HISTOPATHOLOGICAL STUDY OF PROSTATIC LESIONS AND ASSESSMENT WITH AGNOR INDEX AND PROSTATIC BASAL CELL MARKER

DISSERTATION SUBMITTED FOR

M.D., BRANCH – III

PATHOLOGY

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CERTIFICATE

This is to certify that this dissertation entitled

“HISTOPATHOLOGICAL STUDY OF PROSTATIC LESIONS AND ASSESSMENT WITH AGNOR INDEX AND PROSTATIC BASAL CELL MARKER” is the bonafide record work done by DR.K.SUBATHRA submitted as partial fulfillment for the requirements of M.D Degree Examinations, Pathology to be held in April 2012.

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INTRODUCTION

“When the hair becomes grey and scant, when specks of earthly matter begin to be deposited in the tunics of artery, and when there is formed a white zone around the cornea, at the same time, I dare say invariably the prostate increases in volume”.

- Sir Benjamin Brodie.

The prostate is a pear shaped glandular retroperitoneal organ encircling the neck of the bladder and urethra. It weighs about 20 gram in normal adult male. The prostate is a functional conduit that allows urine to pass from the urinary bladder to the urethra, and adds nutritional secretions to the sperm to form semen during ejaculation. Prostatic secretion contributes 20% of total volume of semen. It includes spermine, citric acid, cholesterol, phospholipids, fibrinolysin, fibrinogenase, zinc and acid phosphatase.

Prostatic diseases, benign and malignant are collectively responsible for significant morbidity and mortality in men throughout the world. The ability of this small gland to cause misery for aging male as a consequence of bladder obstruction is astonishing.
Only three pathologic processes affect the prostate gland with sufficient frequency to merit discussion namely inflammation, benign prostatic hyperplasia (BPH) and tumours.

Inflammation of prostate is called as prostatitis. Prostatitis may be divided into several categories such as acute bacterial prostatitis, chronic bacterial prostatitis, chronic abacterial prostatitis and granulomatous prostatitis.

Benign prostatic hyperplasia (BPH) is an extremely common disorder in men over age 50. It is characterized by hyperplasia of prostatic stromal and epithelial cells, resulting in the formation of large, fairly discrete nodules in the periurethral region of the prostate.

Prostate cancer is now the sixth most common cancer in the world. Prostatic adenocarcinoma is the second most common cause of cancer mortality in men next to lung cancer. When the terms "prostate cancer" or "prostate adenocarcinoma" are used without qualifications it refers to the common or acinar variant of prostate cancer. In approximately 70% of cases, carcinoma of the prostate arises in the peripheral zone of the gland, classically in a posterior location, where it may be palpable on rectal examination.
Prostatic cancers are diagnosed by fine needle aspiration cytology, needle biopsies, transurethral resection of prostate (TURP) and prostatectomy.

Interpretation of prostatic biopsies has been a continuous problem for practising pathologist. Various types of difficulties have been encountered while diagnosing and typing prostatic carcinoma and premalignant lesions especially in TURP chips where there is loss of orientation and coagulation of tissue during cauterization.

Prostatic lesions on routine haematoxylin & eosin staining sometimes cause diagnostic dilemma between benign and malignant lesions and especially in premalignant lesions like atypical adenomatous hyperplasia (AAH) and prostatic intraepithelial neoplasia (PIN). An important diagnostic criteria in the differentiation is the loss of basal cell layer in adenocarcinoma and its presence in the benign lesions. Several immunohistochemical markers have been used to stain the basal cells of prostate like High molecular weight cytokeratin (HMWCK), p63 etc. Proliferative markers like silver staining nucleolar organizer regions (AgNOR), proliferating cell nuclear antigen (PCNA) are of great help in differentiating benign premalignant and malignant lesions.
This current study aims at analysis of histopathological features of various non neoplastic and neoplastic lesions of the prostate including the grading of malignant lesions and evaluation of role of basal cell markers and proliferative markers in different benign, premalignant and malignant lesions of prostate.

Histological typing, grading and staging of prostatic carcinoma are vital in planning the treatment strategies and predicting the survival rate.
AIM OF THE STUDY

1. To study the incidence of various prostatic lesions in and around Madurai during the period from May 2009 to July 2011.
2. To analyse the age incidence of various prostatic lesions.
3. To study the histopathology of non neoplastic and neoplastic lesions of prostate.
4. To categorize the prostatic malignancy and to apply Gleason grading system for prostatic carcinoma.
5. To study and compare the role of proliferative marker such as AgNOR and immunohistochemical prostatic basal cell marker such as p63 in different benign, premalignant and malignant lesions of prostate.
REVIEW OF LITERATURE

EMBRYOLOGY

The prostate gland is formed from the upper part of the definitive urogenital sinus. The buds that arise from the mesodermal part of prostatic urethra form the inner glandular zone. The buds that arise from rest of the prostatic urethra (endoderm) form the outer glandular part.

Development and growth of prostate is androgen dependent and 5α reductase is the essential androgen for prostate development.\textsuperscript{24}

![Figure 1: Location of prostate gland](image)
ANATOMY

The first description of the anatomy of prostate dates back to third century. B.C. Heterophilus is credited with being the first to provide anatomic description of prostate.

The prostate is a pyramidal shaped fibro muscular gland which surrounds the prostatic urethra from the bladder base to membranous urethra (Figure 1). The adult prostate weighs approximately 20gm, measures 3cm in length, 4cm in width, and 2cm in diameter.\(^{37}\)

The human prostate is a composite organ, made up of glandular and non glandular components.

Glandular component

The anatomical features and developmental biology of the prostate have been explored over the past decades by Mc Neal JE.\(^{5,1}\) He described zonal anatomy of prostate based on examination of gland in different planes of section.\(^{5,1,2}\)

Zonal anatomy (Figure 2)

The glandular tissue may be subdivided into three distinct zones\(^{24}\):

- **Transition zone** - 5 % of volume, chief source of nodular hyperplasia, and 15-20% of carcinomas.
- **Central zone** - 25% of volume, 10% carcinomas.
- **Peripheral zone** -70% of Volume, 70-75% of Carcinomas.
Figure 2: Zonal anatomy of prostate gland

Non glandular component

It is concentrated anteriomedially and responsible for anterior convexity of the organ. It includes

- Preprostatic sphincter
- Anterior fibromuscular stroma
- Prostatic capsule

HISTOLOGY: (Figure 3)

The prostate is composed of glandular epithelium and fibromuscular stroma. The glands are tubuloalveolar type. The glands are lined by three distinct epithelial cell populations such as secretory, basal, and
neuroendocrine cells. The secretory cells are terminally differentiated columnar cells and stain with prostate specific antigen (PSA) and prostatic acid phosphatase (PAP). Basal cells are peripherally located between the secretory cells and basement membrane. They stain for high molecular weight cytokeratin.\textsuperscript{18} Neuroendocrine cells are irregularly distributed throughout the ducts and acini. These are difficult to recognize without special stains. Most of them contain serotonin and less frequently calcitonin, somatostatin or human chorionic gonadotrophin hormone.

Corpora amylacea are laminated calcified eosinophilic inispissated secretions present within the lumina of the glands.

Figure 3: Normal histology of prostate
Arteries

The prostate is supplied by branches from the inferior vesical, internal pudendal and middle rectal arteries.\textsuperscript{37}

Veins

Prostatic vein drains into the prostatic plexus which empties into the internal iliac vein.\textsuperscript{37}

Lymphatic drainage

Lymphatics from the prostate drains into the internal iliac nodes, some of them drain into external iliac and sacral lymph nodes.\textsuperscript{37}

Innervation

The prostate has an abundant nerve supply from the inferior hypogastric (pelvic) plexus.\textsuperscript{37}

PATHOLOGY OF PROSTATE

Pathological lesions of prostate are categorized into non neoplastic and neoplastic lesions. Nonneoplastic lesions are ectopia, benign prostatic hyperplasia (BPH), prostatitis, infarction, calculi and cystic lesions. Tumour like lesions include postoperative spindle cell nodule and inflammatory pseudotumour. Neoplastic lesions include benign and malignant epithelial tumours, mesenchymal tumours and secondary tumours. Among these the following lesions are common
• Inflammatory lesions
• Benign prostatic hyperplasia (BPH)
• Prostatic adenocarcinoma

I. NONNEOPLASTIC LESIONS

INFLAMMATORY LESIONS OF PROSTATE

Inflammatory lesions of prostate are known as prostatitis. They are classified into Common and uncommon types.\textsuperscript{24}

Common types

Acute bacterial prostatitis
Chronic bacterial prostatitis
Non bacterial prostatitis
Prostatodynia

Uncommon types

Gonococcal prostatitis
Tuberculous prostatitis
Parasitic prostatitis
Mycotic prostatitis
Non specific granulomatous prostatitis
BENIGN PROSTATIC HYPERPLASIA (BPH)

Benign prostatic hyperplasia represents nodular expansion of either prostatic glandular elements or stromal elements or both. Although Morgagni referred to BPH in the early 18th century, it was not until the turn of this century that detailed anatomic observation on the ducts and glands were published.

Histologic evidence of BPH can be seen in approximately 20% of men over 40 years of age, a figure that increases to 70% by age 60 and to 90% by age 80.

**Predisposing factors:**

No predisposing factors (other than castration & intact androgen supply) have been identified. As Badenoch put it, nodular hyperplasia of the prostate occurs “in saints and sinners, in fat men and thin, in persons with large families and monks with none, in postmen and prime ministers.”

