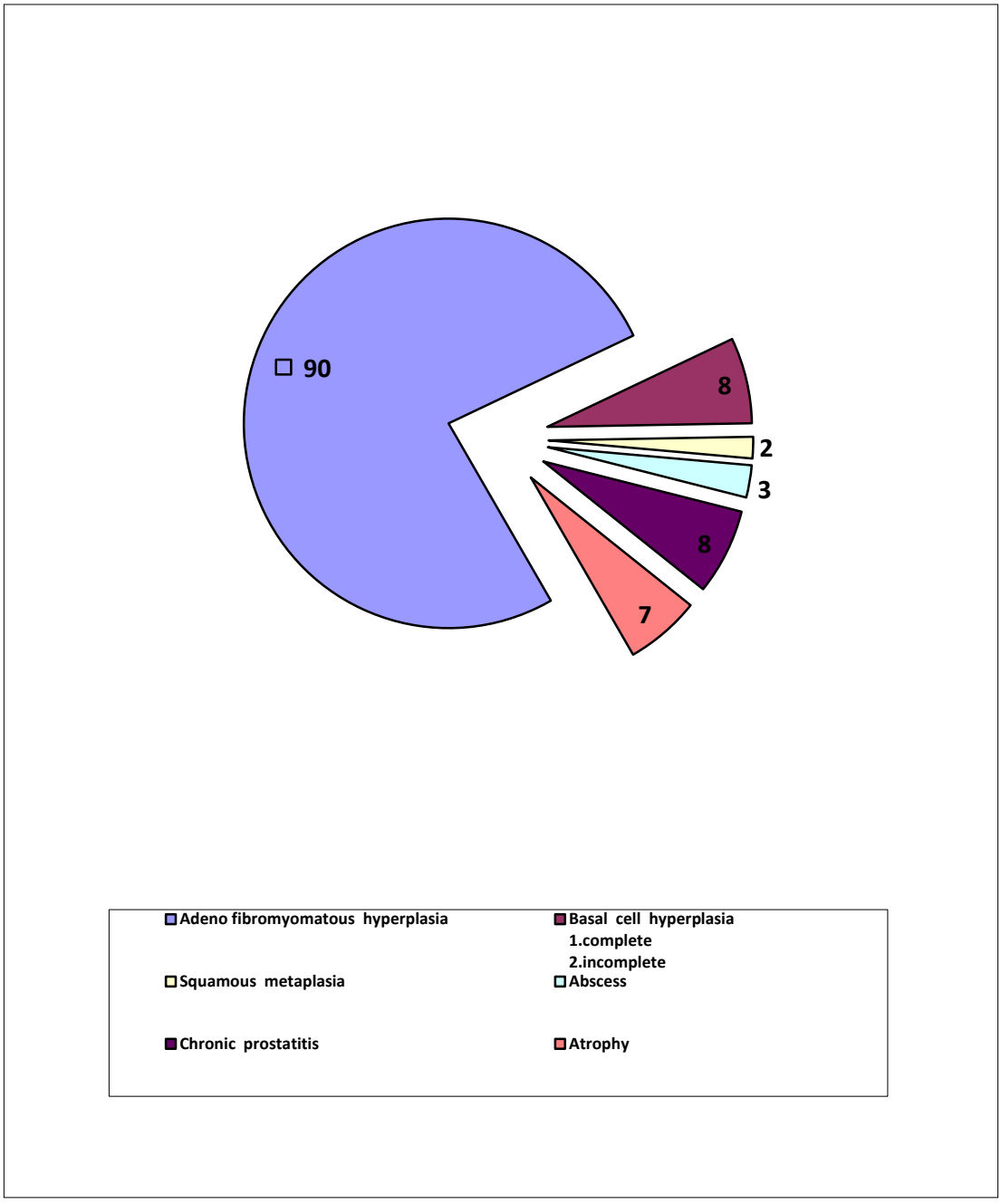
MICROSCOPIC FINDINGS IN BENIGN LESIONS:

Sl.No.	Findings	No.of cases
1	Adeno fibromyomatous hyperplasia	90
2	Basal cell hyperplasia 1.complete 2.incomplete	 2 6
3	Squamous metaplasia	2
4	Abscess	3
5	Chronic prostatitis	8
6	Atrophy	7

Microscopic features in Benign lesions:

In the present study 90 prostatic specimens(fig1A&1B) were showing nodular hyperplasia. The lesions were composed of varying proportion of epithelium and stroma. Corpora amylacea was seen in majority of cases. 8 cases(fig2) were showing chronic inflammatory cell

CHART 5: MICROSCOPIC FINDINGS IN BENIGN LESIONS



infiltrate composed of admixture of lymphocytes and plasma cells. 3 case showed aggregate of neutrophils in and around the acini in the form of abscess.

8 cases were showing nodular hyperplasia associated with basal cell hyperplasia characterised by basal cell proliferation.(fig4A&4B) Out of these 2 showed complete, 6 showed incomplete BCH. 2 cases of nodular hyperplasia were showing squamous metaplasia.(fig3) 7 cases of nodular hyperplasia with atrophy was also found.(fig5) (chart 5)

CHART 6: PROSTATIC INTRAEPITHELIAL NEOPLASIA

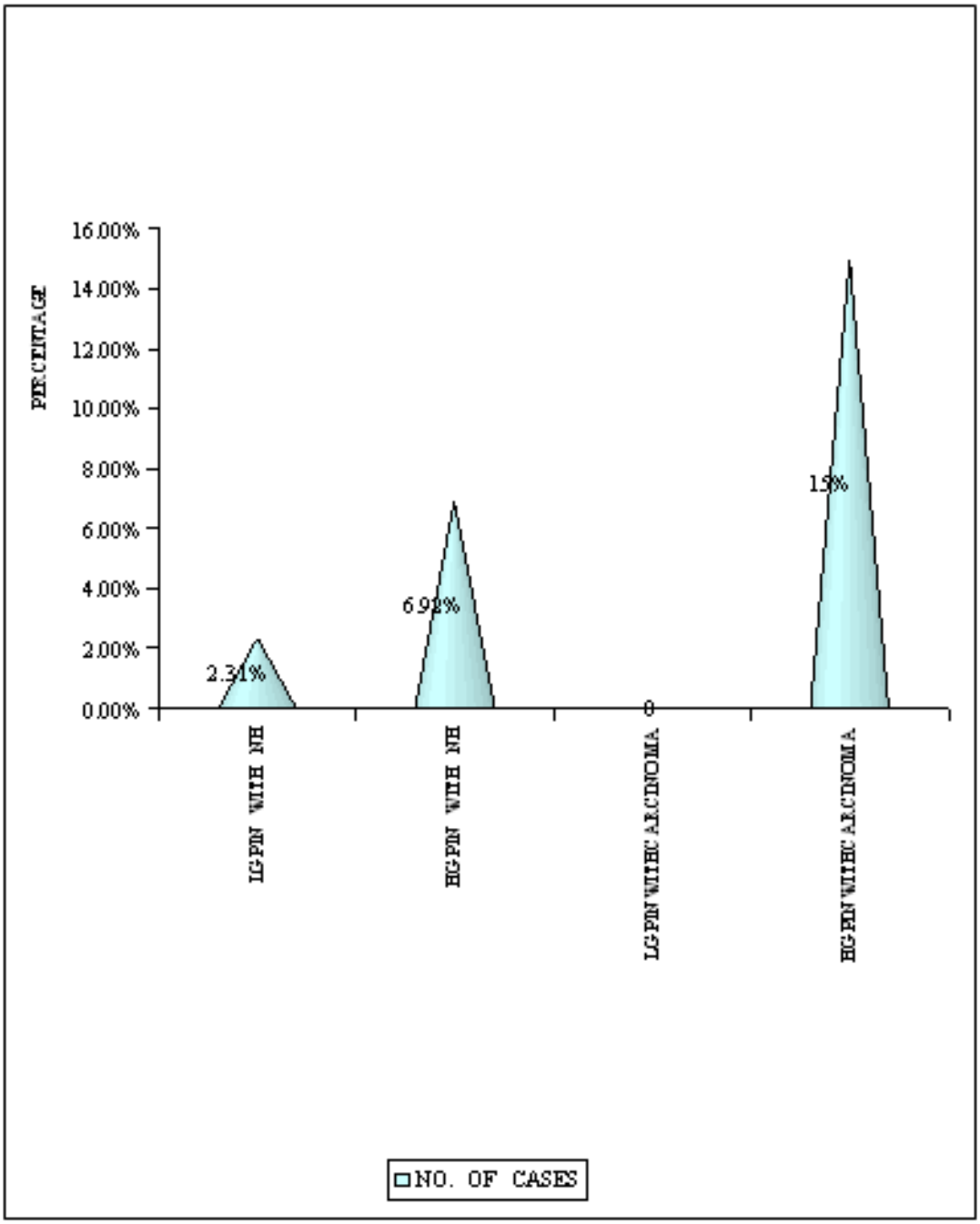


TABLE 6:

PROSTATIC INTRAEPITHELIAL NEOPLASIA :

SL. NO.	PIN LESIONS	NO. OF CASES
1	LGPIN WITH NODULAR HYPERPLASIA	3 (2.31%)
2	HGPIN WITH NODULAR HYPERPLASIA	9 (6.92%)
3	LGPINWITHCARCINOMA	NIL
4	HGPINWITHCARCINOMA	3 (15%)

All the sections of Nodular hyperplasia and Prostatic adenocarcinoma were carefully examined for the evidence of PIN and graded when present.

Low grade PIN was noted in 3 cases(fig7A) and high grade PIN in 9 cases(fig7B) out of 130 cases of nodular hyperplasia & 3 cases of high grade pin out of 20 cases of adenocarcinoma.(figures8-13) (chart 6)

TABLE 7:

GLEASON'S GRADING SYSTEM FOR CARCINOMA :

S. NO.	PATH NO.	HPE DIAGNOSIS	GLEASON'S GRADE	GLEASON'S SCORE
1	500/10	Adenocarcinoma	4+3	7
2	318/10	Adenocarcinoma	4+3	7
3	1185/11	Adenocarcinoma	3+2	5
4	2346/11	Adenocarcinoma	3+3	6
5	2676/11	Adenocarcinoma	4+2	6
6	3036/11	Adenocarcinoma	3+3	6
7	3615/11	Adenocarcinoma	3+4	7
8	3953/11	Adenocarcinoma	3+2	5
9	4083/11	Adenocarcinoma	4+3	7
10	4448/11	Adenocarcinoma	2+2	4
11	812/12	Adenocarcinoma	4+4	8
12	5/12	Adenocarcinoma	4+3	7
13	7/12	Adenocarcinoma	3+3	6
14	115/12	Adenocarcinoma	4+2	6

15	181/12	Adenocarcinoma	3+3	6
16	523/12	Adenocarcinoma	3+4	7
17	1874/12	Adenocarcinoma	3+3	6
18	527/12	Adenocarcinoma	3+4	7
19	1874/12	Adenocarcinoma	4+4	8
20	55/12	Adenocarcinoma	3+4	7

Gleason's score:

All of these 20 malignant cases were graded using Gleason's scoring system. Primary grade is assigned to dominant pattern and secondary grade to subdominant pattern. The two numeric grades are added to obtain the combined Gleason's score. In tumors with one pattern, the number is doubled.

CHART 7: INCIDENCE OF CARCINOMA WITH REFERENCE TO GLEASON'S SCORE

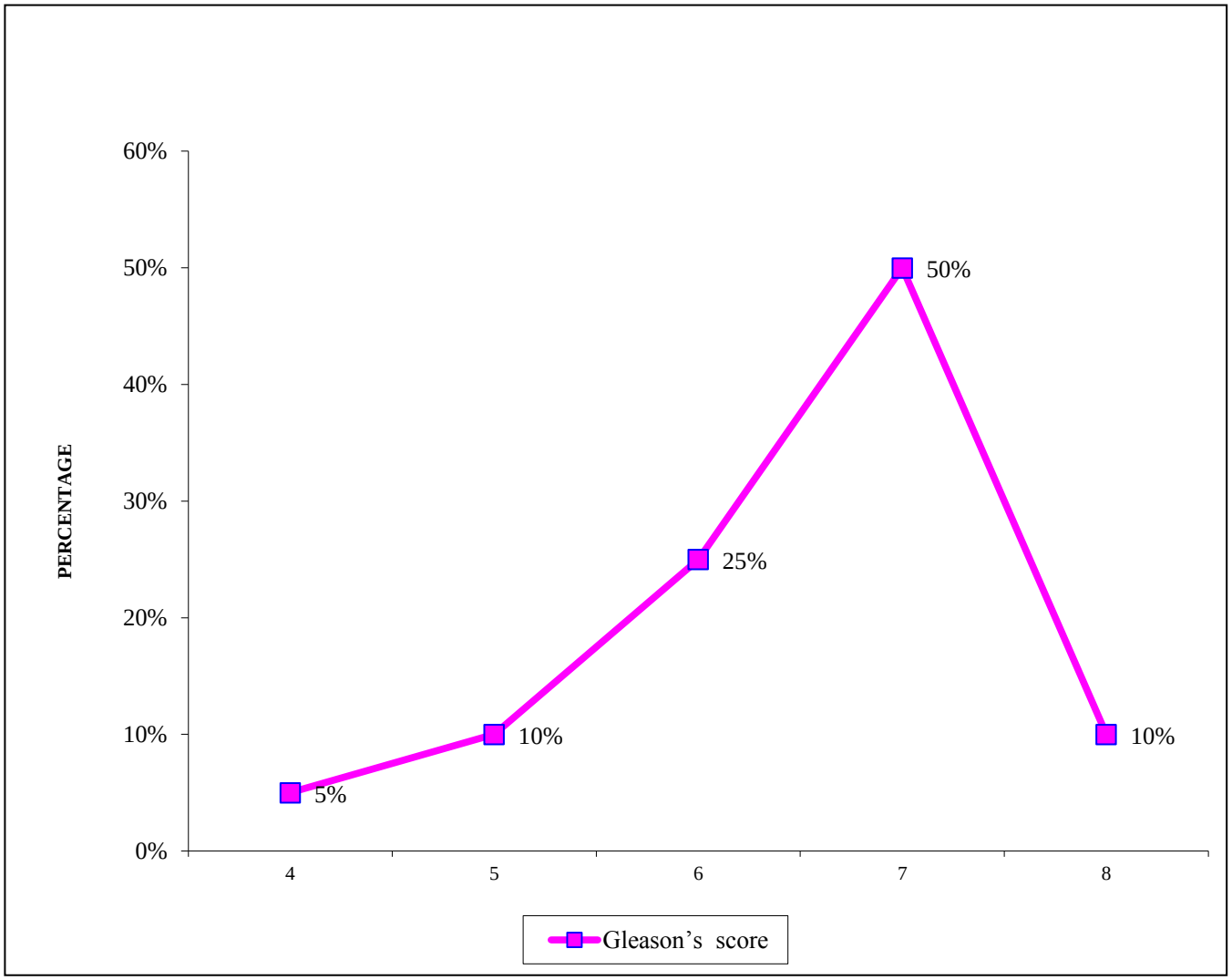


TABLE 8 :

INCIDENCE OF CARCINOMA WITH REFERENCE TO GLEASON'S SCORE

Gleason's score	No. of cases	%
4	**1**	**5**
5	2	10
6	5	25
7	10	50
8	2	10
Total	20	100%

Gleason score of 2-4 was seen in 1 case(5 %). Gleason score of 5-7 was seen in 17 cases(85%). Gleason score of 8-10 (10%) was seen in 2 cases . (chart 7)

