STUDY ON CORRELATION OF SERUM PROSTATE SPECIFIC ANTIGEN (PSA) LEVELS IN VARIOUS LESIONS OF PROSTATE

By

DR. NIKHIL MEHROTRA

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IN

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Under the Guidance of

DR. GIRIJA S. PATIL

Associate Professor, Department of Pathology

BLDE UNIVERSITY'S,

SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL &

RESEARCH CENTRE, VIJAYAPUR,

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Date: **Dr. NIKHIL MEHROTRA**

Place: Vijayapur

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Date:
Place: Vijayapur

DR. GIRIJA S. PATIL
Associate Professor
Department of Pathology,
BLDEU's Shri B.M.Patil
Medical College, Hospital &
Research Centre, Vijayapur,
Karnataka

B.L.D.E UNIVERSITY'S

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL

& RESEARCH CENTRE, VIJAYAPUR

ENDORSEMENT BY HEAD OF DEPARTMENT

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Date:
Place: Vijayapur

DR. B. R. YELIKAR
Professor and H.O.D,
Department of Pathology,
BLDEU's Shri B.M. Patil Medical College, Hospital & Research Centre, Vijayapur, Karnataka.

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SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL

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Date:
Place: Vijayapur

DR. S.P. GUGGARIGOUDAR
Principal,
BLDEU's Shri B.M. Patil
Medical College, Hospital & Research
Centre, Vijayapur, Karnataka.

B.L.D.E UNIVERSITY'S

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL

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Place: Vijayapur

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It is the Supreme Art of the Teacher to Awaken Joy in Creative Expression and Knowledge.- **Albert Einstein**

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Date: **DR. NIKHIL MEHROTRA**

Place: Vijayapur

LIST OF ABBREVIATIONS

BPH	Benign Prostatic Hyperplasia
PSA	Prostatic Specific Antigen
PIN	Prostatic Intraepithelial Neoplasia
TURP	Trans-Urethral Resection of Prostate
H&E	Hematoxylin and Eosin
ELFA	Enzyme Linked Fluorescent Assay
SPR	Solid Phase Reagent
LUTS	Lower urinary tract symptoms
PBRCs.	Population Based Cancer Registries
SD	Standard Deviation
BLDEU	Bijapur Liberal District Education University

ABSTRACT

INTRODUCTION:

Incidence of prostatic diseases, Benign prostatic hyperplasia (BPH) and carcinoma prostate increases with age. BPH, prostate carcinoma and prostatitis are three pathologic processes which frequently affect the prostate gland. Prostate specific antigen (PSA) is a neutral serine protease secreted exclusively by prostatic epithelial cells.

OBJECTIVES:

As the levels of PSA are increased in neoplastic, non-neoplastic and inflammatory conditions of prostate with overlapping values at times, this study was undertaken to correlate the levels of serum PSA in various lesions of prostate.

MATERIALS AND METHODS:

Transurethral resection of prostate (TURP) and biopsy specimens were taken in the study. Tissue was submitted till 4 cassettes were filled, and one additional cassette for each 10 gram of tissue was submitted. When specimen was large, the TURP chips showing soft or rubbery, and yellow grey in colour were chosen for processing.

The sections were cut at 3-5 micron thickness and subsequently were stained by haematoxylin and eosin stain. In case of biopsy specimens, all cores were embedded followed by sectioning and staining similar to TURP specimens was done.

RESULT: Out of total 60 prostatic specimens studied 42 cases were benign. Among benign lesions BPH was the commonest followed by BPH associated with prostatitis, PIN, infarct with squamous metaplasia, cystitis cystica and abscess. 16 cases were of adenocarcinoma of prostate. Majority of adenocarcinoma (8) were in Group 1 with Gleason score ≤ 6 followed by Group 5 adenocarcinoma (4) having Gleason score 9-

10. In majority of benign cases serum PSA levels were in the range of 4-10 ng/mL while majority of adenocarcinoma cases showed PSA >20 ng/mL.

CONCLUSION:

BPH was the commonest lesion followed by adenocarcinoma. Serum PSA levels in the range of 4-10 ng/mL, and values more than 20 ng/mL were significantly associated with benign and malignant lesions respectively in majority of the cases. However PSA is not cancer specific rather prostate specific and elevated serum PSA >20 ng/mL levels do not always result from prostate cancer. BPH along with prostatitis and other associated benign lesions may also cause significant elevations in serum PSA levels.