**Gross features:**

The weight ranges from 40-400gm. On cross-section, the nodules vary in colour and consistency. In nodules that contain mostly glands, the tissue is yellow-pink in colour and soft in consistency. In nodules
composed primarily of fibromuscular stroma, the tissue is pale gray in colour and firm in consistency.

**Histology:**

The hallmark of BPH is nodularity.\textsuperscript{77}

**Frank’s classification of hyperplastic nodules**\textsuperscript{29}

- The stromal (fibrous or fibrovascular) nodule
- The fibromuscular nodule
- The muscular nodule
- The fibroadenomatous nodule
- The fibromyoadenomatous nodule

The hyperplastic glands are dilated or even cystic and may contain corpora amylacea. The lining epithelium is flat to columnar, the cytoplasm is pale and the nuclei are regular and centrally located. The nucleoli are inconspicuous. A continuous basal cell layer is seen above the well-developed basement membrane.

**Special forms of benign prostatic hyperplasia**

- Clear cell and/or cribriform hyperplasia
- Sclerosing adenosis
- Post atrophic hyperplasia of prostate
Basal cell hyperplasia (BCH)

Basal cell proliferation in prostate exhibits a morphological continuum ranging from focal basal cell hyperplasia to florid adenoid cystic carcinoma.24

Patterns of benign basal cell proliferation26, 40

- Typical basal cell hyperplasia
- Atypical basal cell hyperplasia
- Basal cell adenoma

Malignant counterpart

- Adenoid cystic carcinoma

In basal cell hyperplasia two or more cell layer thickness is seen at the periphery of the acini. The cells in basal cell hyperplasia are enlarged, round with large pale ovoid nuclei, finely reticular chromatin and moderate amount of cytoplasm.24

Metaplasia in prostate

- Transitional cell (urothelial) metaplasia
- Mucous gland metaplasia27
- Squamous metaplasia
Association of BPH with prostate cancer

Cancer is found incidentally in 8-10% of TURP specimens but BPH is not a premalignant lesion or a precursor of cancer.

II. NEOPLASTIC LESIONS

PREMALIGNANT CONDITIONS

Foci with the appearance of incipient carcinoma of the prostate in young adults may represent a type of cancer with an extraordinary long latent period. The two proposed histological premalignant lesions of prostate are

- Prostatic intra epithelial neoplasia (PIN)
- Atypical adenomatous hyperplasia (AAH) or adenosis

PROSTATIC INTRA EPITHELIAL NEOPLASIA (PIN)

Definition

Prostatic intraepithelial neoplasia (PIN) is best characterized as a neoplastic transformation of the lining epithelium of prostatic ducts and acini. By definition, this process is confined within the epithelium therefore, intraepithelial.

The term PIN was introduced in 1987 by Bostwick and endorsed by consensus at a 1989 international conference to replace other applications used in the literature for the same lesion. This consensus group also
proposed that PIN to be divided into two grades (low grade and high grade) to replace the previous three grade system (PIN 1 – 3).

**TABLE 1**
PROSTATIC INTRA EPITHELIAL NEOPLASIA (PIN) DIAGNOSTIC CRITERIA

<table>
<thead>
<tr>
<th>Feature</th>
<th>Low grade PIN</th>
<th>High grade PIN</th>
</tr>
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<tbody>
<tr>
<td>Architecture</td>
<td>Epithelial cell crowding and stratification, with irregular spacing.</td>
<td>More crowding and stratification; four patterns; tufting, micro papillary, cribriform and flat.</td>
</tr>
<tr>
<td>Cytology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclei</td>
<td>Enlarged with marked size variation</td>
<td>Enlarged; some size and shape variation.</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Normal</td>
<td>Increased density and clumping.</td>
</tr>
<tr>
<td>Nucleoli</td>
<td>Rarely prominent.</td>
<td>Large and prominent. Similar to invasive carcinoma.</td>
</tr>
<tr>
<td>Basal cell layer</td>
<td>Intact</td>
<td>May show some disruption.</td>
</tr>
<tr>
<td>Basement membrane</td>
<td>Intact</td>
<td>Intact</td>
</tr>
</tbody>
</table>

High Grade PIN (HGPIN)

High grade PIN has high predictive value as a marker for adenocarcinoma.
Architectural patterns of high grade PIN are

- Tufting
- Micropapillary
- Cribriform
- Flat

**Morphological relationship of HGPIN to prostate carcinoma**

The associations of HGPIN and prostate cancer are several:

- The incidence and extent of both lesions increase with the age of the patient.\(^{80}\)
- There is an increased frequency, severity and extent of HGPIN in prostate with cancer.\(^{74, 79}\)
- Both HGPIN and cancer are multifocal with a predominant peripheral zone distribution.\(^{79}\)
- Histological transition from HGPIN to cancer has been described.
- High-grade PIN shares molecular genetics features with cancer.
- HGPIN is more strongly associated with intermediate-high grade prostatic carcinoma.
Histologic variants of high grade PIN

- Signet-ring variant
- Mucinous variant
- Foamy variant
- Inverted variant
- Small cell neuroendocrine variant

ATYPICAL ADENOMATOUS HYPERPLASIA (AAH) OR ADENOSIS:

Although McNeal referred to this lesion as possible premalignant proliferation, to date a convincing argument for it being a precursor lesion has not been made by most studies. ATYPICAL ADENOMATOUS HYPERPLASIA (AAH) OR ADENOSIS is most often found in the central periurethral zone of prostate. It consists of nodular, well circumscribed proliferation of closely packed acini. The individual cells in the acini are cytologically benign. A distinctive feature is the presence of larger infolding glands admixed with smaller glands.

CARCINOMA OF PROSTATE

The first clear description of carcinoma prostate was presented by Sir Henry Thompson in 1854. Mc Neal reported that carcinoma typically arises in the peripheral zone, although any zone can be the site of origin.
Malignant lesions of prostate may be of primary or metastatic in origin. Among the primary prostatic neoplasms epithelial tumours are common. Prostatic acinar adenocarcinoma is the most common type of epithelial tumours. When the terms "prostate cancer" or "prostate adenocarcinoma" are used without qualifications it refers to the common or acinar variant of prostate cancer. Other epithelial tumours are ductal adenocarcinoma, urothelial tumours, squamous and basal cell tumours. A variety of rare benign and malignant mesenchymal tumours arise in the prostate. Leiomyosarcoma of prostate is the most common type of sarcomas in prostate gland among adult patients.

**WHO HISTOLOGICAL CLASSIFICATION OF PROSTATIC TUMORS**:\(^92^:

**Epithelial tumors:**

**Glandular neoplasms**

- **Adenocarcinoma (acinar)**
  - Atrophic
  - Pseudohyperplastic
  - Foamy
  - Colloid
  - Signet ring
- Carcinoma with spindle cell differentiation
  - Carcinosarcoma (Sarcomatoid carcinoma)

- Prostatic intraepithelial neoplasia (PIN)
  - Prostatic intraepithelial neoplasia, grade III (PIN III)

- Ductal adenocarcinoma

- Urothelial carcinoma

- Squamous tumors
  - Adenosquamous carcinoma
  - Squamous cell carcinoma

- Basal cell tumors
  - Basal cell adenoma
  - Basal cell carcinoma

- Neuroendocrine tumors

- Prostatic stromal tumors
  - Stromal tumor of uncertain malignant potential
  - Stromal sarcoma

- Mesenchymal tumors

- Hematolymphoid tumors

- Germ cell tumors

- Metastatic tumors
PROSTATIC ADENOCARCINOMA

Epidemiology

Prostate cancer is now the sixth most common cancer in the world. The incidence of clinically detected adenocarcinoma varies highly among nations worldwide. Prostatic cancer is uncommon in Asians and occurs most frequently among blacks. When compared to other Asian countries, prostatic carcinoma is more common in India. In India, it is the fifth cause of cancer and fourth cause of cancer mortality in men. At some time in their lives approximately 1 in 22 Indian males will be struck by prostatic carcinoma and its incidence is increasing by 3.5 % every year.

Age distribution

Worldwide, about three-quarters of cases occur in men aged 65 or more.

Localization

Most clinically palpable prostate cancers diagnosed on needle biopsy are predominantly located posteriorly and posterolaterally.
Clinical features:

Signs and symptoms:

Most of the prostate cancers are asymptomatic and detected only by digital rectal examination. Rarely, urinary obstruction results from large volume periurethral tumour. Metastatic prostatic adenocarcinoma can present as bone pain, mainly in the pelvic bones and spine.

Aetiology:

Little is known about the aetiology of prostatic cancer. Main factors implicated in the aetiology are

1. Endocrine system
2. Genetic factors
3. Environmental influences
4. Dietary and hereditary factors

Endocrine system:

Androgens play an important role in the development of prostatic cancer.

Genetic factors:

Risk associated loci at 8q24 increases risk among African American men. Fusion of the androgen related gene TMPRSS2 (Transmembrane protease serine 2) and the ETS (E-twenty six) transcription factor family
members particularly ERG (Ets Related Gene) is common and significant 
genomic alteration seen in prostatic cancer.\(^7\)

**Environmental factors:**

Environmental factors as occupational exposure or behavioural factors do not seem to play a clear role.

**Dietary and hereditary factors:**

Increased consumption of fat, lycopenes (found in tomatoes), selenium, soy products and vitamin D have been implicated as the risk factor for prostate cancer, but none has been proven to be causative.\(^7\)

**Macroscopy:**

On section, grossly evident cancers are firm, solid and range in colour from white-grey to yellow-orange.