CHART 8: FINAL HISTOPATHOLOGICAL DIAGNOSIS

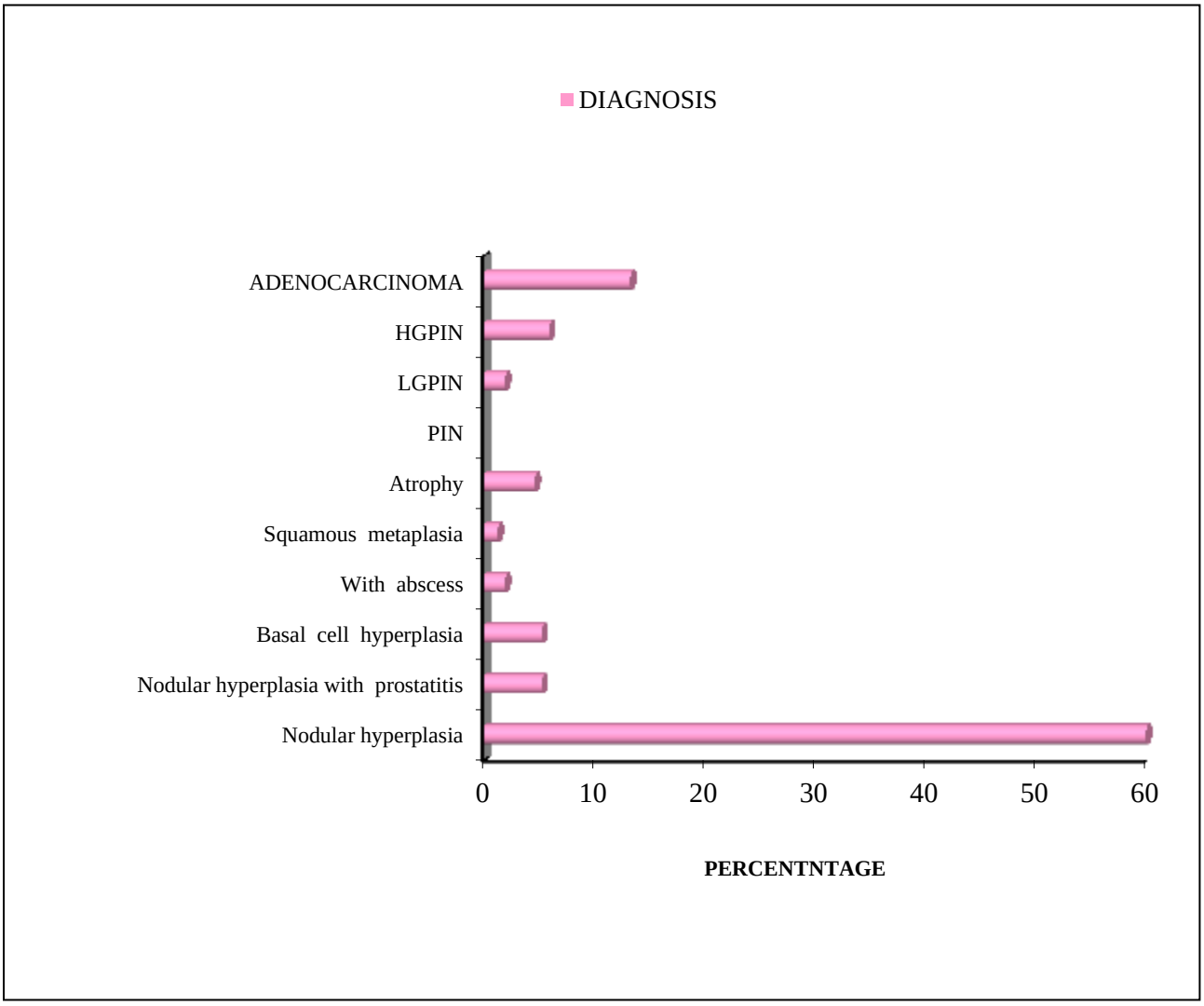


TABLE 9:

Final Histopathological Diagnosis

SL.NO.	DIAGNOSIS	NO. OF CASES	%
1	Nodular hyperplasia With prostatitis	90 8	60 5.33
2	Basal cell hyperplasia	8	5.33
3	With abscess	3	2
4	Squamous metaplasia	2	1.33
5	Atrophy	7	4.68
6	PIN LGPIN HGPIN	 3 9	 2 6
7	Adenocarcinoma	20	13.33

(chart 8)

IMMUNOHISTOCHEMISTRY

A total of 12 cases were selected, comprising 4 cases of benign prostatic hyperplasia,4 cases of PIN , 4cases of prostatic carcinoma to study the immunohistochemical reaction of prostatic basal cells towards HMWCK and P63.

EVALUATION OF IHC

In majority of benign prostatic glands, both antibodies, demonstrated, intense positivity for basal cell - specific immune staining with HMWCK (localized to the cytoplasm) and p63 (localized to the nucleus).

For both stains positive staining was taken as an evidence of benignity whereas negative staining was taken as evidence of malignancy. Basal cell staining was considered positive only if > 10 % of the glands were stained and negative if only ≤ 10 % of the gland were stained.

TABLE 10:

THE RESULT OF FOLLOWING CASES AFTER BEING TREATED WITH HMWCK AND p63 IMMUNOSTANING

SL.NO.	PATH NO.	HPE	HMWCK(+VE/-VE)	p63 (+VE/-VE)
1	3902/10	BPH (Basal cellhyperplasia)	Positive	Positive
2	889/11	BPH (Cystic atrophy)	Positive	Positive
3	530/12	BPH (Crush artifact)	Negative	Positive
4	2413/12	BPH	Negative	Positive
5	4104/12	HGPIN	Positive	Positive
6	3954/11	HGPIN	Positive	Positive
7	3209A/11	HGPIN	Negative	Negative
8	3385/11	HGPIN	Positive	Positive
9	3615/11	Prostatic adenocarcinoma	Negative	Negative
10	704/12	Prostatic adenocarcinoma	Negative	Negative
11	812/12	Prostatic adenocarcinoma	Negative	Negative
12	1185/11	Prostatic adenocarcinoma	Negative	Negative

CHART 9: RESULTS OF HMW-CK STAINING IN BENIGN, PREMALIGNANT AND MALIGNANT PROSTATIC LESIONS

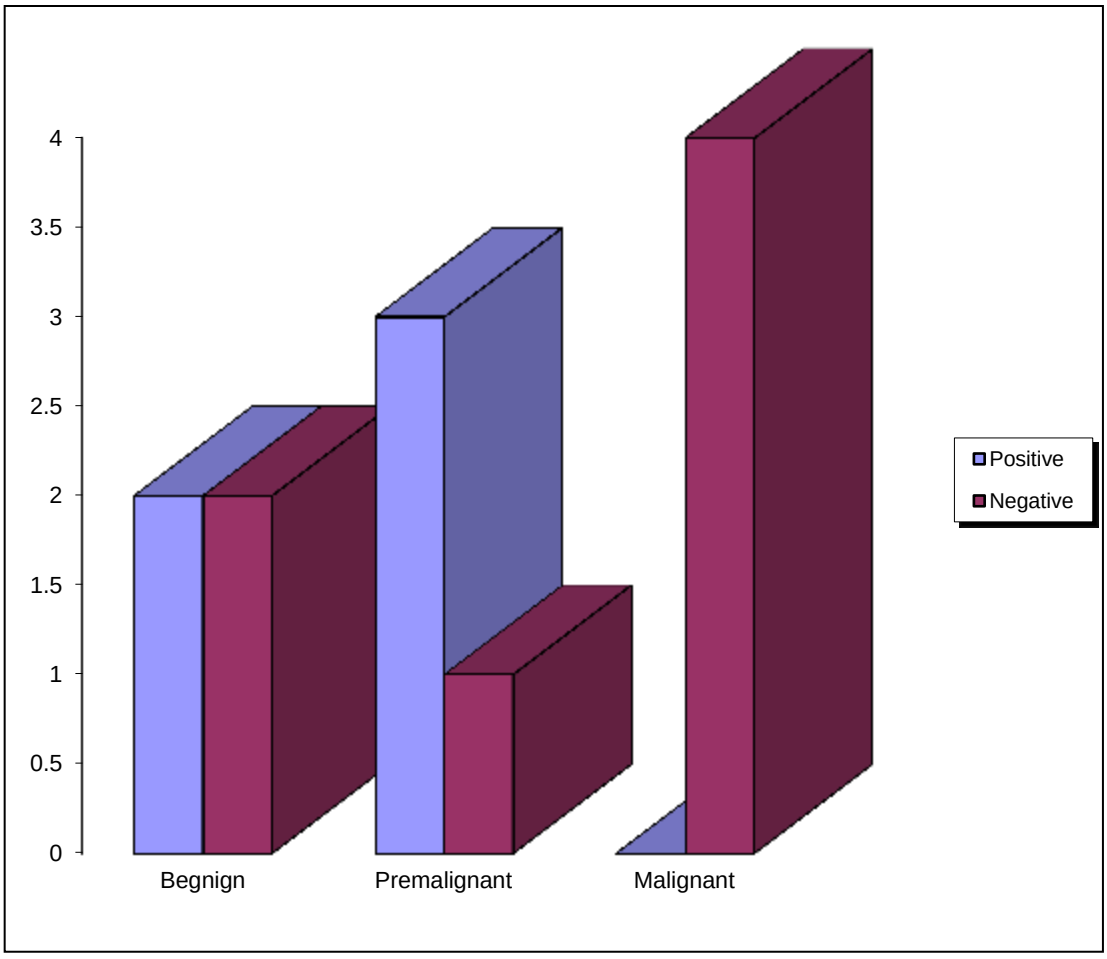


TABLE 11:

RESULTS OF HMW-CK STAINING IN BENIGN, PRE MALIGNANT AND MALIGNANT PROSTATIC GLANDS

RESULTS OF HMWCK STAINING	BENIGN	PREMALIGNANT	MALIGNANT	TOTAL
POSITIVE	2	3	0	5
NEGATIVE	2	1	4	7
TOTAL	4	4	4	12

Sensitivity of HMW-CK = 62.5%

Specificity of HMWCK = 100%

Positive predictive value = 100%

Statistical inference

X^2=4.800, d.f. = 2 & p=.091

p=.091<.05

(chart 9)

CHART 10: RESULTS OF p63 STAINING IN BENIGN, PREMALIGNANT AND MALIGNANT PROSTATIC LESIONS

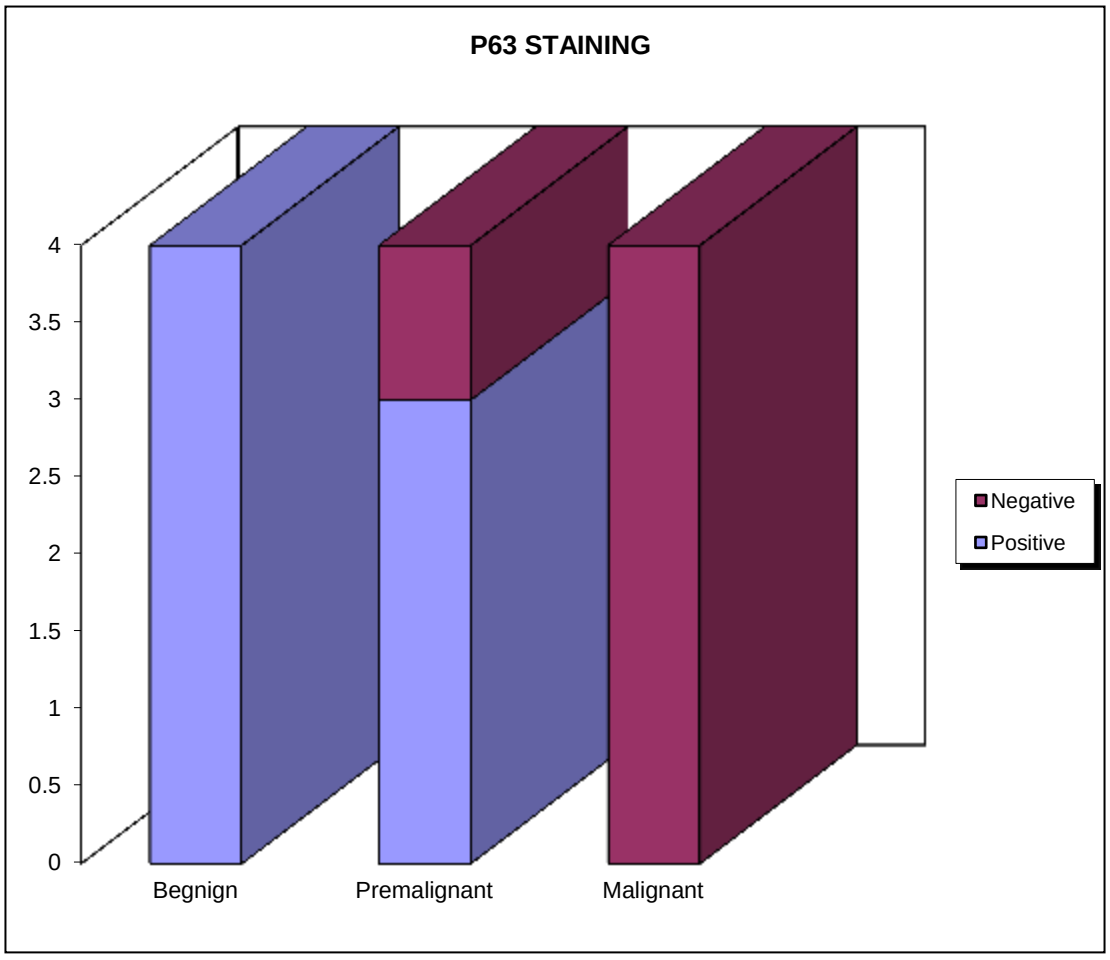


TABLE 12 :

RESULT OF p63 STAINING IN BENIGN, PREMALIGNANT AND MALIGNANT PROSTATIC GLANDS

RESULTS OF p63 STAINING	BENIGN	PREMALIGNANT	MALIGNANT	TOTAL
POSITIVE	4	3	0	7
NEGATIVE	0	1	4	5
TOTAL	4	4	4	12

(chart 10)

Sensitivity of p63 = 87.5%

Specificity of p63 = 100%

Positive predictive value of p63 = 100%

Statistical inference

X^2=8.914,d.f.=2&p=.012

p=.012<.05

From table 11 and 12, it is apparent that all of the malignant glands showed total absence of HMW-CK and p63 staining leading to a specificity of 100% for both HMW-CK and p63 (fig25A&B)

Out of 4 benign glands, only 2 showed positivity for HMWCK and all the 4 showed positivity for p63 staining. (figures 14—21)

Out of 4 premalignant lesions studied with HMWCK and p63, 3 showed positivity for both HMWCK & p63 and 1 showed negativity for the both.(figures 22 A&B, 23A&B)

The sensitivity in identifying basal cells in benign glands was 62.5% and 87.5% for HMW-CK and p63 respectively. The positive predictive value was 100% for both HMW-CK and p63.

The results of our study demonstrates that p63, like HMW-CK, is specific for basal cells in the prostate gland and therefore are negative in areas of prostatic carcinoma. After statistical analysis, p63 is found to be more sensitive than HMWCK in staining benign basal cells in TURP specimens.

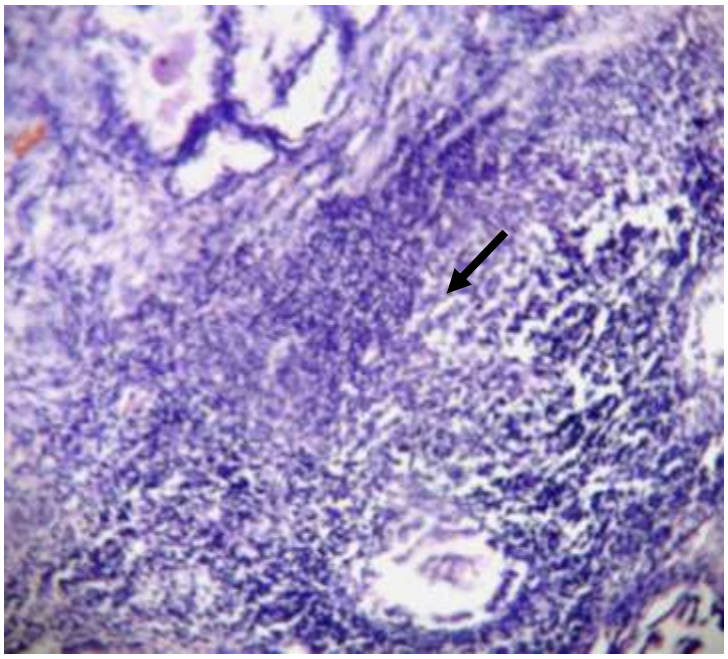


Figure 2 - Chronic prostatitis –showing glands with the admixture of chronic inflammatory cells(H&E) 10X

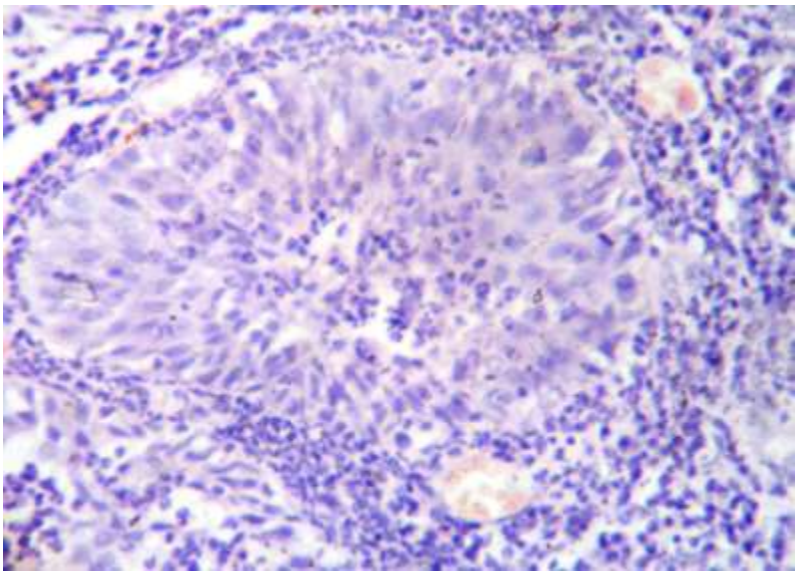
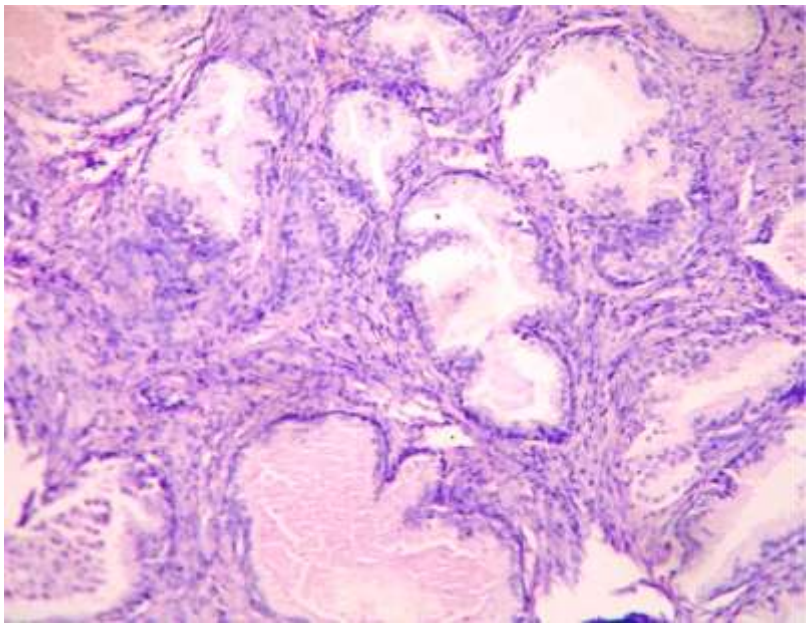