KEY WORDS:

Prostate Specific Antigen, Benign Prostatic Hyperplasia And Prostatitic Intraepithelial Neoplasia

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INTRODUCTION

Incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma prostate increases with age. Benign prostatic hyperplasia, prostate carcinoma and prostatitis are three pathologic processes which frequently affect the prostate gland.[1]

Adult prostatic parenchyma can be divided into four biologically and anatomically distinct zones or regions: peripheral, central, transitional, and periurethral. The type of proliferative lesions are different in each region. Most hyperplastic arise in the transitional zone, whereas most carcinoma originate in the peripheral zone.[2]

Besides histopathological examination of prostatic tissue for various pathologies, estimation of prostate specific antigen (PSA) is advocated. Prostate specific antigen (PSA) is a serine protease secreted exclusively by prostatic epithelial cells lining the acini and ducts of prostate. PSA is organ specific but not cancer specific resulting in limitations of its ability to differentiate carcinoma of the prostate from a number of benign abnormalities that can produce elevated PSA.[3]

As the levels of PSA are increased in neoplastic, non-neoplastic and inflammatory conditions of prostate with overlapping values at times i.e. a case of prostatic carcinoma may have normal PSA levels where as a case of BPH may show significant rise in the levels of PSA. To overcome this dichotomy, this study was undertaken to correlate the levels of serum PSA in various lesions of prostate.

AIMS AND OBJECTIVES

1. To determine the age distribution of patients with prostatic lesions .
2. To determine histological types related with prostate specific antigen.
3. To study prevalence of distribution of various prostatic lesions, admitted in BLDEU's Shri BM Patil Medical College,Hospital and Research Centre Vijayapur.
4. To evaluate the utility of PSA in diagnosis of prostatic lesions

REVIEW OF LITERATURE

Because of location of prostate gland at bladder neck, enlargement of the gland leads to problems related to urinary obstruction. Incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma increases with age.[1]

Benign prostate hyperplasia, prostate carcinoma and prostatitis are three pathologic processes which frequently affect the prostate gland.[2]

Diagnosis of prostatitis is very necessary as they can be successfully treated with antibiotics. Benign prostatic hyperplasia is the usual name applied to a common benign disorder of the prostate that, when extensive, results in varying degrees of urinary obstruction, sometimes requiring surgical intervention. It is extremely common problem in elderly men over the age of 50 years. [1]

Prostatic carcinoma is an important growing health problem, presenting a challenge to urologists, radiologists and pathologists.[4] Incidence of prostatic carcinoma increases with age.Prostate cancer is one of the leading cause of cancer in men and is second only to lung cancer as a leading cause of cancer-related deaths in men.[1]

Prostate-specific antigen (PSA) is a serine protease elaborated almost exclusively by epithelial cells lining the acini and ducts of prostate.Once produced, it is secreted into the prostatic ductal system and is present in high concentraion in seminal plasma in which it serves the purpose of liquefying the seminal coagulum.It gains access to general circulation by seeping through disrupted physiological barrier in diseases affecting the prostate gland.[3]

ANATOMY OF PROSTATE

The prostate is a pyramidal fibromuscular gland which surrounds the prostatic urethra from the bladder base to the membranous urethra. It has no true fibrous capsule, but is enclosed by visceral fascia containing neurovascular tissue. The fascia is firmly adherent to the gland and is continuous with a median septum and with numerous fibromuscular septa which divide the glandular tissue into indistinct lobules.The muscular tissue within the prostate is mainly smooth muscle.[5]

The prostate lies at a low level in the lesser pelvis, behind the inferior border of the symphysis pubis and pubic arch and anterior to rectourethralis and the rectal ampulla, through which it may be palpated. Being somewhat pyramidal, it presents a base or vesical aspect superiorly, an apex inferiorly, posterior, anterior and two inferolateral surfaces.[5]

The prostatic base measures about 4 cm transversely. The gland is 2 cm in anteroposterior and 3 cm in its vertical diameters, and weighs about 8g in young, but almost invariably enlarges with the development of BPH.[5]

It usually weighs 40 g, but sometimes as much as 150 g or even more, after the first five decades of life. The small prostate without BPH is described as a croissant shape (short anterior commissure, prominent apical notch and posterior lip of prostatic tissue), and the enlarged gland is more doughnut-shaped.[5]

The shape of the prostate affects the relationship of the prostatic apex to the external urethral sphincter. This relationship is important when removing the prostate at radical prostatectomy for cancer, and anastomosing the bladder to the urethra to maintain sphincter integrity. The external urethral sphincter is flush to a large doughnut-type gland so a perpendicular incision will separate the prostate and external urethral sphincter accurately.[5]