**Histopathology:**

**Architectural features**

Infiltrative small atypical glands situated in between the larger benign glands.

**Nuclear features**

Nuclear enlargement with prominent nucleoli is a frequent finding.
**Cytoplasmic features**

Glands of adenocarcinoma have a discrete crisp, sharp luminal border and amphophilic cytoplasm.

**Intraluminal features**

Prostatic crystalloids are commonly seen in low grade prostate cancer. Corpora amylacea are rarely seen in prostate cancer.

**Malignant specific features**

- Perineural invasion
- Collagenous micronodules
- Glomerulations

**Histological variants**

**Atrophic variant**

An unusual variant of prostate cancer resembles benign atrophy owing to its scant cytoplasm.

**Pseudohyperplastic variant**

Pseudohyperplastic prostate cancer resembles benign prostate glands in that the neoplastic glands are large with branching and papillary infolding.
**Foamy gland variant**

Foamy gland variant is characterized by having abundant foamy appearing cytoplasm with a very low nuclear to cytoplasmic ratio.

**Colloid & signet ring variant**

Diagnosis of mucinous adenocarcinoma of the prostate gland should be made when at least 25% of the tumor resected contains lakes of extracellular mucin.

**Oncocytic variant**

Prostatic adenocarcinoma is rarely composed of large cells with granular eosinophilic cytoplasm.

**Lymphoepithelioma-like variant**

This undifferentiated carcinoma is characterized by a syncytial pattern of malignant cells associated with a heavy lymphocytic infiltrate.

**Sarcomatoid variant (carcinosarcoma)**

Sarcomatoid carcinoma is composed of glandular component showing variable Gleason score. The sarcomatoid component often consists of a nonspecific malignant spindle-cell proliferation.
OTHER TYPES OF CARCINOMAS

DUCTAL ADENOCARCINOMA

Subtype of adenocarcinoma composed of large glands lined by tall pseudostratified columnar cells. Although ductal adenocarcinomas are not typically graded, they are mostly equivalent to Gleason pattern 4.

UROTHELIAL CARCINOMA

The frequency of primary urothelial carcinoma ranges from 0.7-2.8% of prostatic tumours in adults.\(^{38, 39}\) The full range of histologic types and grades of urothelial neoplasia can be seen in primary and secondary urothelial neoplasms of the prostate.

SQUAMOUS NEOPLASMS

By definition pure squamous cell carcinoma does not contain glandular features and it is identical to squamous cell carcinoma of other origin. With rare exception, it does not express prostate specific antigen (PSA) or prostatic acid phosphatise (PAP).\(^{65, 88}\)

BASAL CELL CARCINOMA

This is a neoplasm composed of prostatic basal cells. It is believed that a subset of basal cell is prostatic epithelial stem cells, which can give rise to a spectrum of proliferative lesions ranging from basal cell hyperplasia to basal cell carcinoma.
NEUROENDOCRINE TUMOURS

Neuroendocrine differentiation in prostatic carcinoma has three forms:

1. Focal neuroendocrine differentiation in conventional prostatic adenocarcinoma
2. Carcinoid tumour
3. Small cell neuroendocrine carcinoma

LEIOMYOSARCOMA

Leiomyosarcomas are the most common sarcomas involving the prostate in adults. Histologically, leiomyosarcoma range from smooth muscle tumors showing moderate atypia to highly pleomorphic sarcomas.

HAEMATOLYMPHOID TUMOURS

Prostate is a rare site of extranodal lymphoma.

SECONDARY TUMOURS INVOLVING THE PROSTATE

Metastases from lung, skin (melanoma), gastrointestinal tract, kidney, testis and endocrine glands have been reported.

GLEASON GRADING SYSTEM (Figure 4)

Although numerous grading systems namely Mostofi –WHO, Schroder-Mostofi, M.D. Anderson Hospital, Gaeta, Muller et al and Gleason grading system have been proposed in the literature, only the Gleason grading system has prevailed.
The Gleason grading system named after Donald F. Gleason is the predominant grading system now and in 1993, it was recommended by WHO consensus conference. The Gleason grading system is based on glandular architecture; nuclear atypia is not evaluated. The following figure shows histological patterns of prostatic adenocarcinoma.

Figure 4: Standardized drawing for Gleason grading system.
This is the most powerful prognostic indicator of prostate carcinoma\(^3\).

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

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

3A. Single, separate, uniform glands, scattered.

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

4A. Fused glands, raggedly infiltrating.

4B. Same, with large pale cells (hypernephroid)

5A. Almost solid, rounded masses, necrosis ("Comedocarcinoma")

5B. Anaplastic, raggedly infiltrating.

**PROLIFERATIVE MARKERS**

**SILVER STAINING NUCLEOLAR ORGANIZER REGIONS (AGNOR)**

The nucleolar organizer regions (NORs) are chromosomal loops of DNA involved in ribosomal synthesis (Gall and Pardue 1969). Some of the nucleolar proteins associated with NORs are stained with silver methods (AgNOR proteins or AgNORs) (Derenzini and Ploton 1991).
AgNORs can be identified as black dots in the nuclei. Their size and number reflect nucleolar and cell proliferative activity of tumors (Derenzini et al. 1990).

Estimation of AgNORs parameters (number, size and distribution) has been applied in tumour pathology both for diagnostic and prognostic purposes. AgNOR number and distribution in the nucleus (configuration) were useful in the detection and prognosis of prostatic neoplasia.60

**IMMUNOPROFILE**

Prostatic immunohistochemical markers can be divided into following categories

- **Prostate lineage specific markers** - Prostate specific antigen (PSA), Prostatic acid phosphatase (PAP), Prostate specific membrane antigen (PSMA), Human glandular kallikrein 2 (Hk2).
- **Basal cell markers** - High molecular weight cytokeratins (34 betaE12), P63, Cytokeratin 5/6 (CK5/6).
- **Prostate cancer specific maker** - Alpha Methyl-CoA racemase AMACR/p504s
- **Proliferation markers** – proliferating cell nuclear antigen (PCNA), KI 67.
**Prostate specific antigen (PSA)**

Prostate specific antigen is a useful immunohistochemical marker relatively high specific for prostatic glandular cells. PSA is diagnostically helpful in distinguishing prostatic adenocarcinomas from other neoplasms secondarily involving the prostate and establishing prostatic origin in metastatic carcinomas of unknown primary.\textsuperscript{28,66}

**Basal cell markers**

In 1953, Totten et al\textsuperscript{85} observed that basal cells were invariably lacking in prostatic adenocarcinoma. They also stated that basal cells were not always present in benign prostatic epithelium. This latter statement is indicative of how inconspicuous basal cells can be on H & E–stained material. It was not until the advent of immunohistochemical staining for cytokeratins that are preferentially expressed in basal cells, that the diagnostic utility of the Totten et al\textsuperscript{85} observation became fully appreciated. In 1985, Brawer et al\textsuperscript{18} clearly outlined the manner in which staining for high molecular weight cytokeratin could be used to distinguish a variety of benign and potentially preneoplastic processes from invasive carcinoma.
The recently cloned gene, p63, is a homologue of the tumor suppressor gene, p53. It is expressed in the basal cell component of the epithelium in a variety of human tissues and appears to be important in epithelial embryogenesis.

The advantages of p63 over High molecular weight cytokeratin in prostate immunohistochemistry are:

1) Stains a subset of 34βE12 negative basal cells.
2) Less susceptible to the staining variability than 34βE12 (particularly in TURP specimens with cautery artifact).
3) Easier to interpret because of its strong nuclear staining intensity and low background.

In a study by Weinstein MH false-negative staining for p63 was less compared with the case of high molecular weight cytokeratin.

**Alpha Methyl-CoA racemase (AMACR)**

AMACR mRNA was recently identified as being over expressed in prostatic adenocarcinoma. AMACR may be used as a confirmatory stain for prostatic adenocarcinoma, in conjunction with H&E morphology and a basal cell specific marker.
PROGNOSIS

The College of American Pathologist has classified prognostic factors into three categories.\(^{10}\)

**Category I: (proven prognostic factors and useful in management)**

- Preoperative serum PSA level
- TNM stage grouping
- Histological grade as Gleason score
- Surgical margin status

**Category II: (remains to be validated)**

- Tumor volume
- Histologic type
- DNA ploidy

**Category III: (not sufficiently studied)**

- Perineural invasion
- Neuroendocrine differentiation
- Microvessel density
- Nuclear roundness
- Chromatin texture
- Other karyometric factors
- Proliferation markers
• PSA derivatives

• Oncogenes, tumor suppressor genes and apoptosis genes
MATERIAL AND METHODS

This present study is a prospective study undertaken in the department of pathology, Madurai Medical College, Madurai, during the period of May 2009 to July 2011. This study was conducted on 108 prostatic specimens of which 56 specimens were from Government Rajaji Hospital, Madurai and 52 were from Madurai Kidney centre, Madurai. (Annexure-IV)

All the 108 specimens received were Trans Urethral Resection of Prostate (TURP) specimens ranging in volume from 1 to 10 grams. These were fixed in 10% neutral buffered formalin for 12 hours. After adequate fixation, the specimens were submitted for processing until four cassettes were filled. Tissue processing was done with automated tissue processor and sections were made manually with microtome of thickness 2-4 microns. Staining was done with routine haematoxylin and eosin (Annexure-III) and examined under light microscope. Silver staining of nucleolar organizer region (AgNOR) method of Smith and Crocker (Annexure-III) was done for all the cases taken for study excluding the cases of Leiomyosarcoma of prostate and contiguous spread of rectal adenocarcinoma to prostate. All the slides were examined under 100X oil immersion objective with 10X eye piece. One hundred lesional nuclei of
epithelial cells were taken at random for the counting procedure. Careful focussing allowed the nucleolar organizer regions (NOR) to be visualised as black dots arranged both in clusters and clumps and as individual “satellites” within the cell nucleolus. The NOR dots were counted per nuclei and an average count was noted.