Figure 3 - Inflammation with squamous metaplasia of glandular epithelium – showing cells with abundant eosinophilic cytoplasm& distinct cell borders(H&E)40X



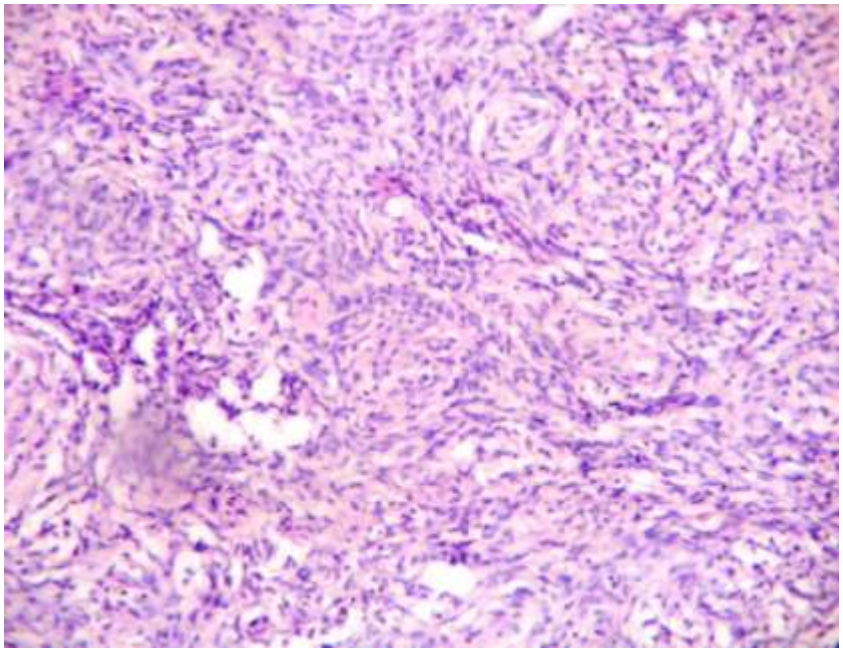


Figure 1A - Benign prostatic hyperplasia – Showing hyperplasia of both glandular and stromal components(H&E)10XFigure 1B - BPH – stromal hyperplasia – showing predominantly stromal component composed mainly of fibrous tissue (H&E)10X

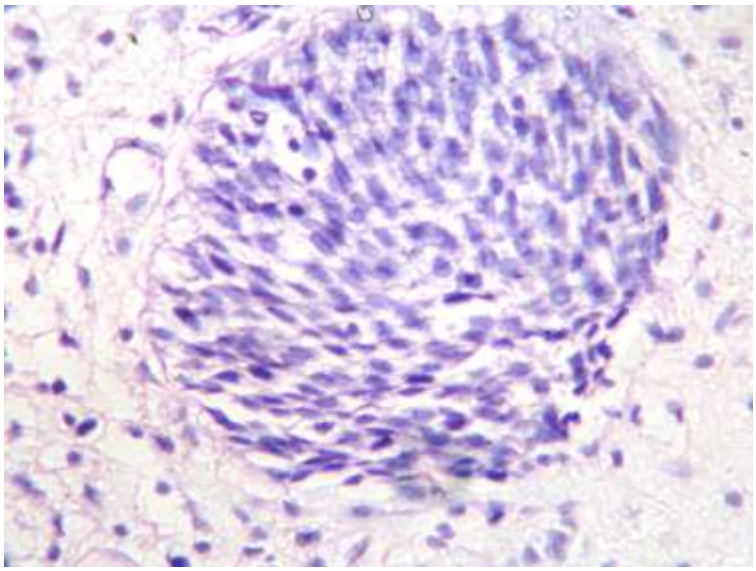


Figure 4A – Basal cell hyperplasia- complete form showing solid nests of cells without luminal differentiation(H&E)40X

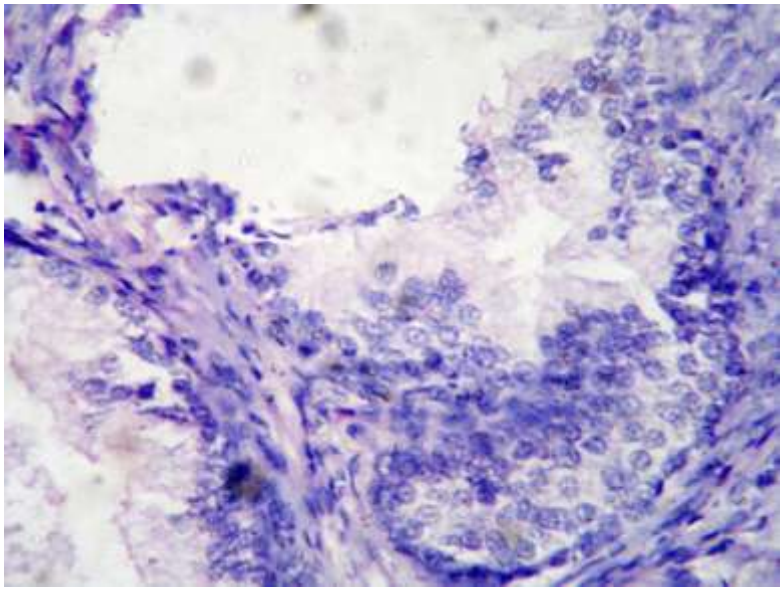


Figure 4B - Basal cell hyperplasia –Incomplete form showing solid nests of basal cells with luminal differentiation(H&E)40X

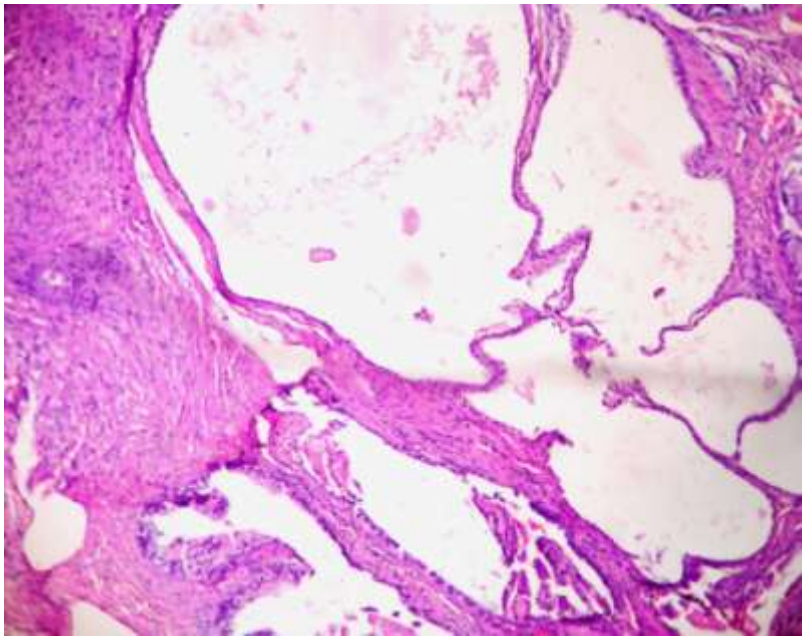


Figure 5 – Cystic atrophy –showing dilated acini, lined by low cuboidal to flattened atrophic cells.(H&E)10X

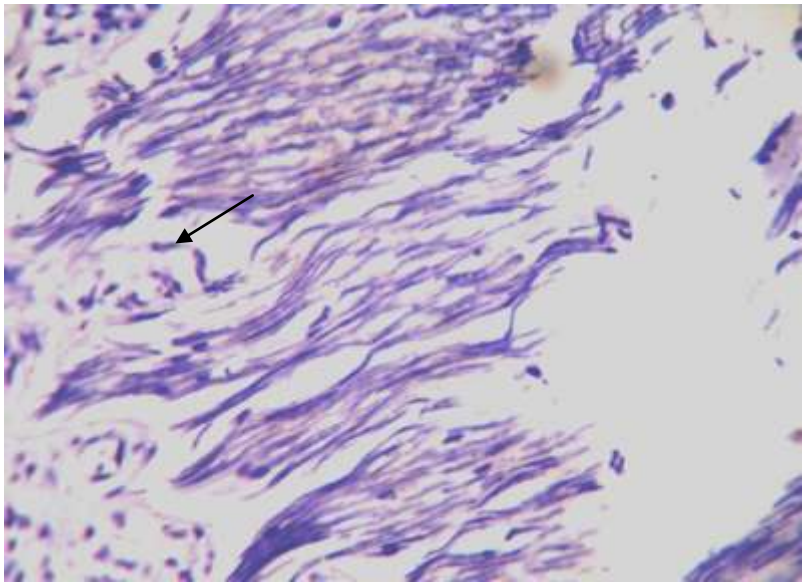


Figure6- Benign prostatic tissue with crush artifact(H&E)10X

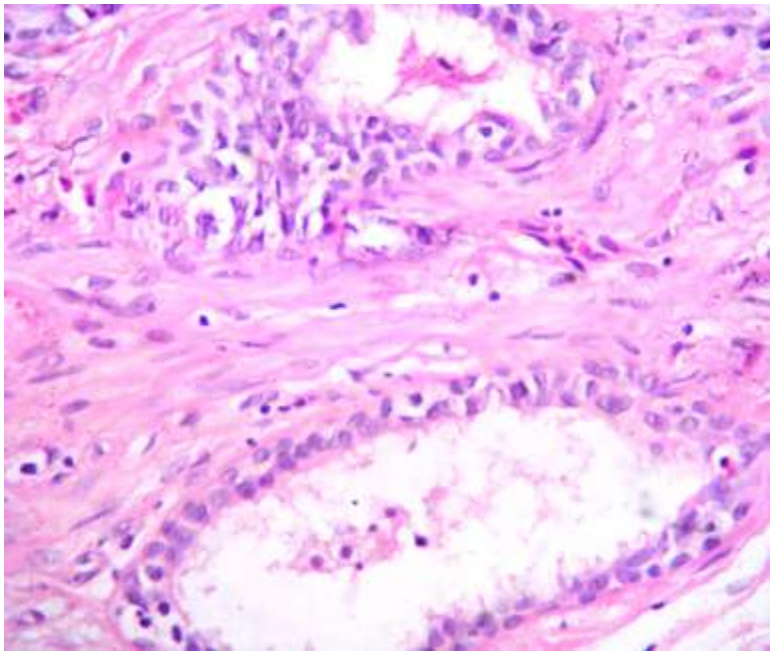


Figure 7A – Low grade prostatic intraepithelial neoplasia –Showing slight enlargement of nuclei (H&E) 40X

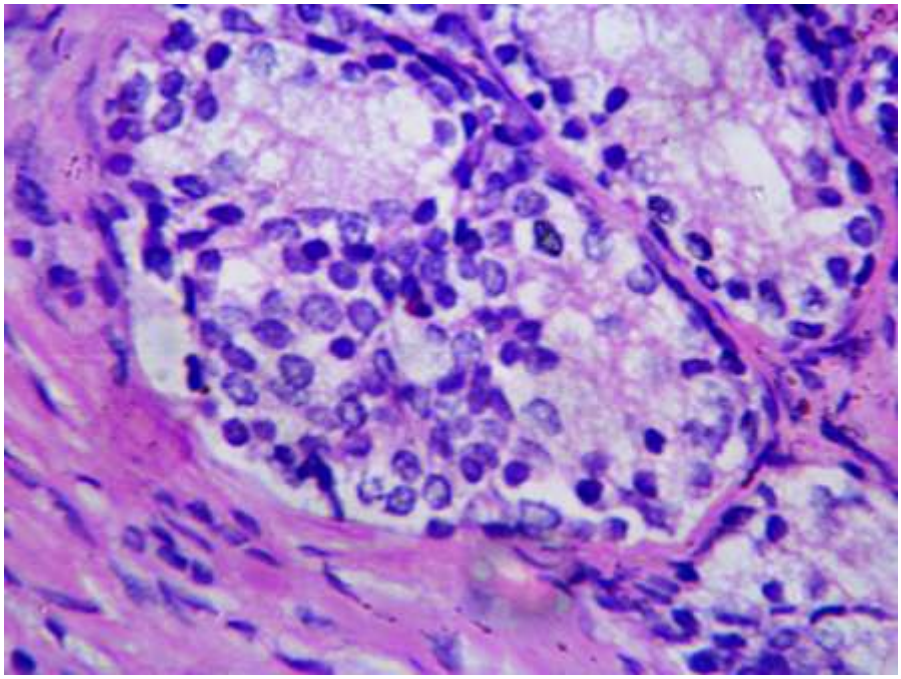


Figure 7B – High grade prostatic intraepithelial neoplasia –showing prostatic gland with stratified lining cells exhibiting cytological atypia(H&E) 40X

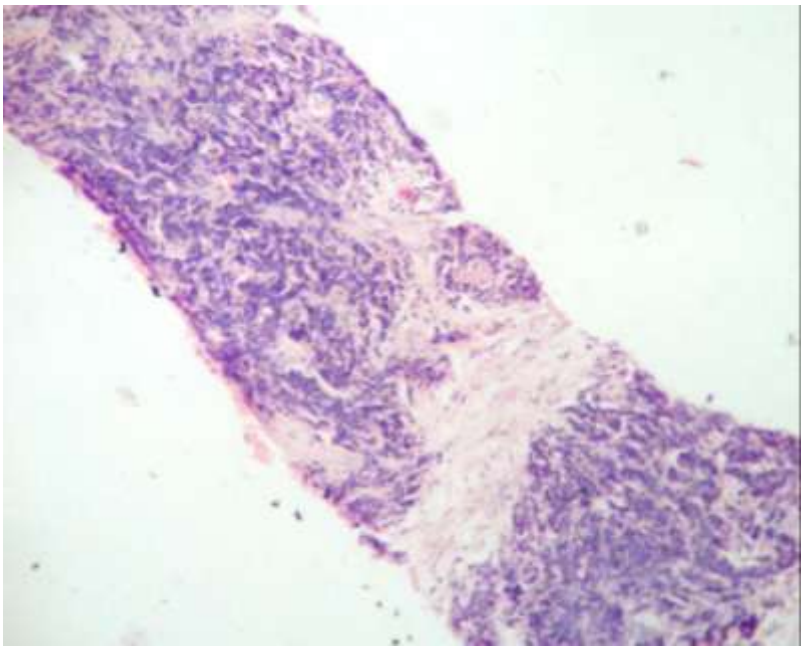


Figure 8– Prostatic adenocarcinoma – needle biopsy –(H&E) 4X

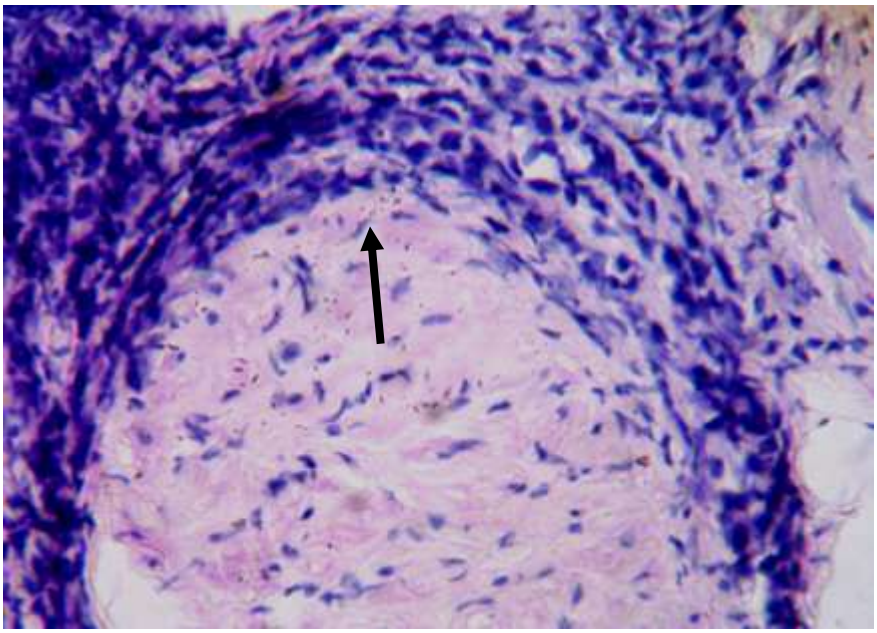


Figure 9– Prostatic adenocarcinoma –Showing characteristic circumferential perineural invasion of tumor cells(H&E) 40X