ZONAL ANATOMY OF THE PROSTATE

The prostate gland was initially thought to be divided into five anatomical lobes, but it is now recognized that five lobes can only be distinguished in the fetal gland prior to 20 weeks gestation. Between then and the onset of BPH, only three lobes are recognizable, two lateral and a median lobe. Clinicians refer to left and right 'lobes' when describing either what can be felt on rectal palpation, or endoscopically visible abnormalities in the diseased state when prostatic anatomy is distorted by BPH.[5]

From an anatomical, and particularly from a morbid anatomical perspective, the glandular tissue may be subdivided into three distinct zones i.e.peripheral (70% by volume), central (25% by volume), and transitional (5% by volume). Non-glandular tissue (fibromuscular stoma) fills up the space between the peripheral zones anterior to the preprostatic urethra. The central zone surrounds the ejaculatory ducts, posterior to the preprostatic urethra, and is more or less conical in shape with its apex at the verumontanum. The transitional zone lies around the distal part of the preprostatic urethra just proximal to the apex of the central zone and the ejaculatory ducts. Its ducts enter the prostatic urethra just below the preprostatic sphincter and just above the ducts of the peripheral zone. The peripheral zone is cup-shaped and encloses the central transitional zone and the preprostatic urethra except anteriorly, where the space is filled by the anterior fibromuscular stroma. Simple mucus-secreting glands lie in the tissue around the preprostatic urethra, above the transitional zone and surrounded by the preprostatic sphincter. These simple glands are similar to those in the female urethra and unlike the glands of the prostate.

The zonal anatomy of the prostate is clinically important because most carcinomas arise in the peripheral zone, whereas BPH affects the transitional zone,

which may grow to form the bulk of the prostate. BPH begins as micronodules in the transitional zone which grow and coalesce to form macronodules around the inferior margin of the preprostatic urethra, just above the verumontanum. Macronodules in turn compress the surrounding normal tissue of the peripheral zone posteroinferiorly, creating a 'false capsule'around the hyperplastic tissue which coincidentally provides a plane of cleavage for its surgical enucleation.[5]

As the transitional zone grows, it produces the appearance of 'lobes' on either side of the urethra. In due course, these lobes may compress or distort the preprostatic and prostatic parts of the urethra and produce symptoms. The central zone surrounding the ejaculatory ducts is rarely involved in any disease. It shows certain histochemical characteristics which differentiate it from the rest of the prostate: it is thought to be derived from the Wolffian duct system (much like the epididymis, vasa deferentia and seminal vesicles), whereas the rest of the prostate is derived from the urogenital sinus.[5]

McNeal proposed zonal anatomy of prostate comprising:[6]

1. Peripheral Zone-65%
2. Central Zone-10%
3. Transitional-25%

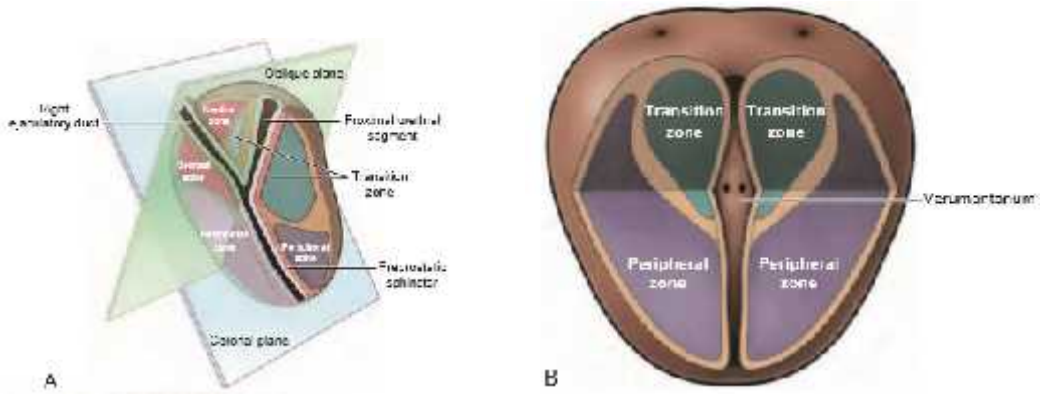


FIG1. Zonal anatomy of the prostate as first described by McNeal. Sagittal(A) and coronal(B)sections of the prostate showing the peripheral zone, transition zone, central zone, verumontanum, and proximal urethral segment, as well as the preprostatic sphincter and ejaculatory duct.