Immunohistochemical study with prostatic basal cell marker p63 (Annexure– III) was done for various types of prostatic lesions. Ten such selected cases include Granulomatous prostatitis, Benign Prostatic Hyperplasia, atypical adenomatous hyperplasia, low grade PIN, high grade PIN, and adenocarcinoma. Expression of p63 was considered as nuclear positivity of the basal cells of prostatic epithelium.

Immunohistochemical study with desmin and actin were done for the case diagnosed as Leiomyosarcoma. Immunohistochemical study with PSA was done for the case of contiguous spread of rectal adenocarcinoma to prostate.

With histopathological examination various prostatic lesions were categorised into non neoplastic and neoplastic lesions such as Granulomatous prostatitis, Benign Prostatic Hyperplasia, atypical adenomatous hyperplasia, low grade PIN, high grade PIN, prostatic adenocarcinoma, Leiomyosarcoma and adenocarcinomatous deposits.
Histological grading was done for all the cases diagnosed as prostatic adenocarcinoma using Gleason grading system and Gleason histological scores were also noted.

The histological data, results of AgNOR staining and results of immunohistochemical staining with basal cell marker, so obtained were analysed and compared with other similar studies. The recent literatures regarding prostatic lesions were also reviewed.
OBSERVATIONS

This prospective study included 108 cases of varied prostatic lesions like benign, premalignant and malignant lesions. They were Granulomatous prostatitis, Benign prostatic Hyperplasia, prostatic intraepithelial neoplasias (PIN), atypical adenomatous hyperplasia (AAH), primary prostatic adenocarcinoma, Leiomyosarcoma, and contiguous involvement of prostate by rectal adenocarcinoma.

INCIDENCE OF VARIOUS PROSTATIC LESIONS:

Benign prostatic hyperplasia was by far the most common type of lesion – 96 cases (88.89%), followed by malignant lesion – 10 cases (9.26%) and inflammatory lesions – 2 cases (1.85%). The incidences of various prostatic lesions are illustrated in Graph 1.

GRAPH 1
INCIDENCE OF VARIOUS PROSTATIC LESIONS
AGE INCIDENCE OF VARIOUS PROSTATIC LESIONS

The age incidence of various prostatic lesions are shown in Table 2.

TABLE 2

AGE INCIDENCE OF VARIOUS PROSTATIC LESIONS

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Age group</th>
<th>Inflammatory condition</th>
<th>BPH</th>
<th>Malignant lesions</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>40-49</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1.85%</td>
</tr>
<tr>
<td>2.</td>
<td>50-59</td>
<td>0</td>
<td>18</td>
<td>2</td>
<td>18.52%</td>
</tr>
<tr>
<td>3.</td>
<td>60-69</td>
<td>1</td>
<td>54</td>
<td>5</td>
<td>55.56%</td>
</tr>
<tr>
<td>4.</td>
<td>70-79</td>
<td>1</td>
<td>20</td>
<td>3</td>
<td>22.22%</td>
</tr>
<tr>
<td>5.</td>
<td>80-89</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1.85%</td>
</tr>
</tbody>
</table>

GRAPH 2

AGE INCIDENCE OF VARIOUS PROSTATIC LESIONS
In our study all the cases were between the ages of 40 – 81 years.

Incidence of both benign and malignant lesions was high in the age group of 60-69 years.

Among the 98 benign lesions, youngest case reported was 41 years old and oldest was 81 years. The mean age group for benign lesions was 63.44.

Among the 10 malignant lesions, youngest case reported was 50 years old and oldest was 77 years. The mean age group for malignant lesions was 63.90.

**HISTOPATHOLOGY OF NON NEOPLASTIC AND NEOPLASTIC LESIONS**

**INFLAMMATORY LESION**

Two cases (1.85%) showed features of granulomatous prostatitis inclusive of both specific and nonspecific types. One case showed disrupted ducts and acini surrounded by granulomatous infiltration of foamy histiocytes multinucleated giant cells and lymphocytes which was suggestive of nonspecific Granulomatous prostatitis (Figure 5,6,7). Other case showed well formed epithelioid cell granulomas with Langhans type of giant cells suggestive of tuberculous Granulomatous prostatitis (Figure 8,9).
BENIGN PROSTATIC HYPERPLASIA

Out of all the prostatic lesions studied, Nodular hyperplasia constituted the bulk of the lesions [88.89 % (96 cases)].

Light microscopic findings in benign prostatic hyperplasia

The light microscopic examination showed hyperplasia of both the glandular and stromal components (Figure 10). The glandular component showed variably sized glands with cystic dilatation of some them. The glandular lining epithelium exhibited papillary buds and infoldings which were prominent than the normal prostatic glands. The glands were lined by inner columnar cells with pale cytoplasm and uniform nuclei and outer intact basal cell layer. The stroma was fibromuscular.

Associated microscopic findings in BPH

Benign prostatic hyperplasia showed other associated microscopic findings such as Lymphocytic infiltration, Corpora amylacea, Basal cell hyperplasia and squamous metaplasia. Incidences of associated microscopic findings in BPH are shown in Table 3.
TABLE 3
ASSOCIATED MICROSCOPIC FINDINGS IN BPH

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Findings</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Lymphocytic infiltration</td>
<td>64</td>
<td>66.67%</td>
</tr>
<tr>
<td>2.</td>
<td>Corpora amylacea</td>
<td>32</td>
<td>29.63%</td>
</tr>
<tr>
<td>3.</td>
<td>Basal cell hyperplasia</td>
<td>10</td>
<td>9.26%</td>
</tr>
<tr>
<td>4.</td>
<td>Squamous metaplasia</td>
<td>2</td>
<td>1.85%</td>
</tr>
</tbody>
</table>

Among the 96 cases of BPH, 64 (66.67%) cases showed minimal non characteristic lymphocytic infiltration (Figure 11). The term BPH prostatitis is used only when there is significant inflammatory cell infiltrate with gland destruction.\textsuperscript{24}

In 32 cases of BPH, glands contained inspissated secretions of glycoprotein called corpora amylacea with areas of calcifications in some of them (Figure 12). Corpora amylacea are common in benign glands and only rarely seen in prostate cancer.\textsuperscript{76}

Foci of basal cell hyperplasia were observed in 10 cases of BPH. Out of which two cases showed symmetric circumferential proliferation of basal cells (Figure 13, 14). Sometimes basal cell proliferation may be mistaken for high grade PIN or carcinoma due to the presence of
cytological abnormalities. These cases are of diagnostic confusion, particularly in needle biopsy specimens.\textsuperscript{24}

Squamous metaplasia is a common response to injury from various causes like TURP, antiandrogen hormonal therapy, infarction and inflammation.\textsuperscript{24} In our study 2 cases of BPH showed squamous metaplasia (Figure 15).

**Prostatic intra epithelial neoplasia (PIN)**

Foci of low grade PIN (LGPIN) and high grade PIN (HGPIN) were observed in benign prostatic hyperplasia. High grade PIN was also associated with prostatic adenocarcinoma. Incidence of Prostatic intra epithelial neoplasia is shown in Table 4.

**TABLE – 4**

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Lesions</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>LGPIN with BPH</td>
<td>12</td>
<td>11.11%</td>
</tr>
<tr>
<td>2.</td>
<td>HGPIN with BPH</td>
<td>1</td>
<td>0.93%</td>
</tr>
<tr>
<td>3.</td>
<td>HGPIN with adenocarcinoma</td>
<td>2</td>
<td>1.85%</td>
</tr>
</tbody>
</table>

Foci of low grade PIN were identified in 12 cases of BPH which showed epithelial cell crowding and stratification. Nuclei were enlarged. Basal cell layer was intact (Figure 16).
Foci of High grade PIN was identified in one case of BPH and two cases of prostatic adenocarcinoma which showed epithelial cell crowding and stratification with tufting and flat pattern. Nuclei were enlarged with prominent nucleoli (Figure 17).

**Atypical adenomatous hyperplasia**

In one case of BPH focal area showed atypical adenomatous hyperplasia in the form of nodular collection of densely packed, small, pale acini which merged with large complex glands (Figure 18).

**MALIGNANT LESIONS OF THE PROSTATE**

**Incidence:**

In our prospective study, malignant lesions constituted the second most common pathology of prostate. This study included a total of 10 cases of malignant lesions of prostate. Incidence of various malignant lesions observed in the study is shown in Table 5.

**TABLE 5**

**MALIGNANT LESIONS OF THE PROSTATE**

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Type of malignant lesion</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Prostatic adenocarcinoma</td>
<td>8</td>
<td>7.41%</td>
</tr>
<tr>
<td>2.</td>
<td>Leiomyosarcoma</td>
<td>1</td>
<td>0.93%</td>
</tr>
<tr>
<td>3.</td>
<td>Local invasion from Rectal adenocarcinoma to prostate</td>
<td>1</td>
<td>0.93%</td>
</tr>
</tbody>
</table>
Adenocarcinoma was the most common [7.41% (8 cases)] type of primary carcinoma encountered. Others were Leiomyosarcoma of prostate invading the bladder [1 case (0.93%)] and the Rectal adenocarcinoma invading the prostate [1 case (0.93%)].