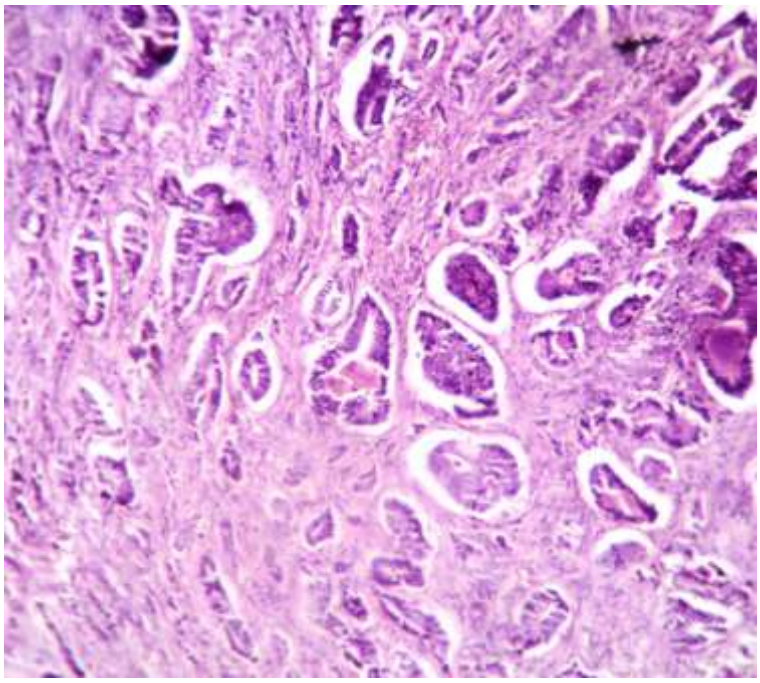
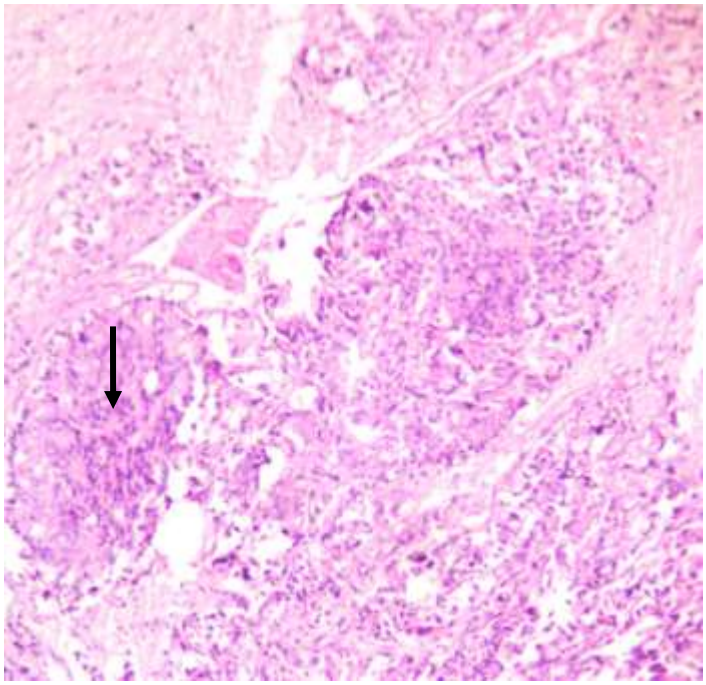


Figure 10- Prostatic adenocarcinoma – Gleason's pattern 2 –composed of less uniform, single, separate, loosely arranged glands(H&E) 10X



igure 11 - Prostatic adenocarcinoma – Gleason's pattern 3 –composed of small to medium sized glands showing angulations with focal cribriform pattern(H&E) 10X

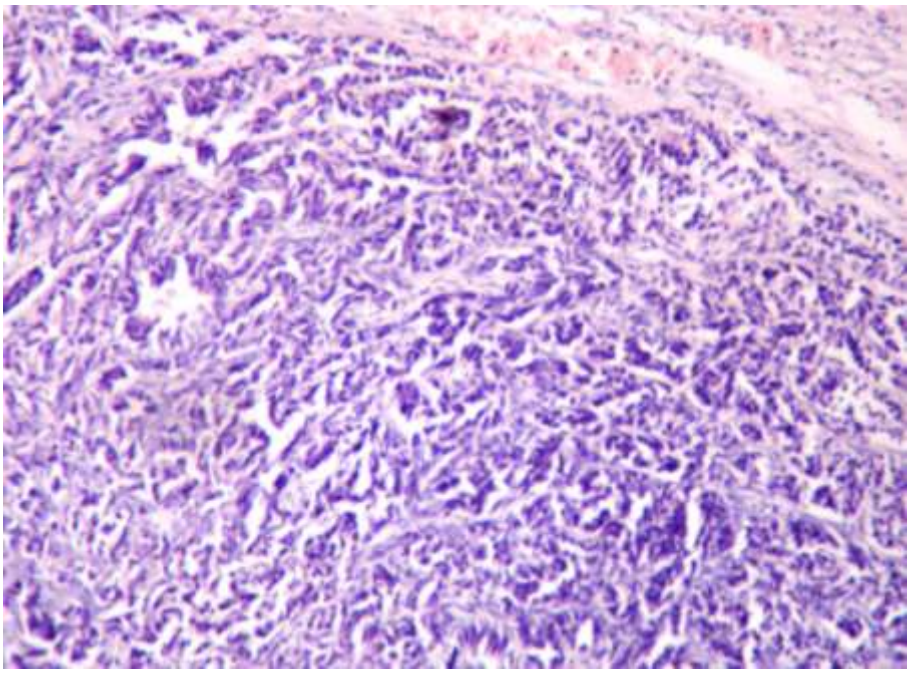


Figure 12A - Prostatic adenocarcinoma – Gleason's pattern 4A – showing fused glands with raggedly infiltrating edges.(H&E)10X

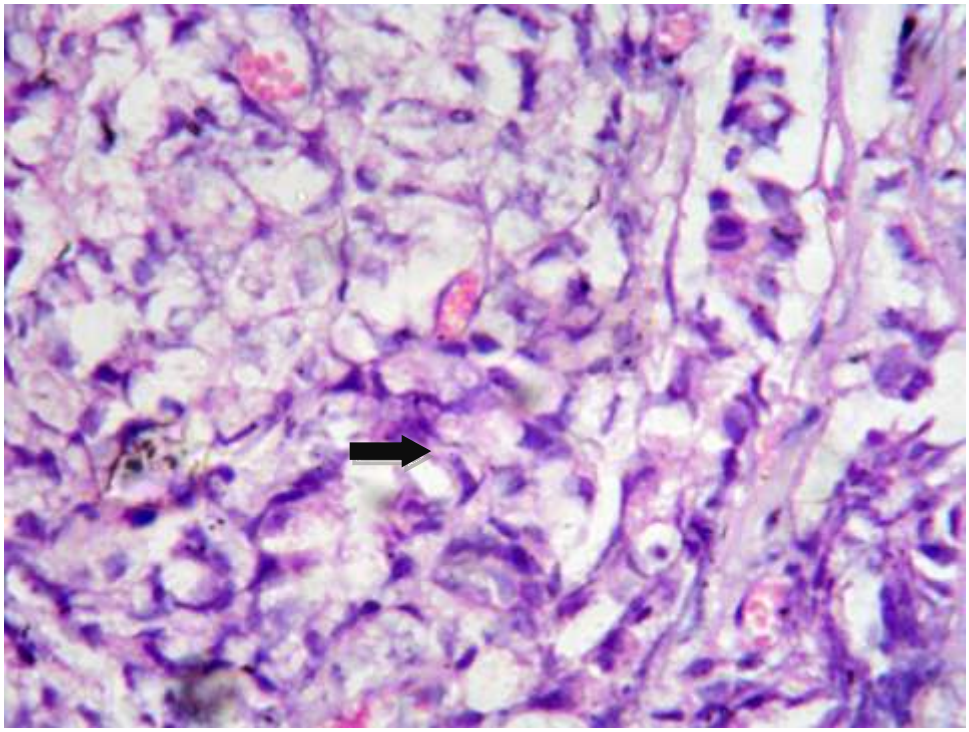


Figure 12B - Prostatic adenocarcinoma – hypernephroid pattern Gleason's grade 4B – showing features same as 4A with large pale cells (H&E)40X

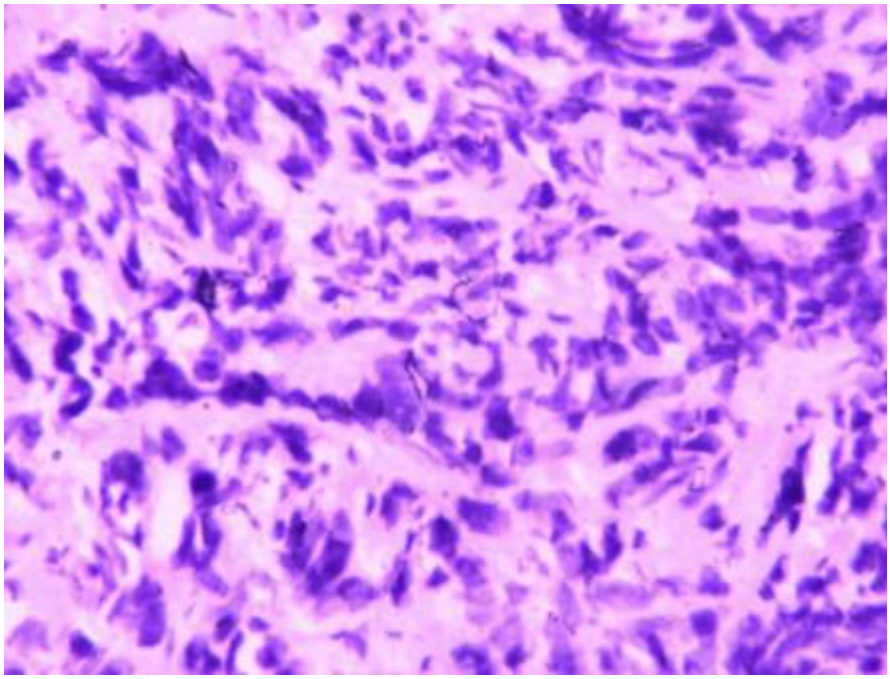


Figure 13 - Prostatic adenocarcinoma – Gleason's pattern 5 –showing solid sheets of cells without glandular differentiation.(H&E) 40X