Transitional and periuretheral regions are exclusive sites of origin of nodular hyperplasia whereas the peripheral zone is most susceptible to inflammation and carcinoma.[2]

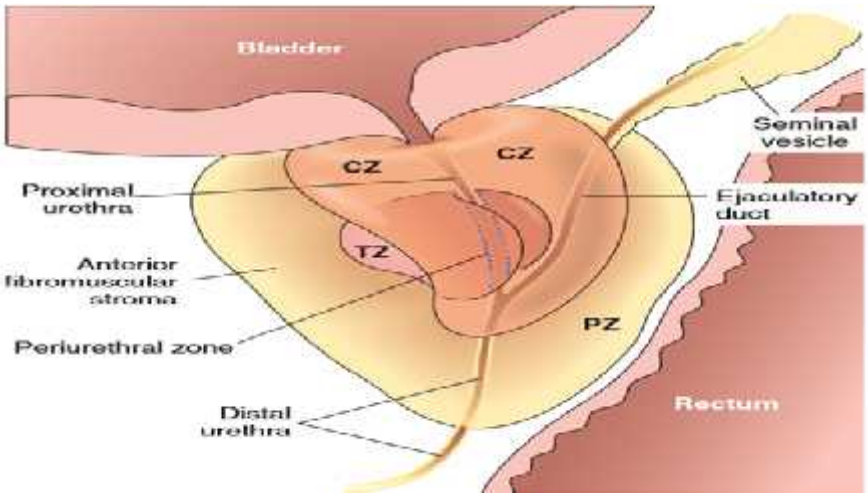


FIG 2. [Adapted from Robbins & Cotran 2014] Adult prostate. The normal prostate contains several distinct regions, including a central zone (CZ), a peripheral zone (PZ), a transitional zone (TZ), and a periurethral zone.

BLOOD SUPPLY

The prostate gland is supplied by branches from the inferior vesicle , middle rectal and internal pudendal arteries. Branches from these arteries form large outer or subcapsularplexus, and a small inner or periuretheral plexus.The greater part of the gland is supplied by subcapsular plexus.[5]

LYMPHATICS

Lymphatics from the prostate drain chiefly into the internal iliac nodes, sacral nodes and partly into the external iliac nodes.[5]

NERVE SUPPLY

The prostatic plexus of nerves is derived from the lower part of the inferior hypogastric plexus.[5]

HISTOLOGY OF THE PROSTATE

The prostate consists of branched tubulo-acinar glands embedded in a fibromuscular stroma. On the other hand, in this gland, there also is a partial capsule enclosing the posterior and lateral aspects of the prostate but the anterior and apical surfaces are bounded by the anterior fibromuscular stroma, which consists, as the name implies, only of collagenous stroma and muscle fibers.[7]

In the past, the prostate was considered to have a huge number of ill-defined lobes. However, this terminology has been replaced by the concept of prostate zones. Thus, this gland is now described as consisting of four zones of unequal size portion, ducts and acini are lined by columnar cells.[7]

- The **transition zone** surrounds the proximal prostatic urethra and comprises about 5% of the glandular tissue.
- The **central zone** (20%) encloses the ejaculatory ducts.
- The **peripheral zone** makes up the bulk of the gland (approximately 70%).
- The **anterior fibromuscular stroma** contains no glandular tissue and is situated anteriorly

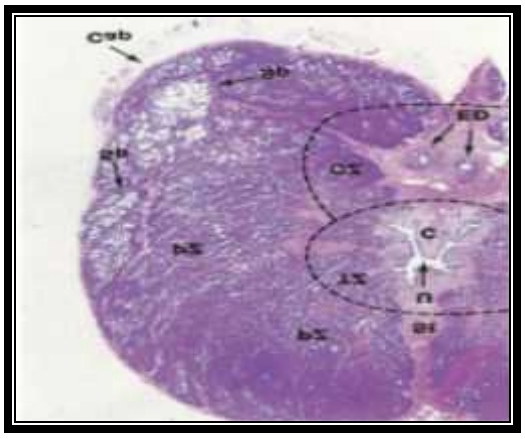


FIG 3: Prostate gland H&E x 5, [adapted from (Young 2007)]. The urethral (U) is localized centrally and surrounded by a fibrous stroma (St). The ejaculatory ducts (ED) are also found in this central stroma as they course towards their junction with the prostatic urethra. The zones of the prostate are not clearly demarcated from each other anatomically. Partial fibrous septa (Sp) separate the gland into lobules. The transition zone (TZ) surrounds the first part of the prostatic urethra. The central zone (CZ) is posterior to the transition zone and encircles the ejaculatory ducts. The peripheral zone (PZ) makes up the main bulk of the prostate. The ducts of the peripheral zone glands empty into the postero-lateral recesses of the urethra on either side of the verumontanum (urethral crest, C).