**PROSTATIC ADENOCARCINOMA**

Among the malignant lesions, prostatic adenocarcinoma account for 80% of cases. Majority of the cases were found in seventh decade. Age wise distribution of prostatic adenocarcinoma is shown in Table 6.

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Age</th>
<th>Prostatic adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>50-59</td>
<td>1</td>
</tr>
<tr>
<td>2.</td>
<td>60-69</td>
<td>4</td>
</tr>
<tr>
<td>3.</td>
<td>70-79</td>
<td>3</td>
</tr>
</tbody>
</table>
Light microscopic findings in prostatic adenocarcinoma

Architectural disturbances:

Closely packed small glands, fused glands, small atypical glands situated in between larger benign glands were identified along with diffusely arranged tumour cells. The glands were lined by single layer of epithelium (Figure 19, 20, 21).

Nuclear features

Variable degree of differences in the size and shape of the nuclei was observed. Majority of the nuclei were large, hyperchromatic and showed prominent nucleoli (Figure 22).

Stromal invasion:

Stromal invasion was found in all the cases of adenocarcinoma.
GRADING OF ADENOCARCINOMA OF THE PROSTATE:

All the cases of primary prostatic carcinoma were graded using Gleason scoring system. Primary grade was assigned to dominant pattern and secondary grade to second dominant pattern and then the two numeric scores were added to obtain combined Gleason score. In tumours with one pattern of arrangement, the number was doubled.

**TABLE 7**

**GLEASON GRADING SYSTEM FOR CARCINOMA**

<table>
<thead>
<tr>
<th>S.NO</th>
<th>PATH NO</th>
<th>HPE DIAGNOSIS</th>
<th>GLEASON GRADE</th>
<th>GLEASON SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3667/09</td>
<td>Adenocarcinoma</td>
<td>3+3</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>3909/09</td>
<td>Adenocarcinoma</td>
<td>2+2</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>2674/10</td>
<td>Adenocarcinoma</td>
<td>3+4</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>36/09</td>
<td>Adenocarcinoma</td>
<td>1+2</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>50/09</td>
<td>Adenocarcinoma</td>
<td>1+4</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>78/10</td>
<td>Adenocarcinoma</td>
<td>3+2</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>25/11</td>
<td>Adenocarcinoma</td>
<td>2+3</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>46/11</td>
<td>Adenocarcinoma</td>
<td>3+4</td>
<td>7</td>
</tr>
</tbody>
</table>
### TABLE 8

**INCIDENCE OF CARCINOMA WITH REFERENCE TO GLEASON SCORE**

<table>
<thead>
<tr>
<th>Serial no</th>
<th>GLEASON SCORE</th>
<th>NO OF CASES</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>3-4</td>
<td>2</td>
<td>25%</td>
</tr>
<tr>
<td>2.</td>
<td>5-7</td>
<td>6</td>
<td>75%</td>
</tr>
</tbody>
</table>

**GRAPH – 4**

**GLEASON SCORE**
Gleason score of 5-7 was the commonest, seen in 6 cases. Gleason score of 3-4 was seen in 2 cases.

**Perineural invasion:**

Only one case showed the evidence of perineural invasion in the present study (Figure 23, 24).

**MICROSCOPIC FINDINGS IN LEIOMYOSARCOMA:**

One case of Leiomyosarcoma was noted in the present study. The tumour was composed of interlacing fascicles of spindle cells with blunt ended nuclei and eosinophilic cytoplasm with nuclear atypia and increased mitotic activity. (Figure 25, 26, 27) This tumour was positive for immunohistochemical staining with desmin (Figure 28) and actin.

**MICROSCOPIC FINDINGS IN CONTIGUOUS SPREAD FROM RECTAL ADENOCARCINOMA**

In one case contiguous involvement of prostate by rectal adenocarcinoma was seen which was found to be negative for immunostaining with PSA. The prostate was removed in piecemeal along with Abdomino Perineal Resection done for rectal adenocarcinoma (Figure 29).
**SERUM PSA LEVEL**

Total serum PSA levels were done in only 33 cases of which 30 cases were benign and 3 cases were malignant. Serum PSA level more than 10ng/ml was seen in 2 benign cases and 3 malignant cases. Serum PSA level of benign and malignant cases is shown in Table 9.

**TABLE – 9**

<table>
<thead>
<tr>
<th>Serum PSA level</th>
<th>Benign lesions</th>
<th>Malignant lesions</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4.0ng/ml</td>
<td>20 (60.61%)</td>
<td>-</td>
<td>20 (60.61%)</td>
</tr>
<tr>
<td>4.1-10.0ng/ml</td>
<td>8 (24.24%)</td>
<td>-</td>
<td>8 (24.24%)</td>
</tr>
<tr>
<td>10.1-20.0ng/ml</td>
<td>2 (6.06%)</td>
<td>2 (6.06%)</td>
<td>4 (12.12%)</td>
</tr>
<tr>
<td>&gt;20ng/ml</td>
<td>-</td>
<td>1 (3.03%)</td>
<td>1 (3.03%)</td>
</tr>
</tbody>
</table>

**GRAPH – 5**

**SERUM PSA LEVEL**
PROLIFERATIVE MARKER STUDY

Results of silver staining nucleolar organizer regions (AGNOR):

Mean AgNOR count:

Mean AgNOR count was higher in malignant lesions when compared to benign lesions. (Figure 30, 31, 32)

TABLE - 10

THE MEAN AgNOR COUNT IN VARIOUS PROSTATIC LESIONS

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Lesions</th>
<th>No of cases</th>
<th>Mean AgNOR count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Granulomatous prostatitis</td>
<td>2</td>
<td>1.9</td>
</tr>
<tr>
<td>2.</td>
<td>BPH with or without prostatitis</td>
<td>83</td>
<td>1.43</td>
</tr>
<tr>
<td>3.</td>
<td>BPH with LGPIN</td>
<td>11</td>
<td>2.08</td>
</tr>
<tr>
<td>4.</td>
<td>BPH with AAH</td>
<td>1</td>
<td>2.3</td>
</tr>
<tr>
<td>5.</td>
<td>BPH with HGPIN</td>
<td>1</td>
<td>3.9</td>
</tr>
<tr>
<td>6.</td>
<td>Adenocarcinoma</td>
<td>8</td>
<td>4.81</td>
</tr>
</tbody>
</table>

Note: LGPIN and AAH were noted in the same case. (1091/10) and included as BPH with AAH in the above table.
TABLE 11
MEAN AgNOR COUNT IN BENIGN AND MALIGNANT LESIONS

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean AgNOR count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>1.2-1.7</td>
<td>1.44</td>
</tr>
<tr>
<td>PIN</td>
<td>1.9-3.9</td>
<td>2.23</td>
</tr>
<tr>
<td>Malignant</td>
<td>4-5.2</td>
<td>4.81</td>
</tr>
</tbody>
</table>

GRAPH – 6
MEAN AgNOR COUNT IN VARIOUS PROSTATIC LESIONS

One way Analysis Of Variance test was used to assess the statistical difference between benign, premalignant and malignant lesions.

The differences in the mean value between benign and pre malignant lesions were statistically significant. (P = < 0.001).
The differences in the mean value between benign and malignant lesions were statistically significant. \((P = < 0.001)\).

**PROSTATIC BASAL CELL MARKER STUDY**

**Results of immunohistochemical staining with P63**

The following cases were selected for immunohistochemical staining with prostatic basal cell marker p63.

**TABLE 12**

<table>
<thead>
<tr>
<th>SERIAL NO</th>
<th>PATH NO</th>
<th>HPE DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21/10</td>
<td>Granulomatous prostatitis</td>
</tr>
<tr>
<td>2</td>
<td>83/10</td>
<td>BPH</td>
</tr>
<tr>
<td>3</td>
<td>1091/10</td>
<td>BPH with AAH &amp; LGPIN</td>
</tr>
<tr>
<td>4</td>
<td>4027/09</td>
<td>BPH with LGPIN</td>
</tr>
<tr>
<td>5</td>
<td>119/11</td>
<td>BPH with LGPIN</td>
</tr>
<tr>
<td>6</td>
<td>37/09</td>
<td>BPH with LGPIN</td>
</tr>
<tr>
<td>7</td>
<td>103/10</td>
<td>BPH with HGPIN</td>
</tr>
<tr>
<td>8</td>
<td>50/09</td>
<td>Adenocarcinoma with HGPIN</td>
</tr>
<tr>
<td>9</td>
<td>36/09</td>
<td>Adenocarcinoma with HGPIN</td>
</tr>
<tr>
<td>10</td>
<td>2674/10</td>
<td>Adenocarcinoma (3+4)</td>
</tr>
</tbody>
</table>

Continuous staining of basal cells was observed in benign glands, foci of low grade PIN and atypical adenoamatus hyperplasia. (Figure 33, 34) Focal discontinuity in basal cell staining was observed in high grade
PIN areas. (Figure 35) Complete absence of basal cell staining was seen in adenocarcinoma. (Figure 36, 37) Interestingly discontinuous basal cell staining was seen in disrupted glands of Granulomatous prostatitis. (Figure 38)