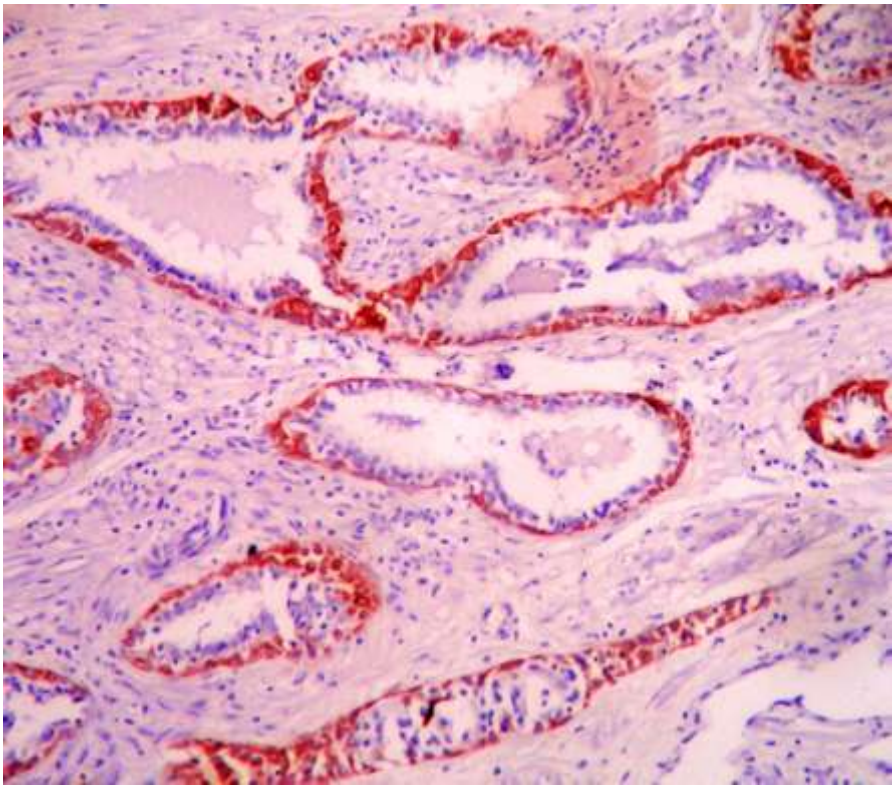


Figure 14 – BPH - Diffuse cytoplasmic positivity for HMWCK –10X

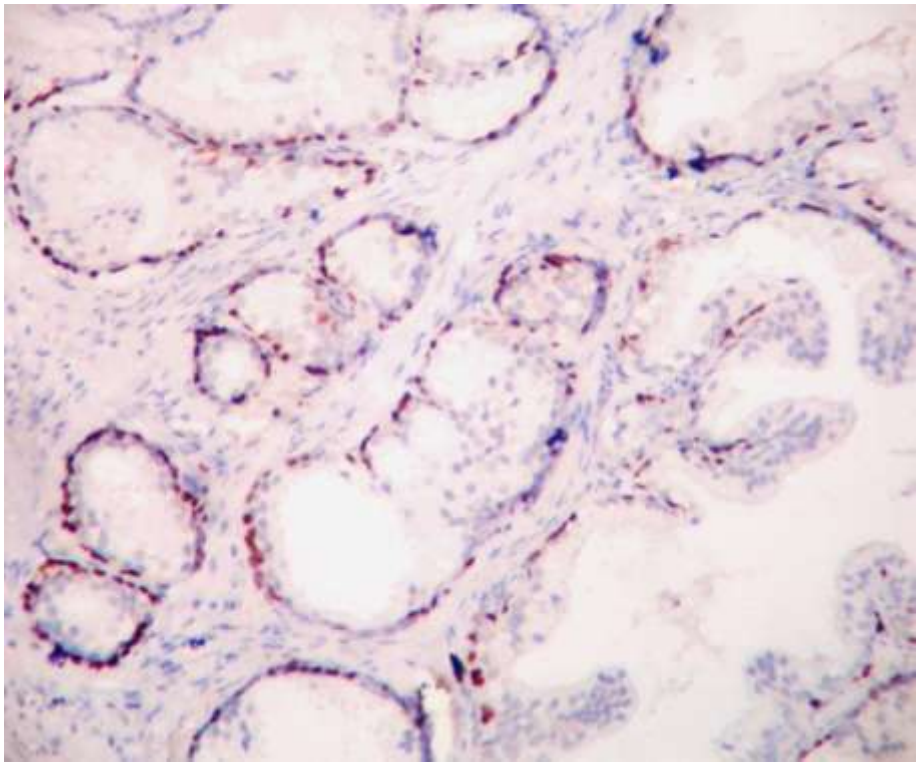


Figure 15 - BPH- Diffuse nuclear positivity for p63 - 10X

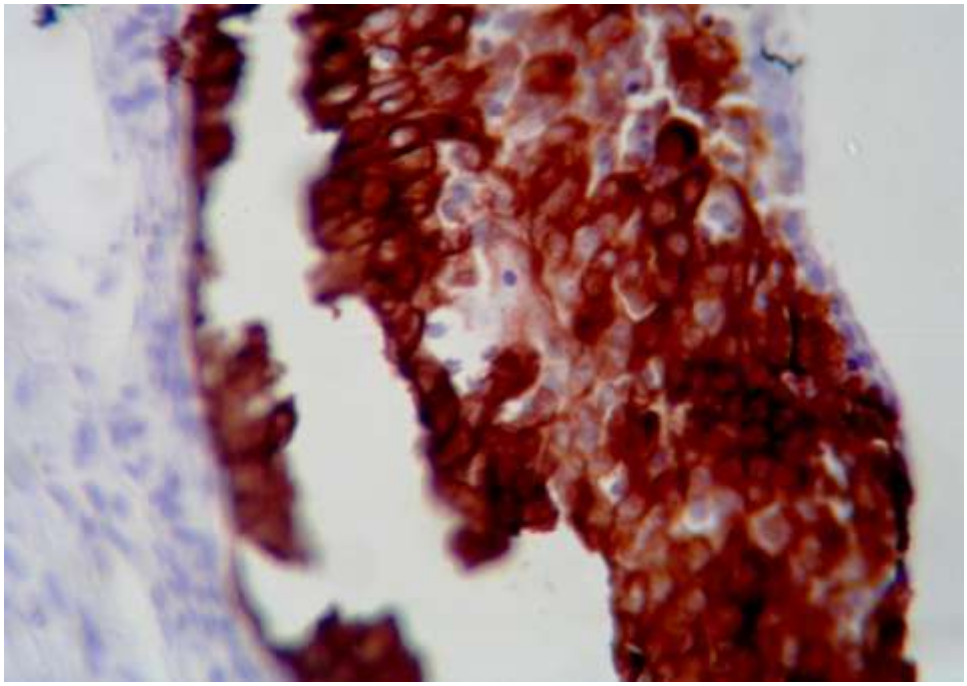


Figure 16 - BCH- Diffuse cytoplasmic positivity for HMWCK-40X

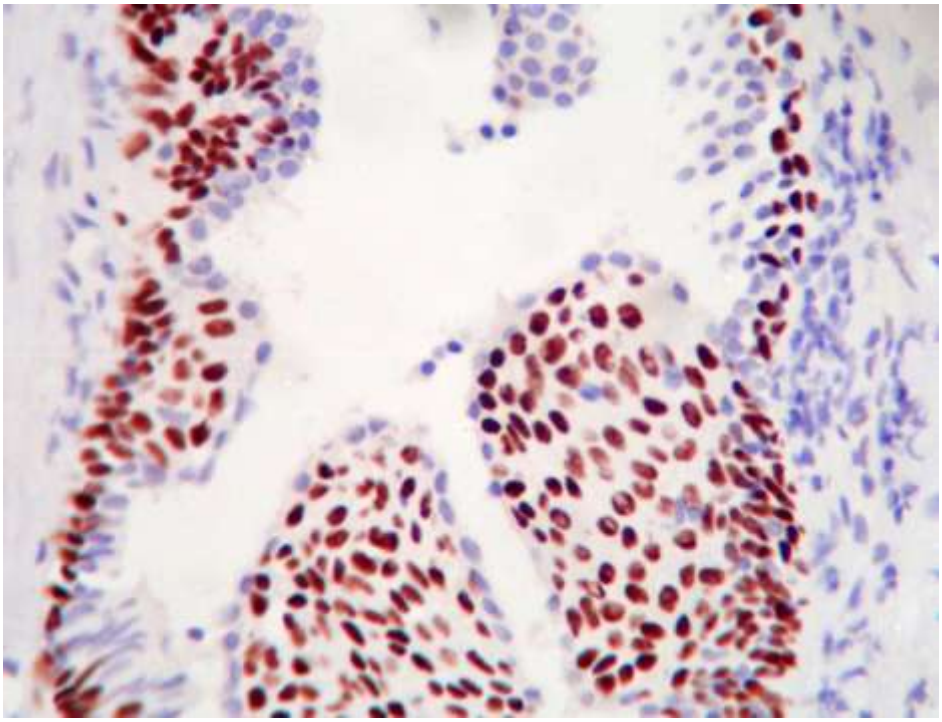


Figure 17 - BCH- Diffuse nuclear positivity for p63 - 10X

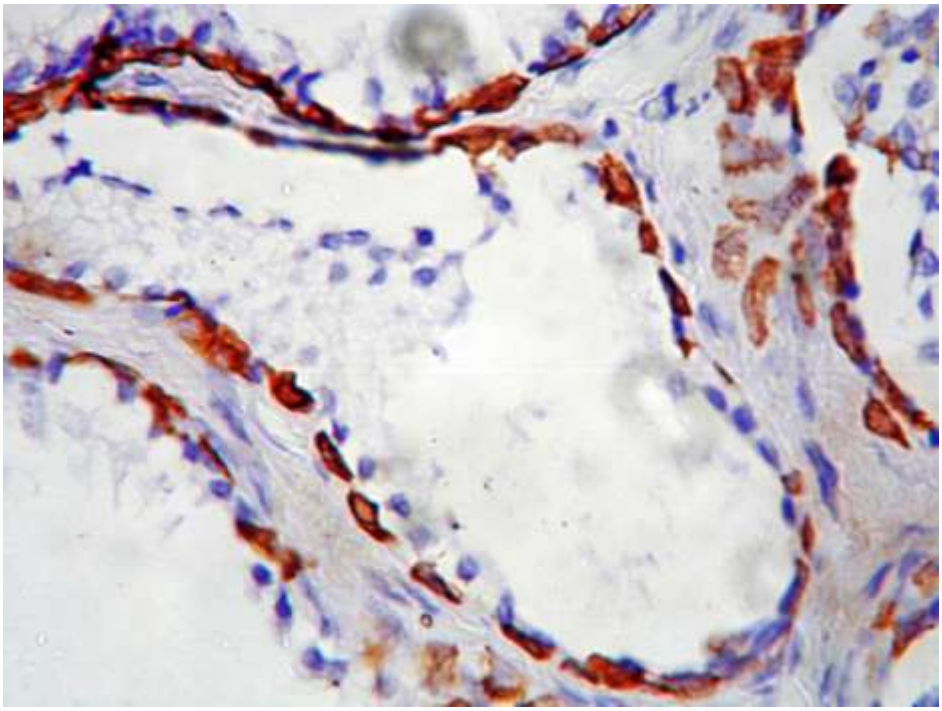


Figure 18 - Cystic atrophy-diffuse cytoplasmic positivity for HMWCK– 40X

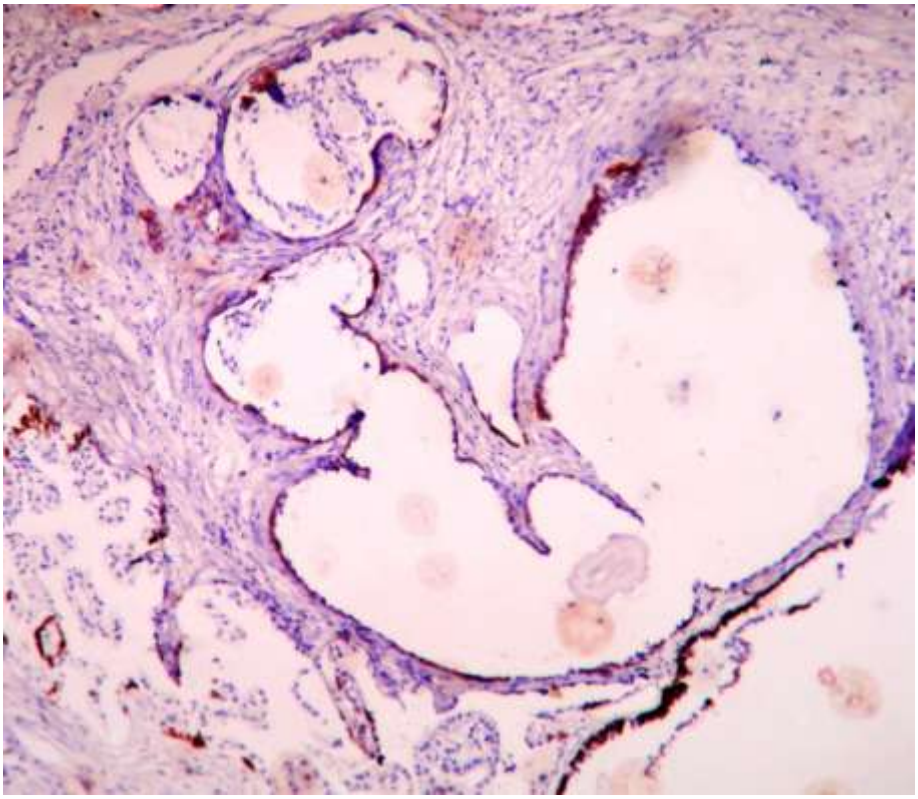


Figure 19 - Cystic atrophy-diffuse nuclear positivity for p63 – 10X

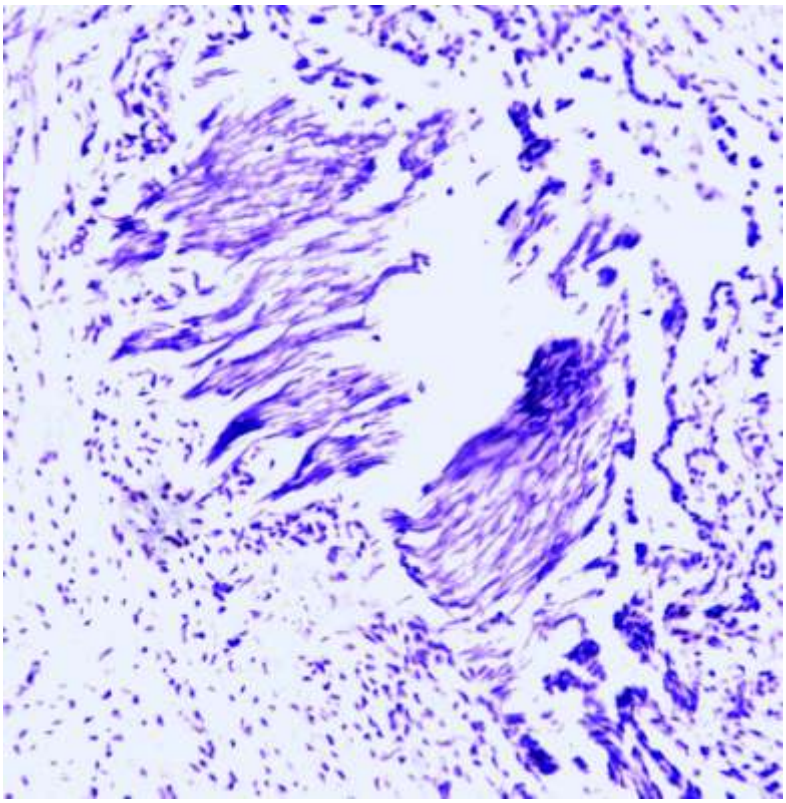


Figure 20 – Crush artifact – Negative for HMWCK– 40X

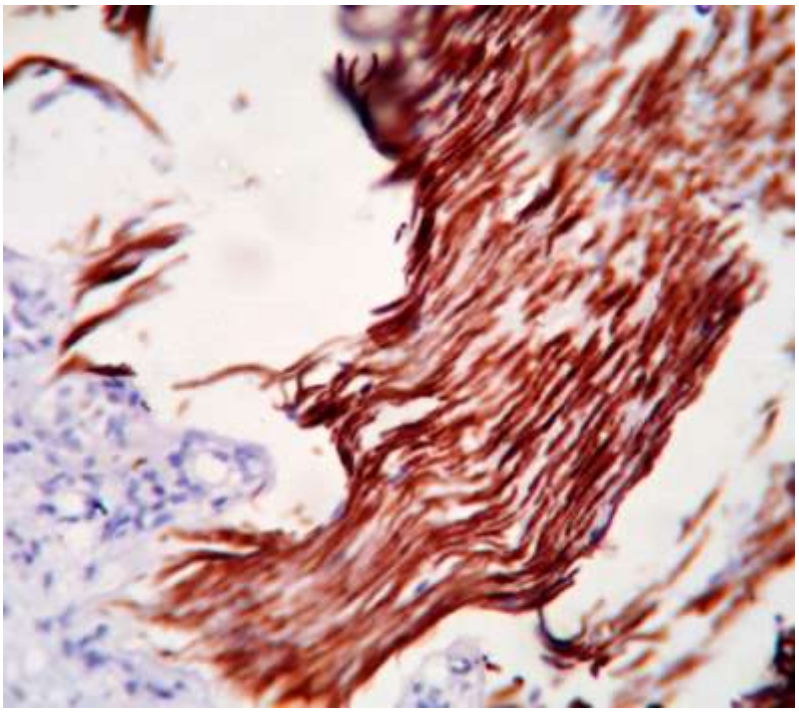


Figure 21 – Crush artifact – Diffuse nuclear positivity for p63 – 40X

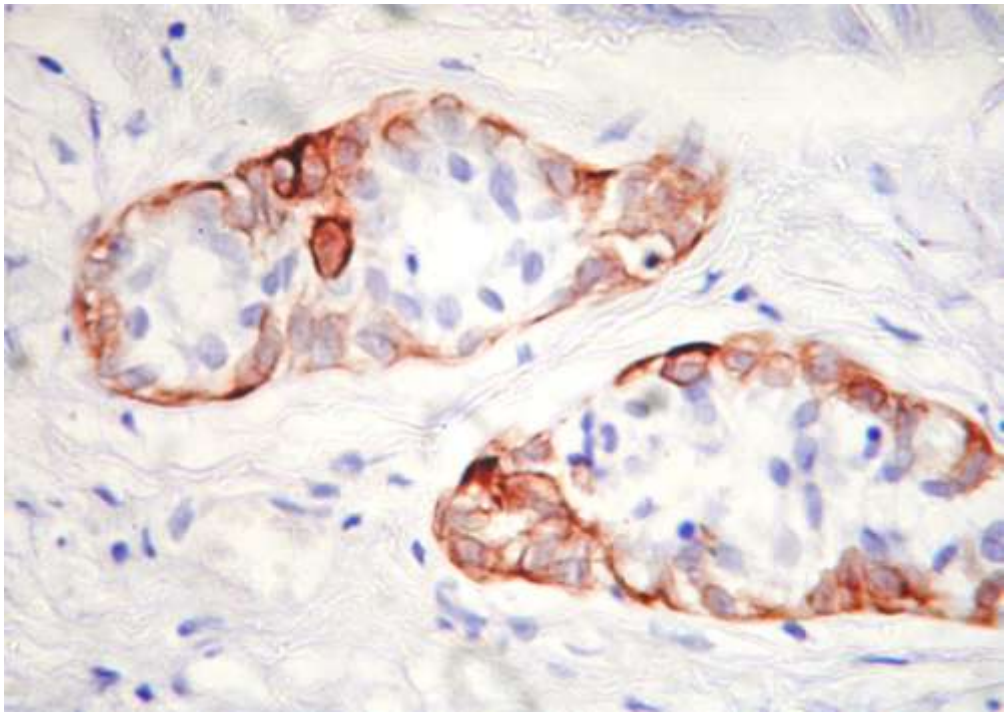


Figure 22A – Low grade prostatic intraepithelial neoplasia – Diffuse cytoplasmic positivity for HMWCK – 40X

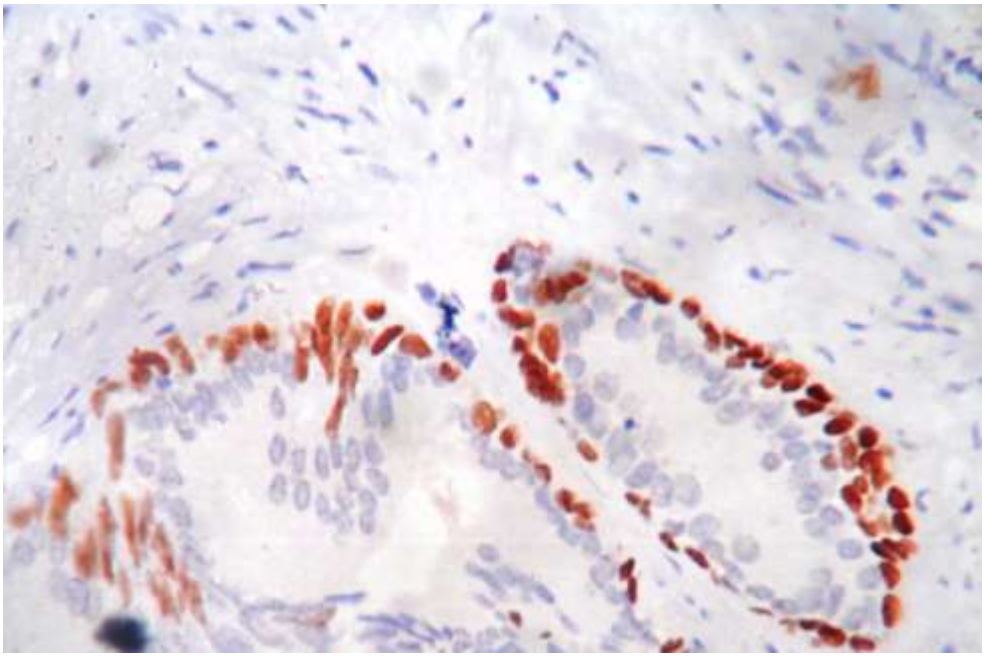


Figure 22B - Low grade prostatic intraepithelial neoplasia – Diffuse nuclear positivity for p63 – 40X

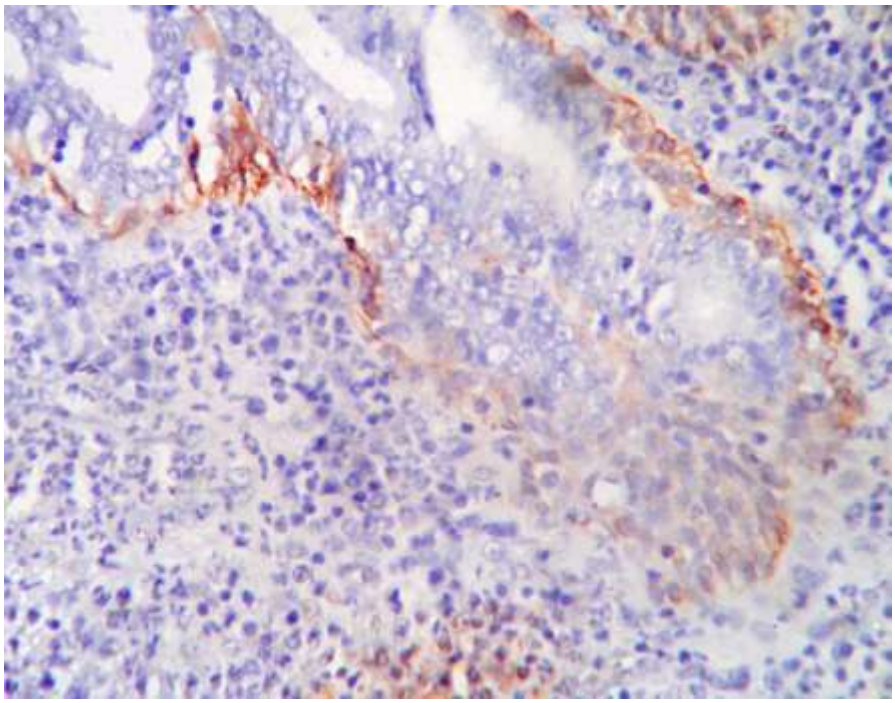


Figure 23A - High grade prostatic intraepithelial neoplasia – Patchy cytoplasmic positivity for HMWCK – 10X