papillary appearance. The secretory product of the prostate, which makes up about half of the seminal fluid volume, is thin and milky, rich in citric acid and hydrolytic enzymes, especially fibrinolysin, which liquefies the coagulated semen after deposition within the female genital tract. Lamellated glycoprotein masses called corpora amylacea (CA) are a feature of ageing, becoming progressively calcified to form prostatic concretions. The stroma of the prostate consists of dense collagen, fibroblasts and haphazardly arranged smooth muscle fibers which, like those of the seminal vesicles and the rest of the tract, are innervated by the sympathetic nervous system that stimulates powerful contractions during ejaculation. Towards the apex of the gland the anterior fibromuscular stroma also contains skeletal muscular fibers.[7]

BENIGN PROSTATIC HYPERPLASIA

Benign prostatic hyperplasia is the most common prostatic disease in men older than 50 years.It results from nodular hyperplasia of prostatic stromal and epithelial cells and often lead to urinary obstruction. It is characterised by the formation of large, fairly discrete nodules in the periuretheral region of the prostate, which when sufficiently large, compress and narrow the urethral canal to cause partial, or sometimes virtually complete, obstruction of the urethra.[2]

Histologic evidence of BPH can be seen in approximately 20% of men 40 years of age, a figure that increases to 70% by age 60 and to 90% by age 80. There is no direct correlation, however, between histologic changes and clinical symptoms. Only 50% of those who have microscopic evidence of BPH have clinically detectable enlargement of the prostate, and of those, and of these individuals, only 50% develop clinical symptoms.[2]

Etiology And Pathogenesis

Despite the fact that there are an increased number of epithelial cells and stromal component in the periuretheral area of prostate, there is no clear evidence of increased epithelial cell proliferation in human BPH. Instead, it is believed that hyperplasia mainly stems from impaired cell death, resulting in accumulation of senescent cells in the prostate. Androgens which are reqiuired for development of BPH, not only increase cellular proliferation, but also inhibit cell death.[2]

The main androgen in the prostate, constituting 90% of the total prostatic, constituting 90% of total prostatic androgens, is dihydroxytestosterone(DHT). DHT is formed in the prostate from testosterone through the action of an enzyme called type 2 5α reductase. This enzyme is located almost entirely in the stromal cells; with the exception of a few basal cells, prostatic epithelial cells do not express type 2 5α reductase. Thus, stromal cells are responsible for androgen-dependent prostatic growth.[2]

Type 1 5α reductase is not detected in the prostate growth,or is present at very low levels. However this enzyme may produce DHT from testosterone in liver and skin, and circulating DHT may act in the prostate by an endocrine mechanism. DHT binds to the nuclear androgen receptor present in both stromal and epithelial prostate cells. DHT is more potent than testosterone because it has a higher affinity for AR and forms a more stable complex with the receptor. Binding of DHT to AR stimulates the transcription of androgen-dependent genes, which induces several growth factors and their receptors. Most important among these are members of the fibroblast growth factor(FGF) and transforming growth factor(TGF)-β .

FGFs, produced by stromal cells, are paracrine regulators of androgen-stimulated epithelial growth during embroynic prostatic development, and some of

these pathways may be “reawakened” in adulthood to produce prostate growth in BPH.TGF- β serves as a mitogen for fibroblasts and other mesenchymal cells, but inhibit epithelail proliferations.[2,8]