**TABLE 13**

**COMPARISON BETWEEN MEAN AGNOR COUNT AND IMMUNOREACTIVITY FOR P63**

<table>
<thead>
<tr>
<th>Type of lesion</th>
<th>Mean AgNOR count</th>
<th>Staining pattern with p63</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>1.44</td>
<td>Continuous</td>
</tr>
<tr>
<td>Low grade PIN</td>
<td>2.08</td>
<td>Continuous</td>
</tr>
<tr>
<td>AAH</td>
<td>2.3</td>
<td>Continuous</td>
</tr>
<tr>
<td>High grade PIN</td>
<td>3.9</td>
<td>Focal discontinuity</td>
</tr>
<tr>
<td>Malignant</td>
<td>4.81</td>
<td>Absent</td>
</tr>
</tbody>
</table>
In this study the AgNOR count which is the marker for proliferative index showed an increase in malignant lesions when compared to that of benign lesions. The normal prostatic basal cell marker is p63. On immunohistochemical staining with p63, basal cells were completely absent in malignant lesions and they were present in benign lesion.
Figure 5: Nonspecific granulomatous prostatitis showing granulomas with destruction of acini. (H & E 100X) (21/10)

Figure 6: Nonspecific granulomatous prostatitis showing disrupted acini surrounded by granulomatous infiltration of foamy histiocytes. (H & E 400X) (21/10)
Figure 7: Nonspecific granulomatous prostatitis showing foamy histiocytes and multinucleated giant cells. (H & E 400X) (21/10)

Figure 8: Tuberculous Granulomatous prostatitis showing epithelioid cell granulomas with Langhans type of giant cells. (H & E 100X) (20/11)
Figure 9: Tuberculous Granulomatous prostatitis showing Langhans type of giant cell. (H & E 400X) (20/11)

Figure 10: Benign prostatic hyperplasia showing nodules of hyperplastic glands. (H & E 100X) (119/11)
Figure 11: Non characteristic lymphocytic infiltration in benign prostatic hyperplasia. (H & E 100X) (3226/09)

Figure 12: Corpora amylacea within the glandular lumina in benign prostatic hyperplasia. (H & E 100X) (119/11)
Figure 13: Benign prostatic hyperplasia showing circumferential proliferation of basal cells. (H&E 100X) (3678/09)

Figure 14: Basal cell hyperplasia highlighted with basal cell immunostain p63. (100X) (50/09)
Figure 15: Squamous metaplasia in benign prostatic hyperplasia. (H&E 100X) (4027/09)

Figure 16: Low grade PIN foci showing epithelial cell crowding and stratification. (H&E 100X) (4027/09)
Figure 17: Foci of High grade PIN showing epithelial cell crowding and stratification in tufting pattern with enlarged nuclei and prominent nucleoli. (H&E 400X)

Figure 18: Benign prostatic hyperplasia showing foci of atypical adenomatous hyperplasia. (H&E 100X) (1091/10)
Figure 19: Prostatic adenocarcinoma Gleason pattern 2 – loosely packed single glands with irregular edges. (H&E 100X) (78/10)

Figure 20: Prostatic adenocarcinoma Gleason pattern 3 – scattered single glands. (H&E 100X) (78/10)
Figure 21: Prostatic adenocarcinoma Gleason pattern 4 – fused infiltrating glandular pattern. (H&E 100X) (2674/10)

Figure 22: Prostatic adenocarcinoma cells showing prominent nucleoli and mitosis. (H&E 400X) (2674/10)
Figure 23: Prostatic adenocarcinoma showing perineural invasion. (H&E 400X) (3667/10)

Figure 24: Prostatic adenocarcinoma showing perineural invasion. (H&E 400X) (3667/10)
Figure 25: Prostatic parenchyma with Leiomyosarcoma. (H&E 100X) (81/10)

Figure 26: Leiomyosarcoma showing interlacing fascicles of tumour cells. (H&E 100X) (81/10)
Figure 27: Leiomyosarcoma showing spindle cells with blunt ended nuclei and eosinophilic cytoplasm with nuclear atypia. (H&E 400X) (81/10)

Figure 28: Leiomyosarcoma showing positivity for desmin with immunohistochemistry. (400X) (81/10)
Figure 29: Rectal adenocarcinoma deposits in prostate.
(H&E 100X)

Inset: Tumour deposits showing negativity for PSA with immunohistochemical study. (100X) (2598/09)

Figure 30: BPH showing occasional AgNOR dots per nuclei.
(AgNOR stain 1000X) (2116/10)
Figure 31: High grade PIN showing two to three AgNOR dots per nuclei. (AgNOR stain 1000X) (103/10)

Figure 32: Prostatic adenocarcinoma showing numerous AgNOR dots per nuclei. (AgNOR stain 1000X) (2674/10)
Figure 33: Foci of low grade PIN showing continuous basal cell immunostaining with p63. (100X) (4027/09)

Figure 34: Foci of Atypical Adenomatous Hyperplasia showing continuous basal cell immunostaining with p63. (100X) (1091/10)
Figure 35: Foci of high grade PIN showing discontinuous basal cell immunostaining with p63. (400X) (103/10)

Figure 36: Prostatic adenocarcinoma showing absent basal cell immunostaining with p63. (100X) (2674/10)
Figure 37: Grade 3 prostatic adenocarcinoma showing infiltrating malignant glands between benign glands with p63 immunostaining. (100X) (2674/10)

Figure 38: Granulomatous prostatitis showing discontinuous basal cell immunostaining with p63 in centre of granuloma. (100X) (21/10)
DISCUSSION

Prostate hosts a number of diseases ranging from inflammation to carcinoma. This leads to a considerable morbidity and mortality worldwide.

This current study aims at the analysis of histopathological features of various non neoplastic and neoplastic lesions of the prostate including the grading of malignant lesions and evaluation of role of basal cell and proliferative markers in different benign, premalignant and malignant lesions of prostate.

INFLAMMATORY LESIONS

GRANULOMATOUS PROSTATITIS

Granulomatous prostatitis is noticed occasionally in TURP specimens. Clinically, it presents as a focal or diffuse area of induration and is often mistaken for carcinoma. Incidence of granulomatous prostatitis was 1.4% in a study by H Mohan et al \(^6^1\) which is similar to our study (1.85%).

BENIGN PROSTATIC HYPERPLASIA (BPH)

The incidence of BPH increases with age. BPH is seen in 20% of the men at 40 years of age, a figure that increases to 70% by age of 60 and to 90% by age of 80.\(^7^7\)
In the present study 108 cases of TURP specimen were examined. Benign prostatic hyperplasia was seen in 96 cases. Highest incidence of nodular hyperplasia was noted in the 7th decade. The number of cases in various age groups is shown in the graph 8

**GRAPH 8**

**AGE DISTRIBUTION OF BPH**

In a classic paper by Berry et al, the prevalence of BPH ranged from 8% for men in their 30s to 88% for men over 80s. In another classic paper Issac and Coffey compared the prevalence of BPH by age in autopsy studies from various countries. This study demonstrated relatively similar prevalence of BPH across a spectrum of countries and ethnicities.
In our study also the incidence of BPH increases with age reaching maximum in 7\textsuperscript{th} decade. The decline in the number of cases beyond the age of 80 years may reflect the average life span of people in our country.

**Associated microscopic findings in BPH**

In BPH minimal periglandular and non characteristic cellular infiltrates are seen in 60\% to 70\% of cases.\textsuperscript{24} In this study 64 cases (66.67\%) of BPH showed focal or diffuse lymphocytic infiltration. The term BPH prostatitis is used when there is significant inflammatory cell infiltrate with gland destruction; however this type of BPH prostatitis is seen in 30\% of all cases.\textsuperscript{24}

In a study by Mittal BV et al basal cell hyperplasia was present in 8.9\% of transurethral specimens.\textsuperscript{59} In our study 10 cases (9.26\%) of BPH showed basal cell hyperplasia which is comparable with the above study.

Squamous metaplasia is a common response to injury from various causes like TURP, antiandrogen hormonal therapy, infarction and inflammation\textsuperscript{24}. In our study two cases of BPH showed squamous metaplasia.
Prostatic Intra Epithelial Neoplasia (PIN)

PIN has high predictive value as a marker for adenocarcinoma. This is particularly true for high grade PIN; if this lesion is identified; close surveillance and follow up biopsy are indicated.\textsuperscript{24} Incidence of cancer after follow up of high grade PIN is shown in Table 14.

**TABLE: 14**

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Investigator</th>
<th>Cases of HGPIN (N)</th>
<th>Cancer on follow up (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Brawer et al\textsuperscript{19}</td>
<td>21</td>
<td>12</td>
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<tr>
<td>2.</td>
<td>Weinstein et al\textsuperscript{90}</td>
<td>19</td>
<td>10</td>
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<td>3.</td>
<td>Davidson et al\textsuperscript{25}</td>
<td>100</td>
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<tr>
<td>4.</td>
<td>Markham et al\textsuperscript{30}</td>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>5.</td>
<td>Berner et al\textsuperscript{6}</td>
<td>37</td>
<td>14</td>
</tr>
</tbody>
</table>

The frequency of HGPIN in transurethral resection of the prostate specimens is between 2.3\% and 4.2 \%.\textsuperscript{8, 32, 57} The present study was comparable well with the above study, stating 2.78\% prevalence of HGPIN in all TURP specimens.

The frequency of HGPIN in prostates involved with cancer is significantly increased when compared with the cancer free prostates.\textsuperscript{24} The
The frequency of high grade PIN in prostates with and without cancer is shown in Table 15.