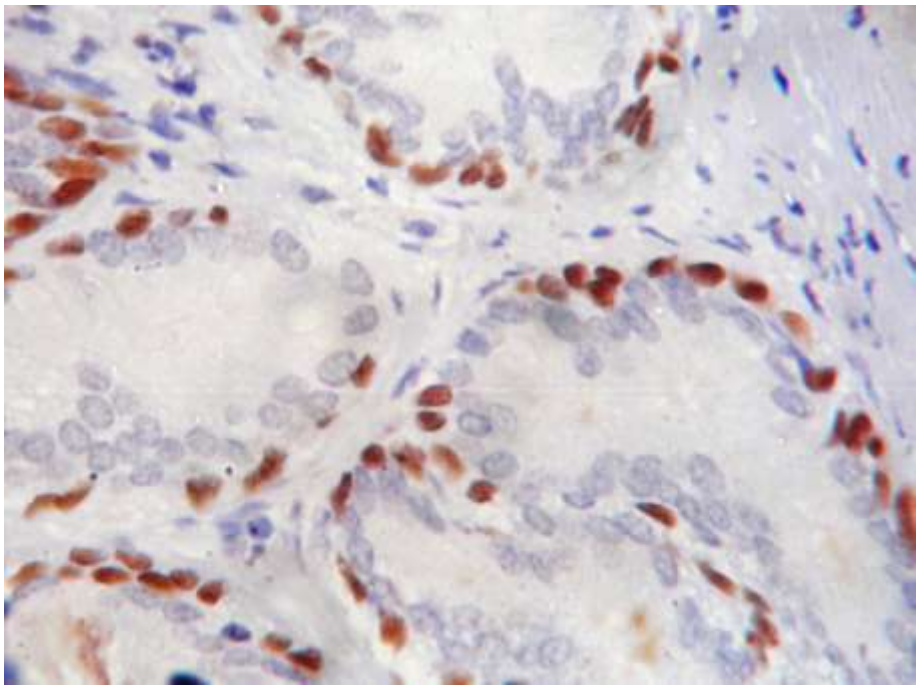


Figure 23B - High grade prostatic intraepithelial neoplasia – Patchy nuclear positivity for p63 – 40X

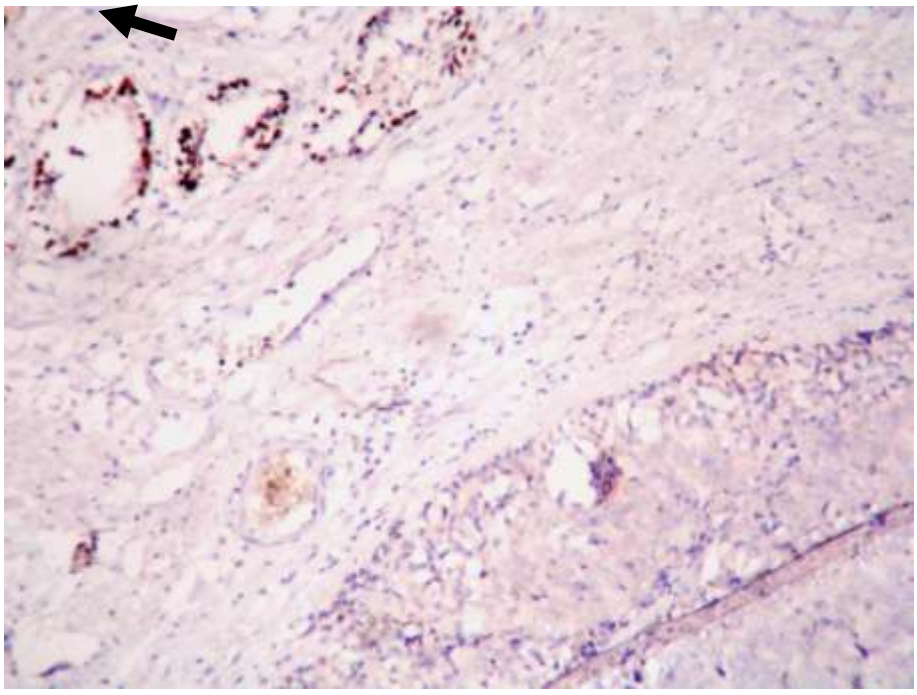


Figure 24 - Adenocarcinoma with normal adjacent glands showing nuclear positivity for p63 ,acting as a good positive internal control – 10X

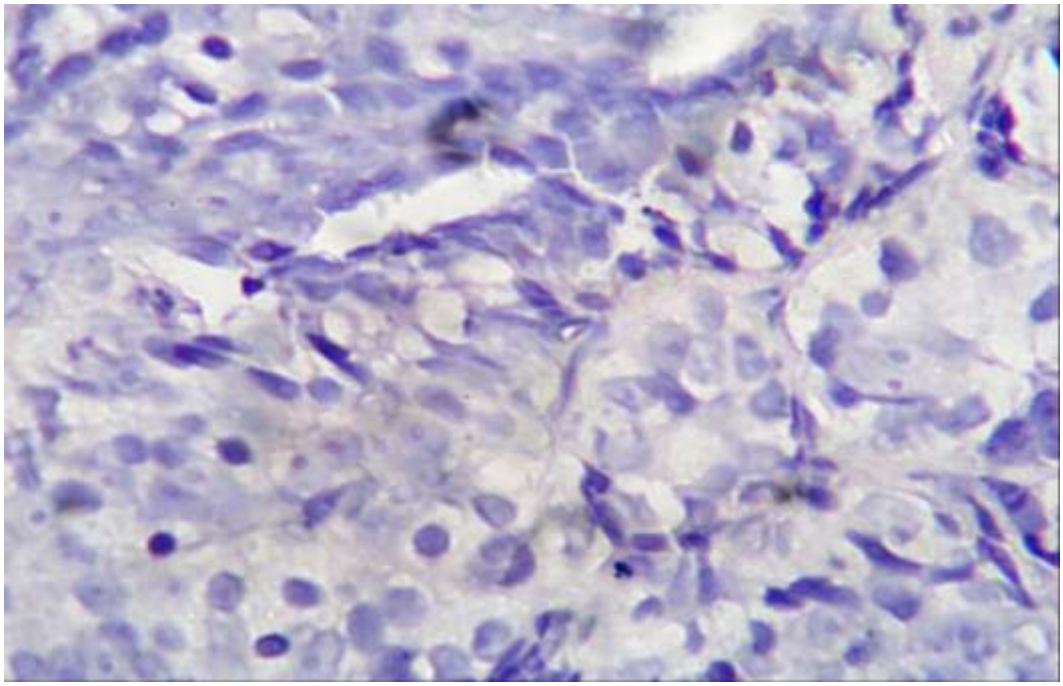


Figure 25A - Adenocarcinoma – Negative for HMWCK – 40X

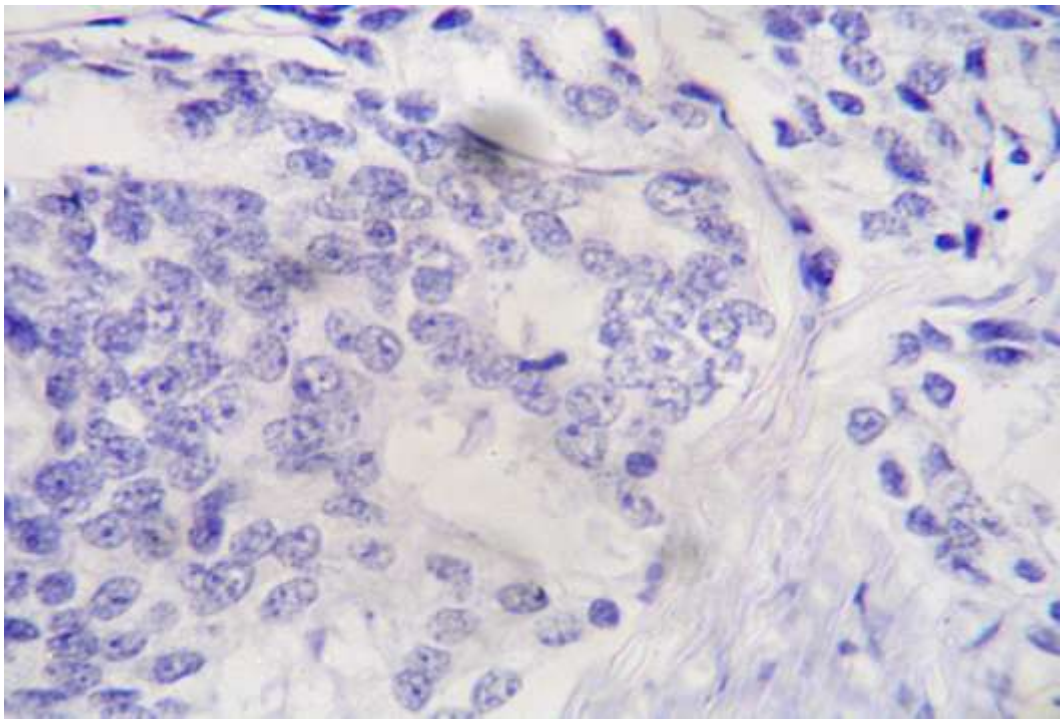


Figure 25B - Adenocarcinoma – Negative for p63 – 40X

DISCUSSION

DISCUSSION

Prostatism is a common malady in the geriatric age group. BPH and carcinoma of the prostate are increasingly frequent with advancing age. The various histological appearances of BPH and prostatic adenocarcinoma are well known and have been described and illustrated extensively in the literature.

These two common urologic conditions among elderly men, share not only a similar hormonal milieu within the prostate, but also several epidemiologic and clinical factors. Both conditions increase with advancing age, both require androgens for growth and development and both respond to antiandrogenic therapy. Both share similar risk factors such as insulin like growth factors, insulin and obesity.

This study was undertaken to evaluate the various histological lesions in the prostatic specimens and to evaluate the role of IHC in diagnostically challenging cases. In this study, 150 prostatic lesions were analysed. These formed 1.42% of the total surgical specimens received during the study period.

HISTOPATHOLOGICAL DIAGNOSIS:

The present study showed that majority, 86.67% of cases were benign lesions of which nodular hyperplasia alone constituted 60% cases, followed by 13.33% of adenocarcinoma.

According to study by Bostwick et al nodular hyperplasia is composed of varying proportion of epithelium and stroma. The most common nodules reported in their study was adenofibromyomatous nodules which contained all elements.[10]

In a study, Mittal et al [14] showed 92.98% of cases of benign lesions followed by 7.02% of malignant cases.

TABLE 13:

HISTOPATHOLOGICAL DIAGNOSIS IN DIFFERENT STUDIES

Sl.No.	HP diagnosis	Mittal BV et al (14)	Elizabeth et al (2005) (30)	Present study
1	Nodular hyperplasia	103 (55.67%)	1029 (88.5%)	90 (60%)
2	Basal cell hyperplasia	10(5.4%)	Nil	8 (5.33%)
3	Squamous metaplasia	19 (10.27%)	Nil	2 (1.33%)
4	Prostatitis	30 (16.24%)	Nil	8 (5.33%)
5	Atrophy	3 (1.62%)	Nil	7 (4.67%)
6	PIN	Nil	7 (0.6)	15 (10%)
7	Carcinoma	13 (7.02%)	127 (0.9%)	20 (13.34%)
8	Total no. of Prostatic specimens	185	1163	150 (100%)

HYPERPLASIAS:

In the present study, the incidence of benign lesions was 86.67 %. nodularhyperplasia alone was noted in 60 %, out of which majority of cases were encountered in the 6th and 7th decade. Other cases includes those in which nodularhyperplasia occurred together with other lesions like PIN, basal cell hyperplasia, metaplasia, prostatitis and atrophy.

TABLE 14:

AGE SPECIFIC INCIDENCE OF NODULAR HYPERPLASIA –

A COMPARATIVE ANALYSIS:

S.No.	Study	40 -49 years	50 – 59 years	60 – 69 years	70 – 79 years, >80
1	Anjorin et al[5]	2.3%	13.6%	40.4%	23.4%
2	Elizabethgeorge and sosama[30]	7.82%	25.97%	32.67%	16.94%
3	Present study	2.3%	24.62%	47.69%	19.24%

BASAL CELL HYPERPLASIA[46] :

Basal cell hyperplasia is usually seen in cases of nodular hyperplasia.Basal cell hyperplasia is typically found in the transition zone and is therefore usually identified in the transurethral resection.

In a present study 8 cases showed Nodular hyperplasia along with basal cell hyperplasia in the age group of 55 - 75 years. It is characterized by small uniform darkly staining basal cells forming solid nests, tubules and cords with peripheral palisading appearance.

There are 2 types in basal cell hyperplasia. In complete form, solid nests of dark blue cells are seen with no secretory cell differentiation, whereas in the incomplete form, secretory cells with clear cytoplasm line the small residual lumina with multiple layers of basal cells surrounding them.

In both the types basal cells show scant cytoplasm with round, oval or spindled hyperchromatic nuclei indistinct nucleoli which may be prominent in some cases. In this study, 2 cases showed complete hyperplasia. 6 Cases showed incomplete hyperplasia.

In a study by clearly et al,[18] all the patients were above the age of 60 years and all had nodular hyperplasia, in addition to basal cell hyperplasia.

The present study showed 2 cases of squamous metaplasia, in addition to nodular hyperplasia, thus accounting for 1.33% of total cases studied. However study by Mittal et al [14] showed Metaplastic epithelium in 10.27% of cases.

PROSTATITIS:

TABLE 15:

INCIDENCE OF PROSTATITIS:

Chronic Prostatitis	8 (72.72%)
Abscess	3 (27.28%)
Total	11 (100%)

In the present study, out of 150 cases 11 cases had Prostatitis.

In a study by Stillwell et al, 25 cases of prostatic abscess showed sheets of neutrophils in and around the acini.

In cases of chronic nonspecific prostatitis, lymphocytes, plasma cells and macrophages were seen. Bostwick in his study has reported more cases of chronic abacterial as compared to bacterial prostatitis.

ATROPHY[46] :

Glandular atrophy of prostate is commonly seen in areas of nodular hyperplasia.Atrophy is more common in peripheral zone but it can be seen the central and transitional zone also.

According to the pattern,the atrophy can be classified as lobular, sclerotic, cystic, linear or streaming . But in all the types cytological features are similar in the form of shrunken dark cells with high N/C ratio, uniform nuclei with no nuclear membrane or chromatin abnormality. In areas the cytological features are difficult to appreciate because of marked secretory cell atrophy.

In the present study, 7 cases had atrophy along with Nodular hyperplasia out of 150 cases. Mittal BV et al[14] showed 1.32% cases of atrophy, present along with Nodular hyperplasia in their study. Wenle WangMD et al [98] showed 4.35% of cases with partial atrophy.

PROSTATIC INTRAEPITHELIAL NEOPLASIA

In a present study, 15 cases showed PIN . 3 cases of LGPIN was associated with nodular hyperplasia and 3 cases showed HGPIN associated with Prostatic carcinoma. 9 cases showed HGPIN with Nodular hyperplasia.

LGPIN was characterized by epithelial crowding, stratification and anisonucleosis.HGPIN was characterized by pronounced epithelial crowding, nuclear enlargement, hyperchromasia and luminal bridging giving a cribriform appearance. Prominent nucleoli was also seen. Adjacent area showed small glands infiltrating the stroma.

The prevalence and extend of PIN increases with patient age. Most foci of PIN in young men were low grade with increasing frequency and volume of high grade PIN with advancing age.

Race and geographic location also appear to influence the incidence of PIN. African - American men had a greater prevalence of PIN than Causatians in the 50 - 60 years of age group. African - American also had a highest incidence of cancer.

TABLE 16:

INCIDENCE OF PIN WITH AND WITHOUT PROSTATIC CARCINOMA.

Authors	PIN without carcinoma %	PIN with carcinoma %
McNeal f Bostwick et al[13]	43%	82%
Troncosa et al[13]	17.9%	72.1%
Kovi et al[56]	46%	59.3%
Rekhi B et al[81]	11.2%	86.9%
Present study	9.23%	15%

According to this study, PIN was found in 15% of Prostate with carcinoma and 9.23% Prostate without carcinoma.

TABLE 17:

INCIDENCE OF HGPIN IN PROSTATES WITH CARCINOMA.