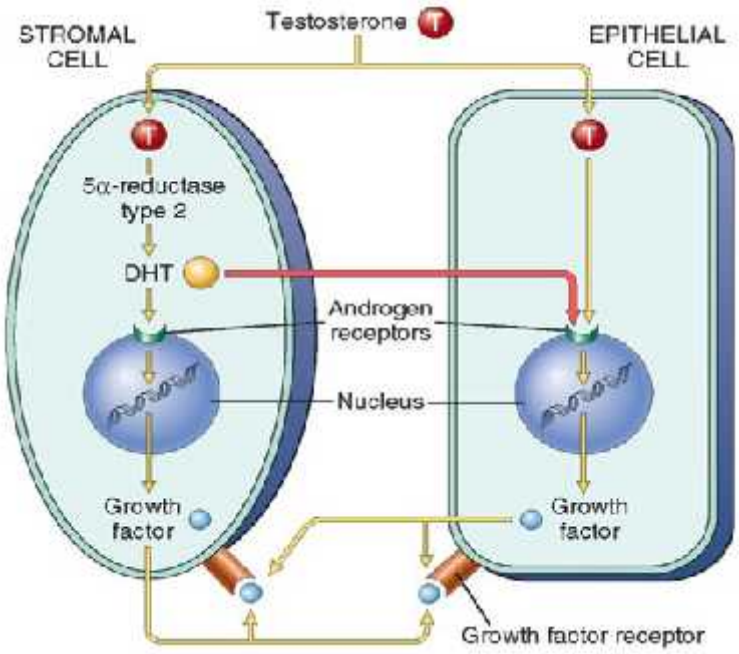


FIG 4.[Adapted from Robbins&Cotran 2014].Simplified scheme of the pathogenesis of prostatic hyperplasia. The central role of the stromal cells in generating .dihydrotestosterone (DHT) is important.

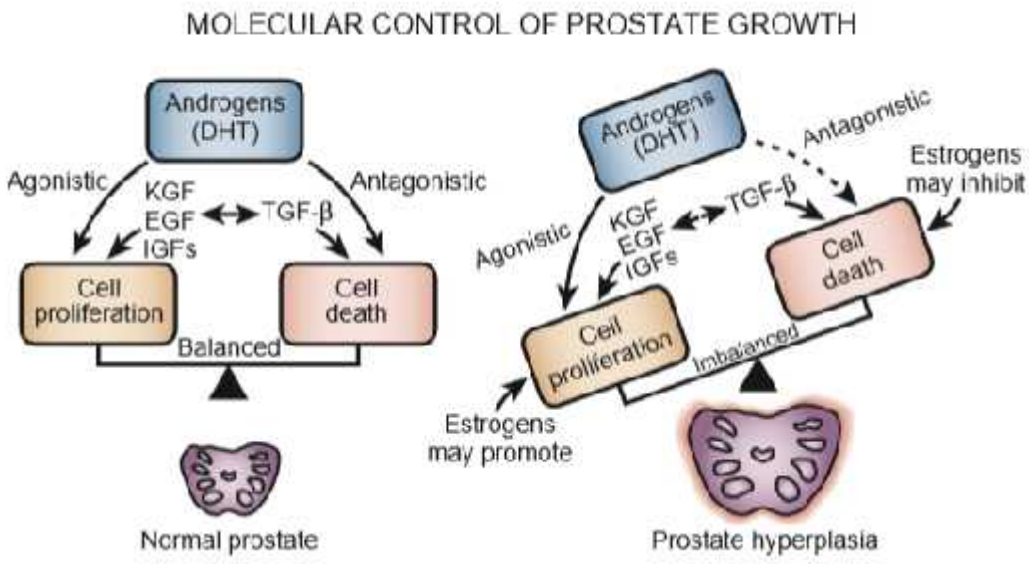


FIG 5 [Adapted from Walsh Urology] Prostate hyperplasia is probably due to an imbalance between cell proliferation and cell death. Androgens play a necessary but probably permissive role. Growth factors are likely to be sites of primary defects .DHT, dihydrotestosterone; EGF ,epidermal growth factor; IGFs ,insulin-like growth factors; KGF, keratinocyte growth factor;TGF-β,transforming growth factor-β

MORPHOLOGY OF BENIGN PROSTATIC HYPERPLASIA

In the usual case of benign prostatic enlargement, the prostate weighs between 60 and 100 gm. Nodular hyperplasia of the prostate originates almost exclusively in the inner aspect of the prostate gland (transition zone). The early nodules are composed almost entirely of stromal cells, and later predominantly epithelial nodules arise. From their origin in this strategic location the nodular enlargements may encroach on the lateral walls of the urethra to compress it to a slit like orifice. In some cases, nodular enlargement may project up into the floor of the urethra as a hemispheric mass directly beneath the mucosa of the urethra, which is termed **median lobe hypertrophy**.[2]

On cross-section, the nodules vary in colour and consistency depending on their cellular content. Nodules that contain mostly glands are yellow-pink and soft, and exude a milky white prostatic fluid.[2]

Nodules composed primarily of fibromuscular stroma are pale gray and tough; these nodules do not exude fluid and are less clearly demarcated from the surrounding prostatic tissue. Although the nodules do not have true capsules, the compression of surrounding prostatic tissue creates a plane of cleavage about them.[2]