**TABLE: 15**

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Authors</th>
<th>Specimen source</th>
<th>HGPIN with carcinoma</th>
<th>HGPIN without carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Mc Neal and Bostwick(^5^5) 1986</td>
<td>Autopsy</td>
<td>82%</td>
<td>43%</td>
</tr>
<tr>
<td>2.</td>
<td>Wael A. Sakr and Alan W. Parti(^8^9)(2001)</td>
<td>Autopsy</td>
<td>63% -93%</td>
<td>25% - 43%</td>
</tr>
<tr>
<td>3.</td>
<td>Present study</td>
<td>TURP</td>
<td>25%</td>
<td>1%</td>
</tr>
</tbody>
</table>

The incidence of high grade PIN is low in our study because all the specimens were TURP which does not have enough material compared to whole prostate specimen examined in other studies. In a study by Pacelli A and Bostwick DG the incidence of high grade PIN in TURP specimens without carcinoma was 2.8\(^6^9\). The incidence of PIN in prostatic malignancy, as quoted in the literature, varies from 33% to 100%, depending on the nature of specimen.\(^1^2, 4^5, 5^6, 7^5, 8^7\) In our study, we observed high grade PIN in 25% of the carcinomas.
Low grade PIN foci were identified in 12 cases of BPH. Interobserver agreement on HGPIN is “good to excellent,” whereas that for Low grade PIN may be too great to justify its diagnostic use. Despite this concern LGPIN is been reported, recognizing that this for research purpose.\textsuperscript{24}

Atypical Adenomatous Hyperplasia (AAH)

Gaudin and Epstein estimated the incidence of AAH as 1.6\% in TURP specimens.\textsuperscript{11, 30, 31} In the present study the incidence of Atypical Adenomatous Hyperplasia (0.93\%) is slightly lower than the above study.

MALIGNANT LESIONS OF PROSTATE

In this study, malignant lesions account for 9.26\% (10 cases) of cases. Among the malignant lesions incidence of primary prostatic adenocarcinoma is high [8cases (80\%)].

PROSTATIC ADENOCARCINOMA

Prostate cancer is now the sixth most common cancer in the world.\textsuperscript{71}

The prevalence of prostatic adenocarcinoma in this study is 7.41\% (8 cases). All these cases were incidental adenocarcinoma which were identified in transurethral resection of the prostate (TURP) done for BPH. According to WHO study, when TURP is done without clinical suspicion
of cancer, prostate cancer is incidentally detected in approximately 8-10% of the specimens\textsuperscript{92}, which is in correlation with our study.

The risk of prostate cancer rises very steeply with age. Worldwide, about three-quarters of all cases occur in men aged 65 or more.\textsuperscript{92} In our study also maximum numbers of cases were found in the age group of 60-69 years.

**GLEASON GRADING SYSTEM:**

Gleason scoring system is the most widely used and officially recommended system for scoring prostatic adenocarcinoma.\textsuperscript{2, 35} Gleason score correlates with prognosis after radical prostatectomy and with outcome following radiotherapy. Gleason grade on biopsy can influence mode of treatment.

We applied Gleason grading system for all adenocarcinoma. (Table 7)

The original Gleason grading system does not account for tertiary patterns occupying less than 5% of the tumour. When this tertiary pattern accounted is pattern 4 or 5, it should be reported in addition to the Gleason score, even if it is less than 5% of the tumour since it is associated with adverse prognosis.\textsuperscript{70}

Tertiary high grade Gleason patterns were observed in two cases.
According to Association of Directors of Anatomic and Surgical Pathology (ADASP) Prostate Carcinoma Guideline (Updated September 2006, Version 1.4) in TURP, enucleation, and radical prostatectomy specimens, the Gleason score is based on the primary (most common) and secondary (next most common) pattern. If there is a third pattern or if the second pattern occupies less than 5% of the specimen, then this pattern is reported as a tertiary pattern.¹

**LEIOMYOSARCOMA**

Leiomyosarcoma of prostate is the most common type of sarcomas in prostate gland among adult patients. This tumour, in general accounts for less than 0.1% of prostate malignancies.⁴⁸ In this study one case (0.93%) of Leiomyosarcoma was observed which was confirmed by immunohistochemical study with desmin and actin.
CONTIGUOUS SPREAD FROM RECTAL ADENOCARCINOMA

Prostate carcinoma and colorectal carcinoma constitute 2 of the 3 leading malignancies in males both in term of frequency of diagnoses and mortality. Given the anatomic proximity of the 2 organs, locally advanced Prostate carcinoma can involve adjacent colorectal tissue. Similarly, advanced colorectal carcinoma can rarely invade into prostate.

In this study one case (0.93%) of local invasion from rectal adenocarcinoma was noted and it was found to be negative for immunostaining with PSA, thus ruling out the primary prostatic adenocarcinoma.

SERUM PSA (PROSTATE SPECIFIC ANTIGEN) LEVELS:

In the present study only 33 cases had serum PSA level estimated. Out of 33 cases 30 were benign. A total of 8 cases (24.24%) of BPH showed modest elevation of serum PSA (4.1-10.0ng/ml). Studies of patients with histologically confirmed BPH have shown that 21% to 86% have an elevated serum PSA. Conditions that disrupt barriers for PSA access into the vasculature result in elevation of serum PSA. Such serum elevation can be caused by benign conditions like BPH, prostatic inflammation, infarct or prostatic manipulation and malignant diseases.
Two cases of Granulomatous prostatitis showed elevation of PSA more than 10ng/ml.

High levels of serum PSA is seen in prostatic cancer and it is the most important tumour marker for adenocarcinoma of prostate. In this study two case of prostatic adenocarcinoma showed serum PSA levels between 10.1-20.0ng/ml and one case showed PSA level >20ng/ml.

Serum PSA lacks high sensitivity and specificity for prostate cancer. This problem has been partially overcome by calculating several PSA-related indices (PSA density, Prostate-specific antigen epithelial density. PSA velocity and PSA doubling time). PSA tests are also useful to detect recurrence and response of cancer following therapy.

**AgNOR COUNT**

Tumor differentiation and proliferative activity are important predictors of biological behavior. While routine histological evaluation is fairly adequate to assess differentiation, tumor proliferative activity is difficult to measure. Silver staining for nucleolar organizer regions (AgNORs) is reported to be helpful for assessing tumor proliferation.

AgNOR value is significantly higher in Prostatic carcinoma than BPH, AAH &PIN. It is also significantly higher in PIN than BPH.
Our study showed identical results with the study done by Asim Kumar Manna et al.\textsuperscript{3} Kawase\textsuperscript{43} found AgNOR counts were higher in carcinoma (4.2 +/- 1.57) than in benign lesions (1.9 +/- 0.24). Wael A sakr found that AgNOR study is helpful in assessing tumour proliferation.\textsuperscript{81}

\textbf{TABLE 17}

\textbf{COMPARISON OF MEAN AGNOR COUNT IN VARIOUS STUDIES}

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Studies</th>
<th>BPH</th>
<th>PIN</th>
<th>Prostatic adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Sakr, W. A\textsuperscript{81}</td>
<td>1.836</td>
<td>3.129</td>
<td>4.737</td>
</tr>
<tr>
<td>2.</td>
<td>Asim Kumar Manna\textsuperscript{3}</td>
<td>1.3</td>
<td>4.7</td>
<td>4.91</td>
</tr>
<tr>
<td>3.</td>
<td>Present study</td>
<td>1.44</td>
<td>2.23</td>
<td>4.81</td>
</tr>
</tbody>
</table>

Results of the present study are comparable with the above studies.

\textbf{IMMUNOHISTOCHEMISTRY WITH P63}

P63 is most abundantly represented in normal prostate basal cells and it is a reliable prostate basal cell marker. Because basal cells with p63 protein are consistently undetectable in prostate cancers, p63 expression may be used in the differential diagnosis between benign and malignant lesions of the prostate.\textsuperscript{58}
This marker has the disadvantage that a diagnosis of cancer is based on negative staining. Benign conditions like atrophic glands (25%), basal cell hyperplasia (12%) and atypical adenomatous hyperplasia (10-90%) may show negative staining with basal cell markers. So it is critical to study the immunostained sections with a positive internal control. Benign glands with a strong positive signal were taken as controls.

A combination of basal cell markers and $\alpha$-methylacyl-CoA racemase (AMACR), has increased the sensitivity for the diagnosis of prostate cancer rather than basal cell markers. $^{47}$

Granulomatous prostatitis is a distinctive form of prostatitis that can be misdiagnosed as carcinoma clinically, $^{44, 83, 84}$ radiologically$^{20, 78}$, and histopathologically.$^{73}$ Interestingly in our study the glands in the centre of the granuloma showed absence of basal cells. This shows that while interpreting basal cell marker immunostaining, attention should be given to surrounding inflammation also. This is the disadvantage of using basal cell marker alone as a diagnostic tool.

Increasing grades of PIN were associated with progressive disruption of basal cell layer.$^8$ In this study basal cell layer disruption was seen in foci of high grade PIN areas.
In our study suspected areas of atypical adenomatous hyperplasia in benign prostatic hyperplasia showed continuous staining with p63 which proved that the lesion was benign. As definite diagnosis was arrived with p63 in this case AMACR was not done. So p63 staining is useful in diagnosing gray zone cases.

In this study malignant glands consistently failed to express immunoreactivity to antibody against p63, whereas normal prostatic acini invariably were stained for basal cells.