Authors	Incidence of HGPIN in Prostatic adenoca %
McNeal Bostwick et al (1986)[13]	33%
Kovi et al[56]	33%
Present study	15%

The prevalence of high grade PIN in TURP for carcinoma is remarkably high reflecting the strong association with malignancy.

There are many evidences to suggest the relationship of HGPIN and Prostatic adenocarcinoma.

1. The incidence and extent of both lesions increases with patient age.
2. There is an increased frequency, severity and extent of HGPIN in prostatic carcinoma.
3. Both HGPIN and carcinoma are multifocal with a predominant peripheral zone distribution .

Histological atypia observed in HGPIN is virtually indistinguishable from that of Prostate cancer except that in HGPIN the basal membrane is still intact. As HGPIN progresses, the likelihood of basal cell layer disruption increases.[49]

PROSTATIC CARCINOMA

Prostatic cancer contributes to the overall cancer burden, being the most frequent malignancy in men world wide. The number of cases had continuously increased over the past decades, due to higher life expectancy, western life style characterized by a high calorie diet and lack of physical exercise.

It is the second most frequently diagnosed cancer of men and fifth most common cancer overall. Incidence rates of prostate cancer vary by more than 25 fold worldwide, highest rates are in Australia/Newzealand, Western and Northern Europe, North America, largely because the practice of PSA testing and subsequent biopsy has become widespread in those regions.[43]

Epidemiological data suggest the black people are more susceptible followed by white people, while the Asians have the lowest risk.[28,53]

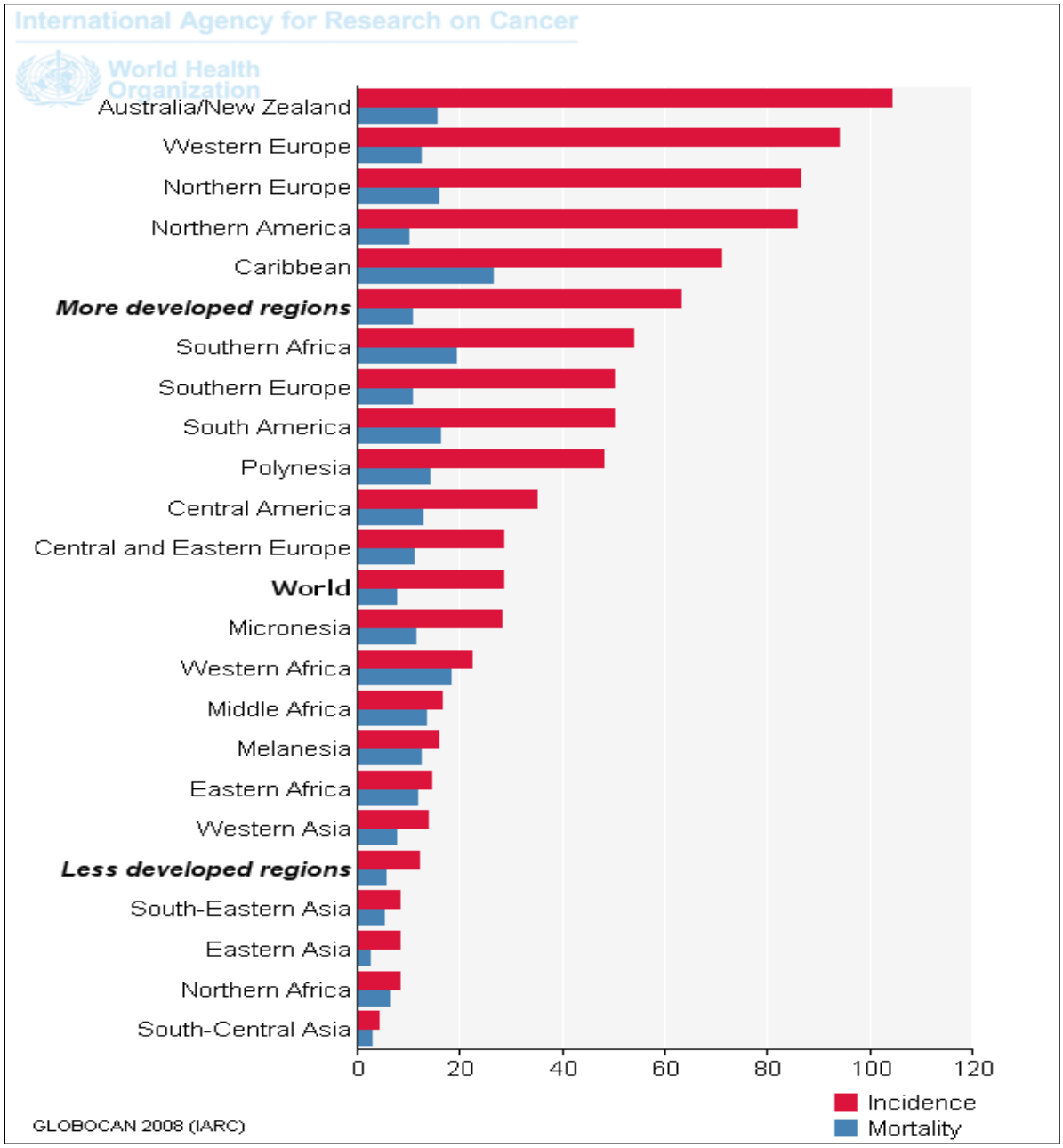

International Agency for Research on Cancer
World Health Organization
Australia/New Zealand
Western Europe
Northern Europe
Northern America
Caribbean
More developed regions
Southern Africa
Southern Europe
South America
Polynesia
Central America
Central and Eastern Europe
World
Micronesia
Western Africa
Middle Africa
Melanesia
Eastern Africa
Western Asia
Less developed regions
South-Eastern Asia
Eastern Asia
Northern Africa
South-Central Asia
0
20
40
60
80
100
120
Incidence
Mortality
GLOBOCAN 2008 (IARC)

TABLE 18 :

COMPARISION OF INCIDENCE OF PROSTATIC CARCINOMA[73]

S.no	Name and year of study	Prevalence
1	Population based cancer registry Delhi 2001-2003	2.7%
2	Population based cancer registry Mumbai 2001 – 2003	2.8%
3	Population based cancer registry Bangalore 2001 - 2003	2.5%
4	Population based cancer registry Sikkim 2003 - 2004	0.5%
5	Population based cancer registry Bhopal 2001 – 2003	2.3%
6	Population based cancer registry Assam 2007 – 2008	0.7%
7	Population based cancer registry Chennai 2001 – 2003	1.6%
8	Present study 2010 - 2012	2.26%

The prevalence of prostate cancer as indicated by various studies in the journals and the literature is given in the above table. In our study, the prevalence was 2.26% , which is in close correlation with other studies.

TABLE 19:

AGE INCIDENCE OF PROSTATIC CARCINOMA IN DIFFERENT STUDIES

AUTHORS	40 -49	50 -59	60 -69	70 -79	>80
Lee and Shanmugaratnam et al [99]	4.3%	8.3%	10.6%	13.6%	20%
L Stanford et al[44]	0.6%	6%	20%	18.3%	Nil
Hamwakyoma et al[29]	0.8%	16.7%	39.5%	31.6%	Nil
Roberto Deangless et al[83]	2%	2.3%	33%	64%	Nil
F Aragona et al[33]	1.5%	4.5%	7.1%	11%	Nil
Anjorini et al[5]	2.3%	13.6%	40.4%	23.4%	Nil
Present study	0%	25%	45%	15%	15%

In the present study, peak incidence of prostatic carcinoma was seen in age group of 60 - 69 a decade earlier than PIN.

Many recent studies show a higher incidence of prostatic carcinoma in the age group of 60 - 80.

TABLE 20:

FREQUENCY DISTRIBUTION OF GLEASON'S SCORE AT PRESENTATION.

Author	Gleason's score	No.of pts.	% age
Dr.Hamwakyoma and Dr. JLMagandi[29]	2 -4	6	5.3%
	5 -7	69	61.1%
	8 -10	38	33.6%
	Total	113	100%

PRESENT STUDY	2 -4	1	5%
	5 -7	17	85%
	8 -10	2	10%
	Total	20	100%

In the present study, 20 cases of adenocarcinoma prostate were seen accounting for 13.33% of the cases.

All these 20 malignant cases were graded using Gleason's scoring system. Majority of our cases showed moderate to poor differentiation.

IMMUNO HISTOCHEMISTRY

Immunohistochemical detection of basal cells is widely used to help in the diagnosis or exclusion of prostatic carcinoma in a diagnostically challenging cases. HMW-CK has thus far been the most commonly used IHC stain in the diagnosis of prostatic carcinoma.

When dealing with small foci of atypical glands with some suspicious (but not diagnostic) architectural or cytologic features of prostatic carcinoma, negative HMW-CK staining in the atypical glands would favour a diagnosis of adenocarcinoma.

p63 has recently generated much interest due to its expression in the basal cells of the prostate, and it is essential for prostate development. Signorett et al [88] also highlighted the role of p63 in the development of prostate gland and showed that p63 is expressed in virtually all the basal cells of prostatic glands, including a subset negative for HMW-CK.

The resuls of our study demonstrates that p63, like HMWCK is specific for basal cells in the Prostate gland.

None of the 4 case with histologically unequivocal prostatic carcinoma demonstrated immunoreactivity for either HMWCK or p63 (100% specificity).

Among the 8 cases which included both benign and premalignant lesions, with regard to HMWCK staining in our study in 5 cases [2 Benign and 3 Premalignant (PIN)] showed positivity, 3 cases (2Benign and 1 premalignant) showed negativity. Absence of basal cell staining in these cases was due to the effects of prolonged formalin fixation, as extended formalin fixation decreases the HMWCK antigeniciy.[50]

With regard to p63 staining in our study out of 8 cases, 7 cases [4 benign and 3 premalignant (PIN)] showed positivity and 1 case [1premalignant] showed negativity. This correlated with the study of shah et al [89] who reported the absence of basal cel staining both with HMWCK and p63.

This absence of basal cell staining may be attributed to the diminished or absence gene expresson of basal cell markers, technical variables, including those resulting from surgical procedures and antigen retrieval methods could be another important source of negative basal cell IHC reactions.[69,50]

Multhaupt et al,[68] also found that 88% benign gland in the transition zone obtained by trans urethral resections of the prostate lost their HMWCK antigenicity if antigen retrival was not used.

In our study, one case of benign prostatic hyperplasia with crush artifact, showed, lack of staining of basal cells with HMWCK but showed positivity with nuclear p63 staining. This correlated with the study of Michael et [64] who showed same effect as above.

In one case of prostatic adenocarcinoma(fig24) good positive internal control staining was seen with p63. That means, no staining was seen in malignant glands but the basal cells in benign glands that was present adjacent to the malignant gland were stained with p63.

Our study showed that the sensitivity in identifying basal cells in benign glands is 62.5% and 87.5% for HMWCK and p63, respectively.

Hence, p63 is slightly more sensitive in identifying basal cells than HMWCK according to our study.

Shah et al [89] similarly found that p63 is more sensitive than HMWCK in identifying the basal cells, particularly in TURP specimens, offering slight advantage over HMWCK in diagnostically challenging cases. p63 may be used as an alternative to HMWCK stain for difficult prostatic lesion.

CONCLUSION

CONCLUSION

In the present retrospective study, comprising of 150 cases of prostatic lesions, histopathological analysis, the role of basal cell markers [IHC] are studied during the period from Jan 2010 to March 2012 . The following are the salient observation noted in this study.

1. Prostatic specimens constituted 1.42% total number of surgical specimens received during the same period.
2. Out of 150 cases studied, the commonest pathology encountered was benign lesion constituting 86.67% and malignant lesions were 13.33% .
3. Among the benign lesions, benign nodular hyperplasia is the most commonly observed pathology of prostate.
4. The age incidence of nodular hyperplasia is between 4^{th} and 8^{th} decade.
5. The incidence of LGPIN is 2.31% and HGPIN is 6.92% in TURP specimen of nodular hyperplasia.
6. Among the 130 cases of benign lesion,90 cases were diagnosed as nodular hyperplasia, 8 cases with prostatitis. Basal cell hyperplasia in 8 cases, squamous metaplasia in 2 cases and atrophy in 7 cases.

7. Among the malignant neoplasm of the prostate, adenocarcinoma is the commonest
8. Incidence of carcinoma was 13.33% and peak age group affected was between 60-69 yrs.
9. Gleason's score of 5-7 was seen in 85% of the cases. Gleason score of 8 and 10 was seen in 10% of cases.
10. With regard to IHC studies 12 cases were selected and tested with HMWCK and p63 and comparative study was done.
11. It is found that p63 is more sensitive than HMWCK in identifying basal cells according to our study.

In summary, we found that immunohistochemical p63 staining is diagnostically reliable in identifying basal cells in TURP specimens and compares favourably with high molecular weight cytokeratin staining. In TURP specimens in which cautery artifact can impair the ability to detect high molecular weight cytokeratin , staining for p63 appears superior. In addition, p63 staining which shows a nuclear reaction is easy to interpret than HMWCK which shows cytoplasmic reaction.

APPENDIX

APPENDIX - I

HAEMATOXYLIN AND EOSIN STAINING.

PREPARATION OF SOLUTIONS:

HARRIS HAEMATOXYLIN

Distilled water - 1000 ml

Ammonium alum - 100 g

Haematoxylin - 5 g

Absolute ethyl Alcohol - 50 ml

Mercuric Oxide - 2.5 g

100 g of Ammonium alum dissolved in 1000 ml of distilled water by heating and shaking at 60° C. Add solution of 5 g of Haematoxylin in 50 ml of Ethylalcohol and bring rapidly to boil. When it begins boil, remove from flame and acid 2.5 g of Mercuric Oxide. Mix by Swirling gently.

EOSIN STAIN

EOSIN Y - 1 g

Distilled water - 20 ml

95% Ethanol - 80 ml

Glacial acetic acid - 0.2 ml

Dissolve 1 g Eosin Y in 20 ml of water and add 95% ethanol and glacial acetic acid.

PROCEDURE:

1. Dewax the sections through two changes of Xylene and hydrate the sections through descending grades of alcohol to water.

2.Stain in Harris's hematoxylin for 5 minutes.

3.Quickly rinse in running tap water.

4.Differentiate in 1% acid alcohol (2 - 3 quick dips).

5.Blue the sections in running tap water for 10 minutes.

6.Wash in running tap water for 10 - 20 minutes.

7.Stain in 1% Eosin for 15 seconds to 2 minutes.

8.95% alcohol - 2 changes.

9.Absolute alcohol - atleast 2 changes.

10.Xylene - 2 changes.

11.Mount in DPX moutant.

APPENDIX - II

IMMUNOHISTOCHEMISTRY

Preparation of gelatin coated slide:

Chrome alum - 0.05 gm

Gelatin - 0.3 gm

Distilled water - 100 ml

First chrome alum is added to distilled water and then the distilled water is heated to 60° C Gelatin is added slowly to the heated distilled water. Glass slides are then dipped in this solution and dried overnight.

Preparation of TRIS BUFFERED SALINE (TBS): 0.005 M TBS

Distilled water - 10 litres

Sodium Chloride - 80 g

TRIS (Hydroxy methylamine) - 6.05 g

I M Hcl - 44 ml

Final PH is adjusted to 7.6 with either I M Hcl or 0.2 M Tris solution.

Preparation of CITRATE buffer solution (antigen retrieval solution):

Trisodium Citrate - 2.94 gms

IN Hcl - 5 ml

Distilled water - 1000 ml

Final PH is adjusted to 6.0 with IN Hcl.

Antigen Retrieval:

The slides are placed in citrate buffer in the coplin jar and capped. The jar is then heated in a 750 w domestic microwave oven for 15 minutes (5 minutes in low power (40) 5 minutes in medium power (60) and 5 minutes in full power (80) pausing only to top up the fluid.

Procedure adopted for IHC:

1.Dewax the sections in Xylene (1/2 hour, two changes and bring sections to distilled water.

2.Antigen retrieval using TBS by microwave oven heating.

3.Cool to room temperature in running tap water for 20 minutes.

4.Bring sections to TBS for 5 minutes.

5.Drain and wipe off excess TBS around sections.

6.Incubate in endogenous peroxidase blocking reagent for 15 - 20 minutes.

7.Gently wash the slides in TBS for 5 minutes.

8.Wipe off the excess fluid and incubate in power block reagent for 15 - 20 minutes.

9.Wipe the excess fluid and incubate in Primary Antibody for 60 minutes.

10.Repeat steps 4 and 5.

11.Incubate in super enhancer for 30 minutes.

12.Repeat steps 4 and 5.

13. Incubate in enzyme labeled polymer secondary antibody (supersensitive poly HRP) for 30 minutes.

14.Repeat steps 4 and 5.

15.Incubate in DAB (Diamino Benzidine) substrate solution for 2 - 10 minutes.

(To prepare DAB substrate, add 1 ml of substrate buffer, 1 drop of liquid DAB, and 1 drop of substrate DAB).

16.Wash in distilled water, counter stain with Hematoxylin, clear in Xylene and mount with DPX.