Microscopically, glandular proliferation takes the form of aggregations of small to large to cystically dilated glands lined by two layers of cells, an inner columnar layer and an outer layer of cuboidal or flattened epithelium. Occasionally foci of reactive squamous metaplasia mimicking urothelial carcinoma are seen adjacent to prostatic infarcts in prostates with prominent BPH. The diagnosis of BPH cannot be usually made on needle biopsy because such biopsies are too small to appreciate the nodularity of the process and do not usually sample the transition zone where BPH occurs.[2]

ADENOCARCINOMA OF PROSTATE

Adenocarcinoma of the prostate is the most common form of cancer in men. There is a one in six lifetime probability of being diagnosed with prostate cancer. It demonstrates a remarkably wide range of clinical behaviours, from very aggressive lethal cancers to incidentally discovered clinically insignificant cancers.[2]

Incidence

Prostate cancer is a disease with a long natural history, with progression commonly related to stage and grade of tumor and lack of differentiation.[9] Cancer of the prostate is typically a disease of men older than age 50 years.[2]Several reports have described that more than 65% of all prostate cancers are diagnosed in men over 65 years old.[10]

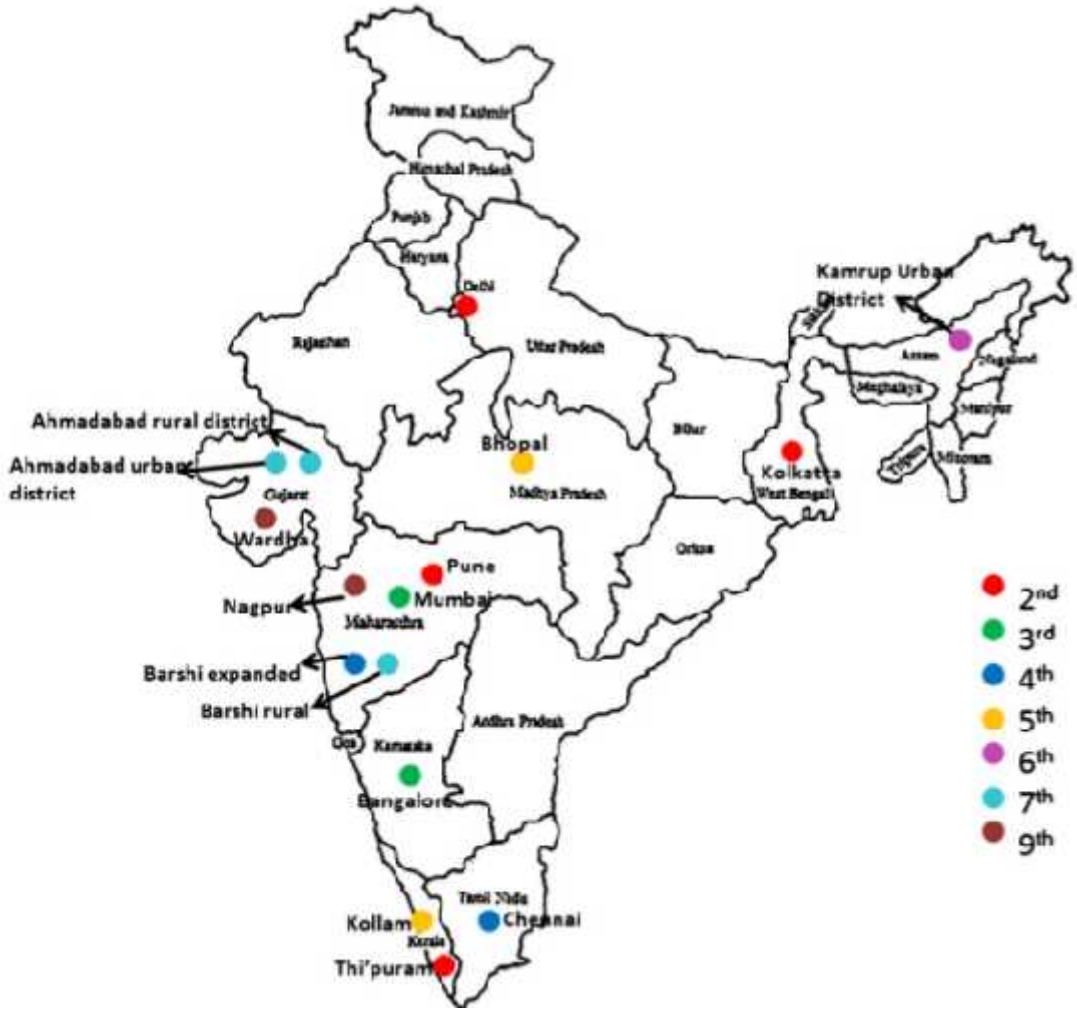
Based on autopsy studies, its incidence increases from 20% in men in their 50s to approximately 70% in men between the ages of 70 and 80 years.[2]