When the results of AgNOR and p63 staining were compared AgNOR index (the proliferative activity) and invasiveness (lack of basal cell layer) increases from benign to malignant end in the spectrum of prostatic lesions.
SUMMARY

In the present prospective study comprising 108 cases of prostatic lesions which were evaluated with light microscopy, AgNOR staining and Immunohistochemistry, following conclusions were made and presented.

1. BPH was the most common lesion affecting the prostate in elderly [96 cases (88.89%)].
2. The age incidence of Nodular Hyperplasia was high in 7th decade [54 cases (56.25%)].
3. Chronic non specific inflammatory cell infiltration [64 cases(66.67%)], foci of basal cell hyperplasia [10 cases (29.63%)] and squamous metaplasia [2 cases(1.85%)] were seen associated with BPH.
4. Granulomatous prostatitis was rarely encountered [2 cases (1.85%)].
5. HGPIN had high degree of association with prostatic carcinoma (25%).
6. Among the malignant lesions of the prostate, primary prostatic adenocarcinoma was the commonest (80%).
7. According to Gleason Grading system higher grades were more commonly observed as the predominant pattern.
8. Mean AgNOR counts (proliferative activity) were higher in malignant lesions (4.81) when compared with the benign lesions (1.44).

9. With Immunohistochemical staining invasiveness increased from benign (continuous staining) to malignant (absence of staining) end in the spectrum of prostatic lesions.

10. Two rare cases, Leiomyosarcoma of prostate and contiguous spread of rectal adenocarcinoma to prostate were observed in the present study which were confirmed with immunohistochemical study with desmin and PSA respectively.
CONCLUSION

Interpretation of prostatic biopsies has been a continuous problem for practising pathologist. Various types of difficulties have been encountered while diagnosing and typing prostatic carcinoma and premalignant lesions especially in TURP specimens. Mean AgNOR counts are significantly higher in adenocarcinoma when compared to benign and premalignant lesions and correlated with histological grade of the tumour. Prostatic basal cell marker p63 expression may be used in the differential diagnosis between benign and malignant lesions of the prostate with its limitations. We conclude that basal cell markers and proliferative markers have significant role in the diagnosis of prostatic lesions especially which fall in the premalignant category and which create difficulty in the diagnosis by routine histopathological study.
ANNEXURE – I

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ANNEXURE - II
PROFORMA

Serial no:  Name:  
Age:  

Path no:  Address:  

Serum PSA:  

Provisional diagnosis:  

Nature of specimen received: Biopsy, TURP, Prostatectomy.  

Gross examination:  

Weight: size: colour: shape: consistency:  

Presence of nodules, cysts, calculi & suspicious area of carcinoma:  

Histopathological examination:  

BPH  
PIN: low grade, high grade  
Malignancy: primary, secondary  
Adenocarcinoma-Gleason grading  
Associated PIN  
Perineural/ lymphatic invasion  
Inflammatory lesion  

Proliferative marker:  

AgNOR,  

Immunohistochemistry:  

P63 – prostatic basal cell marker
ANNEXURE- III

1. HAEMATOXYLIN AND EOSIN STAINING METHOD

1. Sections were dewaxed with xylene for 20 minutes.
2. Sections were hydrated through descending concentrations (absolute alcohol, 90%, 70%, 50%) of ethanol to water solutions.
3. Sections were rinsed in distilled water.
4. Sections were placed in Ehrlich haematoxylin stain for 20-30 minutes.
5. Rinsed with water.
6. Differentiation was done by immersing the sections in 1% acid alcohol for 10 seconds.
7. Rinsed with water.
8. Blueing was done by keeping the sections in scott’s tap water for 2-10 minutes.
9. Counterstained with 1% aqueous eosin for 1-3 minutes.
10. Rinsed with water.
11. Dehydrated through increasing concentration of ethanol solutions (50%, 70%, 95%, absolute alcohol) and cleared with xylene.
12. Mounted with DPX
2. **AgNOR STAINING OF SMITH AND CROCKER:**

1. Sections were dewaxed with xylene for 20 minutes.

2. Sections were hydrated through descending concentrations of (absolute alcohol, 95%, 70%, 50%) ethanol to water solutions.

3. Sections were rinsed in distilled deionised water.

4. Sections were treated with freshly prepared working solution made up of one volume of 2gm/ml gelatine in 1% formic acid solution and two volumes of 50% aqueous silver nitrate solution for 45 minutes in dark at room temperature.

5. Washed with distilled deionised water for 1 minute.

6. Dehydrated through increasing concentration of ethanol (50%, 70%, 95%, absolute alcohol) solutions and cleared with xylene.

7. Mounted with DPX.
3. IMMUNO HISTOCHEMICAL STAINING FOR P63

1. 3-5 microns thick sections were cut from the blocks and sections were received on slides coated with poly- L – lysine.

2. Slides were kept in hot air oven at 60°C for 3 hrs.

3. Sections were dewaxed in two changes of xylene each for 10 minutes.

4. Sections were hydrated in graded ethanol solution (95%, 70%, and 50%) each for 3 minutes and in running tap water for 3 minutes.

5. Heat induced antigen retrieval was done with Retrieval buffer solution (Tris buffer 1.81gm + EDTA 0.55gm + Distilled water 1500ml) in pressure cooker.

6. Sections were washed with distilled water for 5 minutes.

7. Then sections were washed with Tris buffer solution of PH 7.4-7.6 (Tris 24gm + Sodium chloride 21.5gm + distilled water 2.5 litre + Tween 20 5µl/lr) for 5 minutes.

8. Sections were treated with 1-2 drops of hydrogen peroxide (H₂O₂ 3ml+dist water 97ml) for 5-10 minutes to block endogenous peroxidise enzyme activity.

9. Sections were washed with Tris buffer solution for 5 minutes.

10. Sections were treated with primary antibody p63 for 1 hour.
11. Sections were washed with Tris buffer solution for 5 minutes.

12. Secondary antibody polymer HRP (Horse Radish Peroxidase) was applied for 45 minutes.

13. Sections were washed in two changes of Tris buffer solution each for 5 minutes.

14. Sections were treated with chromogen Diamino Benzidine (DAB) for 15 minutes.

15. Sections were washed with Tris buffer solution for 5 minutes.

16. Then washed in running tap water for 2 minutes.

17. Counterstained with Haematoxylin for 1-2 minute.

18. Mounted with coverslip.
ABBREVIATIONS USED IN MASTER CHART

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>PSA</td>
<td>PROSTATE SPECIFIC ANTIGEN</td>
</tr>
<tr>
<td>FMH</td>
<td>FIBRO MUSCULAR HYPERPLASIA</td>
</tr>
<tr>
<td>BCH</td>
<td>BASAL CELL HYPERPLASIA</td>
</tr>
<tr>
<td>PIN</td>
<td>PROSTATIC INTRAEPITHELIAL NEOPLASIA</td>
</tr>
<tr>
<td>AgNOR</td>
<td>SILVER STAINING OF NUCLEOLAR ORGANIZER REGION</td>
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<td>IHC</td>
<td>IMMUNO HISTOCHEMISTRY</td>
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<td>BPH</td>
<td>BENIGN PROSTATIC HYPERPLASIA</td>
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<td>LGPIN</td>
<td>LOW GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA</td>
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<td>HGPIN</td>
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## ANNEXURE - IV MASTER CHART

<table>
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<th>Name</th>
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<th>Biopsy no</th>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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**Notes:**
- BPH: Benign Prostatic Hyperplasia
- LGPIN: Low Grade Prostatic Intraepithelial Neoplasia
- HGPIN: High Grade Prostatic Intraepithelial Neoplasia
- Tuberculous granulomatous prostatitis
- Desmin positive
- Leiomyosarcoma of prostate
- Prostatic adenocarcinoma (3+2) score 5
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ABSTRACT

BACKGROUND

Interpretation of prostatic biopsies has been a continuous problem for practising pathologist. Various types of difficulties have been encountered while diagnosing and typing prostatic carcinoma and premalignant lesions especially in TURP specimens.

AIM

This current study aims at the analysis of histopathological features of various non neoplastic and neoplastic lesions of the prostate including the grading of malignant lesions and evaluation of role of basal cell and proliferative markers in different benign, premalignant and malignant lesions of prostate.

METHOD

One hundred and eight transurethral resection of prostate specimens were studied with haematoxylin and eosin and AgNOR staining. In ten selected cases immunohistochemical study with p63 was done.

RESULTS

BPH was the most common lesion affecting the prostate in elderly {96 cases (88.89%)}. The age incidence of Nodular Hyperplasia was high
in 7th decade Granulomatous prostatitis was rarely encountered (2 cases (1.85%)). HGPIN had high degree of association with prostatic carcinoma (25%). Among the malignant lesions of the prostate, primary prostatic adenocarcinoma was the commonest (80%). According to Gleason Grading system higher grades were more commonly observed as the predominant pattern. Mean AgNOR counts (proliferative activity) were higher in malignant lesions (4.81) when compared with the benign lesions (1.44). With Immunohistochemical staining invasiveness increased from benign (continuous staining) to malignant (absence of staining) end in the spectrum of prostatic lesions. Two rare cases, Leiomyosarcoma of prostate and contiguous spread of rectal adenocarcinoma to prostate were observed in the present study which were confirmed with immunohistochemical study with desmin and PSA respectively.

CONCLUSION

Basal cell markers and proliferative markers have significant role in the diagnosis of prostatic lesions especially which fall in the premalignant category and which create difficulty in the diagnosis by routine histopathological study.

KEYWORDS

Benign prostatic hyperplasia, prostatic adenocarcinoma, AgNOR, p63