MASTER CHART

MASTER CHART

SL. NO.	PATH NO.	IP NO.	AGE/ SEX	CLINICAL DIAGNOSIS	HP DIAGNOSIS	BIOPSY SPECIMEN
1	64/10	1058764	60/M	BPH	NODULAR HYPERPLASIA	TURP
2	72/10	1061005	65/M	BPH	NODULAR HYPERPLASIA	TURP
3	PP 84/10	-	73/M	BPH	NODULAR HYPERPLASIA	TURP
4	107/10	1060338	55M	BPH	NODULAR HYPERPLASIA	TURP
5	318/10	1065154	60/M	CA PROSTATE	PROSTATIC ADENOCARCINOMA	TURP
6	500/10	1065866	55/M	CA PROSTATE	PROSTATIC ADENOCARCINOMA	TURP
7	676/10	1065181	80/M	BPH	NODULAR HYPERPLASIA	TURP
8	595/10	1069744	72/M	BPH	NODULAR HYPERPLASIA	TURP
9	862/10	1072749	67/M	BPH	NODULAR HYPERPLASIA	TURP
10	946/10	1071214	65/M	BPH	NODULAR HYPERPLASIA WITH CHRONIC PROSTATITIS	TURP
11	1055/10	1073271	70/M	BPH	BENIGN PROSTATIC HYPERTROPHY WITH BASAL CELL HYPERPLASIA	TURP
12	1474/10	1076800	60/M	BPH	NODULAR HYPERPLASIA	TURP
13	1475/10	1075834	42/M	BPH	NODULAR HYPERPLASIA OF PROSTATE WITH CHRONIC PROSTATITIS	TURP

14	1574/10	1080994	65/M	BPH	NODULAR HYPERPLASIA	TURP
15	1778/10	1080751	65/M	BPH	NODULAR HYPERPLASIA WITH FOCAL PIN	TURP
16	1875/10	1083417	55/M	BPH	NODULAR HYPERPLASIA OF PROSTATE	TURP
17	1877/10	1083596	70/M	BPH	NODULAR HYPERPLASIA OF PROSTATE	TURP
18	2288/10	0322485	63/M	BPH	NODULAR HYPERPLASIA	TURP
19	2291/10	0322486	65/M	BPH	NODULAR HYPERPLASIA	TURP
20	2342/10	0322490	80/M	BPH	NODULAR HYPERPLASIA	TURP
21	2396/10	1085782	53/M	BPH	NODULAR HYPERPLASIA	TURP
22	2451/10	1088471	80/M	BPH	NODULAR HYPERPLASIA	TURP
23	2530/10	1091129	42/F	BPH	NODULAR HYPERPLASIA	TURP
24	2859/10	1084536	50/M	BPH	NODULAR HYPERPLASIA	TURP
25	2858/10	1090445	60/M	BPH	NODULAR HYPERPLASIA	TURP
26	2979/10	1096307	60/M	BPH	NODULAR HYPERPLASIA	TURP
27	3139/10	1096299	60/M	BPH	NODULAR HYPERPLASIA	TURP
28	3228/10	1100278	79/M	BPH	NODULAR HYPERPLASIA	TURP
29	3308/10	109856	60/M	BPH	NODULAR HYPERPLASIA	TURP
30	3497/10	1100264	70/M	BPH	NODULAR HYPERPLASIA	TURP

31	3902/10	1106534	60/M	BPH	NODULAR HYPERPLASIA WITH INCOMPLETE BASAL CELL HYPERPLASIA	TURP
32	4060/10	1201290	50/M	BPH	NODULAR HYPERPLASIA	TURP
33	4314/10	1202643	55/M	BPH	NODULAR HYPERPLASIA	TURP
34	4314/10	1202643	55/M	BPH	NODULAR HYPERPLASIA	TURP
35	4316/10	1203296	60/M	BPH	NODULAR HYPERPLASIA	TURP
36	4443/10	1205816	62/M	BPH	NODULAR HYPERPLASIA	TURP-
37	311/11	1303111	50/M	BPH	NODULAR HYPERPLASIA	TURP
38	458/11	1303511	55/M	BPH	NODULAR HYPERPLASIA	TURP
39	557/11	1306100	62/M	BPH	NODULAR HYPERPLASIA	TURP
40	609/11	1306549	56/M	BPH	NODULAR HYPERPLASIA	TURP
41	889/11	1306549	56/M	BPH	NODULAR HYPERPLASIA WITH PROSTATITIS	TURP
42	1185/11	1311457	52/M	CA PROSTATE	PROSTATIC ADENOCARCINOMA	TURP
43	1186/11	1314107	70/M	CA PROSTATE	NODULAR HYPERPLASIA OF PROSTATE	TURP
44	1254/11	1311557	60/M	BPH	BENIGN PROSTATIC HYPERPLASIA	TURP
45	1573/11	1316922	80/M	CA PROSTATE	NODULAR HYPERPLASIA	TURP
46	1571/11	1319294	70/M	?CA PROSTATE	NODULAR HYPERPLASIA WITH BCH	TURP

47	1575/11	1319092	55/M	?CA PROSTATE	NODULAR HYPERPLASIA WITH PROSTATITIS	TURP
48	1576/11	1319096	75/M	CAPROSTATE	NODULAR HYPERPLASIA WITH BCH	TURP
49	1806/11	1319095	76/M	BPH	NODULAR HYPERPLASIA	TURP
50	1806/11	1319095	76/M	BPH	NODULAR HYPERPLASIA OF PROSTATE	TURP
51	1927/11	1319294	70/M	BPH	NODULAR HYPERPLASIA, CHRONIC PROSTATITIS	TURP
52	2144/11	1326208	58/M	BPH	NODULAR HYPERPLASIA ,BCH , CHRONIC PROSTATITIS	TURP
53	2281/11	1325578	65/M	BPH	NODULAR HYPERPLASIA	TURP
54	2306/11	1322765	70/M	BPH	NODULAR HYPERPLASIA ,PIN II CHANGES	TURP
55	2346/11	1297100	55/M	CA PROSTATE	PROSTATIC ADENO CA	TRUCUT BIOPSY
56	2405/11	1322767	60/M	BPH	NODULAR HYPERPLASIA ,PIN I-II CHANGES	TURP
57	2468/11	1324472	78/M	BPH	NODULAR HYPERPLASIA	TURP
58	2465/11	1328467	60/M	BPH	NODULAR HYPERPLASIA	TURP
59	2467/11	1327117	52/M	BPH	NODULAR HYPERPLASIA	TURP
60	2581/11	1461111	65/M	CA PROSTATE	NODULAR HYPERPLASIA,PIN CHANGES	TRUCUT BIOPSY

61	2676/11	1333873	47/M	CA PROSTATE	ADENOCA PROSTATE	TRUCUT BIOPSY
62	2724/11	1331546	72/M	BPH	NODULAR HYPERPLASIA, PIN I CHANGES	TURP
63	2727/11	1331577	61/M	BPH	NODULAR HYPERPLASIA OF PROSTATE	TURP
64	2775/11	1331244	55 /M	BPH	NODULAR HYPERPLASIA WITH PIN II CHANGES	TURP
65	2813/11	1334592	63/M	BPH	NODULAR HYPERPLASIA	TURP
66	2814/11	1331954	58/M	BPH	NODULAR HYPERPLASIA	TURP
67	2954/11	1333515	62/M	BPH	NODULAR HYPERPLASIA	TURP
68	2955/11	1333870	50/M	BPH	NODULAR HYPERPLASIA	TURP
69	3036/11	1336998	56/M	CA PROSTATE	ADENOCARCINOMA OF PROSTATE	TRUCUT BIOPSY
70	3209/11	1336485	62/M	BPH	PIN I-II ,NODULAR HYPERPLASIA OF PROSTATE	TURP
71	3210/11	1338508	65/M	BPH	NODULAR HYPERPLASIA, CHRONIC PROSTATITIS	TURP
72	3265/11	1338294	66/M	BPH	NODULAR HYPERPLASIA	TURP
73	3371/11	1338893	58/M	BPH	NODULAR HYPERPLASIA, CHRONIC PROSTATITIS	TURP
74	3385/11	1339922	62/M	BPH	NODULAR HYPERPLASIA WITH PIN I	TURP

75	3524/11	1342583	58/M	BPH	NODULAR HYPERPLASIA OF PROSTATE	TURP
76	3527/11	1349815	66/M	BPH	NODULAR HYPERPLASIA OF PROSTATE	TURP
77	3615/11	1338878	65/M	BPH	ADENOCA PROSTATE	TURP
78	3748/11	1341764	60/M	CA PROSTATE	BENIGN PROSTATIC HYPERPLASIA	TURP
79	3800/11	1345504	55/M	BPH	NODULAR HYPERPLASIA	TURP
80	3801/11	1344382	60/M	CA PROSTATE	PROSTATIC HYPERPLASIA	TURP
81	3802/11	1344711	64/M	BPH	NODULAR HYPERPLASIA, PIN-2 CHANGES	TURP
82	3824/11	1343165	62/M	BPH	NODULAR HYPERPLASIA	TURP
83	3926/11	1342577	58/M	BPH	NODULAR HYPERPLASIA	TURP
84	3927/11	1346999	60/M	BPH	NODULAR HYPERPLASIA	TURP
85	3953/11	1348233	65/M	CA PROSTATE	ADENOCA PROSTATE	TRUCUT BIOPSY
86	3954/11	1343674	65/M	BPH	PIN 2	TURP
87	3952/11	1348644	60/M	?CA PROSTATE	NODULAR HYPERPLASIA ,ACUTE PROSTATITIS	TURP
88	4014/11	1348466	66/M	?CA PROSTATE	NODULAR HYPERPLASIA	TURP
89	4015/11	1348588	55/M	BPH	NODULAR HYPERPLASIA,PIN 2 CHANGES	TURP
90	4043/11	1395709	58/M	BPH	NODULAR HYPERPLASIA	TURP
91	4043/11	1395709	58/M	BPH	NODULAR HYPERPLASIA	TURP

92	4083/11	1351447	60/M	CA PROSTATE	PROSTATIC ADENO CA	TRUCUT
93	4084/11	1349568	80/M	CA PROSTATE	NODULAR HYPERPLASIA	TRUCUT
94	4104/11	1347323	75/M	BPH	NODULAR HYPERPLASIA,PIN II CHANGES	TURP
95	4107/11	1351383	60/M	CA PROSTATE	NODULAR HYPERPLASIA ,PIN 2 CHANGES	TRUCUT BIOPSY
96	4108/11	1350467	70/M	CA PROSTATE	BASAL CELL HYPERPLASIA	TRUCUT BIOPSY
97	4109/11	1359402	70/M	BPH	NODULAR HYPERPLASIA OF PROSTATE	TRUCUT BIOPSY
98	4363/11	1353260	80/M	BPH	NODULAR HYPERPLASIA WITH ACUTE PROSTATITIS	TURP
99	4448/11	1354724	81/M	CA PROSTATE	PROSTATIC ADENOCA	TRUCUT BIOPSY
100	4576/11	1355973	60/M	CA PROSTATE	PROSTATIC ADENOCA	TRUCUT BIOPSY
101	4604/11	1355477	70/M	BPH	BENIGN PROSTATIC HYPERPLASIA WITH PIN I CHANGES	TURP
102	4607/11	1352733	60/M	BPH	NODULAR HYPERPLASIA	TURP
103	4663/11	1351091	65/M	BPH	NODULAR HYPERPLASIA	TURP
104	4669/11	1352729	60/M	BPH	NODULAR HYPERPLASIA	TURP
105	4753/11	1349969	70/M	BPH	NODULAR HYPERPLASIA	TURP
106	4755/11	1358402	50/M	BPH	NODULAR HYPERPLASIA	TURP
107	4811/11	1359012	52/M	BPH	NODULAR HYPERPLASIA	TURP

108	4833/11	1354390	65/M	BPH	NODULAR HYPERPLASIA	TURP
109	4838/11	1359167	60/M	BPH	NODULAR HYPERPLASIA	TURP
110	5/12	1358710	80/M	CA PROSTATE	PROSTATIC ADENO CA	TRUCUT BIOPSY
111	7/12	1359269	63/M	CA PROSTATE	PROSTATIC ADENO CA	TRUCUT BIOPSY
112	8/12	386011	70/M	CA PROSTATE	NODULAR HYPERPLASIA PIN I-II CHANGES	TRUCUT BIOPSY
113	9/12	1358721	50/M	BPH	NODULAR HYPERPLASIA	TURP
114	53/12	1359043	62/M	BPH	NODULAR HYPERPLASIA	TURP
115	58/12	1357633	75/M	BPH	PROSTATIC ADENOCA	TURP
116	116/12	1354819	70/M	BPH	NODULAR HYPERPLASIA WITH CHRONIC PROSTATITIS	TURP
117	174/12	130732	75/M	BPH	NODULAR HYPERPLASIA WITH CHRONIC PROSTATITIS	TURP
118	179/12	1358993	58/M	BPH	NODULAR HYPERPLASIA	TURP
119	181/12	1359031	65/M	BPH	PROSTATIC ADENOCA	TURP
120	180/12	1359302	60/M	BPH	NODULAR HYPERPLASIA	TURP
121	202/12	1360702	58/M	BPH	NODULAR HYPERPLASIA	TURP
122	244/12	1361976	60/M	BPH	NODULAR HYPERPLASIA	TURP
123	248/12	1363441	65/M	BPH	NODULAR HYPERPLASIA	TURP
124	523/12	1362955	65/M	BPH	PROSTATIC ADENO CA	TRUCUT BIOPSY
125	530/12	1365655	62/M	BPH	NODULAR HYPERPLASIA	TURP

126	527/12	1362955	65/M	CA PROSTATE	PROSTATIC ADENOCA	TRUCUT BIOPSY
127	606/12	1365181	60/M	BPH	NODULAR HYPERPLASIA	TURP
128	767/12	136545	40/M	BPH	NODULAR HYPERPLASIA	TURP
129	812/12	1371050	66/M	BPH	PROSTATIC ADENO CA	TURP
130	813/12	1370458	61/M	BPH	NODULAR HYPERPLASIA	TURP
131	814/12	1362812	74/M	BPH	BENIGN NODULAR HYPERPLASIA , CHRONIC PROSTATIS	TURP
132	958/12	1368033	70/M	CA PROSTATE	NODULAR HYPERPLASIA WITH PIN CHANGES	TRUCUT BIOPSY
133	1026/12	1372983	61/M	BPH	NODULAR HYPERPLASIA WITH SQUAMOUS METAPLASIA	TURP
134	1114/12	1372826	56/M	BPH	NODULAR HYPERPLASIA	TURP
135	1162/12	1374590	56/M	BPH	BENIGN NODULAR HYPERPLASIA WITH CHRONIC PROSTATITIS	TURP
136	1208/12	1372988	68/M	BPH	NODULAR HYPERPLASIA	TURP
137	1209/12	1373175	60/M	BPH	NODULAR HYPERPLASIA	TURP
138	1211/12	1371929	60/M	BPH	NODULAR HYPERPLASIA	TURP
139	1332/12	1375846	60/M	BPH	NODULAR HYPERPLASIA	TURP
140	1359/12	1374270	59/M	BPH	NODULAR HYPERPLASIA	TURP
141	1595/12	1381142	65/M	CA PROSTATE	NODULAR HYPERPLASIA	TURP

142	1597/12	1381145	45/M	BPH	NODULAR HYPERPLASIA	TURP
143	1640/12	1382356	61/M	BPH	NODULAR HYPERPLASIA	TURP
144	1642/12	1382358	65/M	BPH	NODULAR HYPERPLASIA	TURP
145	1760/12	1384570	60/M	BPH	NODULAR HYPERPLASIA	TURP
146	1762/12	1384573	65/M	CA PROSTATE	NODULAR HYPERPLASIA	TRUCUT BIOPSY
147	1874/12	1396234	83/M	CA PROSTATE	ADENO CARCINOMA PROSTATE	TRUCUT BIOPSY
148	1875/12	1396235	65/M	CA PROSTATE	NODULAR HYPERPLASIA WITH BASAL CELL HYPERPLASIA	TURP
149	2063/12	1401214	60/M	BPH	NODULAR HYPERPLASIA	TURP
150	1994/12	1401193	64/M	BPH	NODULAR HYPERPLASIA	TURP

BPH - BENIGN PROSTATIC HYPERPLASIA

BCH – BASAL

PIN - PROSTATIC INTRAEPITHELIAL NEOPLASIA

CA-CARCINOMA.

TURP – TRANS URETHRAL RESECTION OF PROSTATE

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ABSTRACT

Prostatic nodular hyperplasia and adenocarcinoma are common diseases that account for considerable morbidity and mortality in the aging population. Interpretation of prostatic biopsies has been and continues to be a challenge to the pathologist. In such situations, immunohistochemical detection of basal cells is widely used to help in the diagnosis or exclusion of prostatic carcinoma. We analysed 150 cases of prostatic lesions histopathologically,out of which 130 cases were benign lesions and 20 were malignant. Among premalignant lesions 12 cases were found along with nodular hyperplasia &3 cases were found along with carcinoma. We selected 12 cases for IHC studies and studied the role of p63 verses HMWCK in distinguishing prostatic carcinoma from its benign lesions and its precursors. We found that immunohistochemical p63 staining is diagnostically reliable in identifying basal cells in TURP specimens and compares favourably with HMWCK. In addition, p63 staining which shows a nuclear reaction is easy to interpret than HMWCK which shows cytoplasmic reaction.