Compared with the White population, the incidence of prostate cancer is approximately 60% higher in Black men, while native Japanese and Chinese population have a low risk of incidence and mortality[11]. African American men generally are diagnosed with more advanced stages of prostate cancer at an earlier age.[10]

Besides genetics-characteristics, social and environmental factors (especially diet and lifestyle) may act as the determining factors, which may explain why some individuals have higher risk for developing prostate cancer than others.[10]

Prostate is the second leading site of cancer among males in large Indian cities like Delhi, Kolkatta, Pune and Thiruvananthpuram, third leading site of cancer in cities like Bangalore and Mumbai and it is among the top ten leading sites of cancers in the rest of the PBRCs (Population Based Cancer Registries) of India.

The data shows that almost all regions of India are equally affected by this cancer. The incidence rates of this cancer are constantly and rapidly increasing in all the PBRCs. The cancer projection data shows that the number of cases will become doubled by 2020.[12]



A map of India showing the rank of prostate cancer among top ten leading sites of all cancers, for different population based cancer registries of India.[12]

Etiology and Pathogenesis

Several factors, including age, race,family,hormones levels and environmental influences are suspected to play a role. Androgens play an imporant role in prostate cancer. Like their normal counterparts, the growth and survival of prostate cancer cells depend on androgens, which bind to the androgen receptor(AR) and induce the expression of pro-growth and pro-survival genes. The importance of androgens in maintaining the growth and survival of prostate cancer cells can be seen in the the therapeutic effect of castration or treatment with antiandrogens, which usually induce disease regression.[2]

Compared with men with no family history, men with first-degree relative prostate cancer have twice the risk of developing prostate cancer.Men with a strong family history of prostate cancer also tend to develop the disease at an earlier age. Men with germline mutations of the tumour suppressor BRCA2 have a 20 fold increased risk of prostate cancer, and a germline mutation in HOXB13, a homeobox gene encoding a transcription factor that regulates prostatic development, also confers a substanciallly increased risk in the small percentage of families.However, the vast majority of familial prostate cancers are due to variation in other loci that confer a small increase in cancer risk.[2]

Prostate adenocarcinoma typically proceeds through a series of defined stages, from prostatic intraepithelial neoplasia (PIN), to invasive and metastatic cancer.[13]
The niche is a cell environment that provides critical signals to maintain stem cells and to support their undifferentiated phenotype of progenitor cells. These relevant signals include the Hedgehog, Wnt or Notch pathways and all of them are important in early oncogenesis and cell differentiation and proliferation control. In cancer, the cell-cell and cell-matrix interactions are overlaid on top of other features of tumor

physiopathology microenvironment, including the presence of hypoxia, low pH and nutrient deprivation.

Fluctuations of these parameters have profound effects on the activity of cancer stem cells and their potential niche.[13]

Hypoxia is an important characteristic of the niche because it is intrinsically linked to the formation of neovasculature and the regulation of the production of proangiogenic factors. [14]

It is well characterized that several genes are expressed in hypoxic environment, and the most of these genes are controlled by hypoxia-inducible factor-1 (HIF-1).[14] The gene expression may be altered toward an immature phenotype, under hypoxic conditions (3 - 5% O2), promoting de-differentiation of prostate tumor cells into more “stem-like” ones.[15]

The hypoxic cells express higher levels of the embryonic stem-ness gene octamer-binding transcription factor 4 (OCT-4) due to the interactions between HIF-transcription factors (HIF-1α and HIF-2α). OCT-4 is a direct target of HIF-2α, and its induction could contribute to the formation and maintenance of cancer stem cells.[16]

A number of potentially carcinogenic viruses have been detected in human prostatic tissues, such as the oncogenic human papovavirus BK or the human gammaretrovirus Xenotrophic MuLV-related virus (XMRV) in premalignant lesions . [17,15]

These ideas have improved the hypothesis of prostate oncogenesis, where PIN is preceded by aninflammatory atrophy with prostatic epithelial cells showing an increased Ki-67- marked proliferation[13] as shown in the flow chart.

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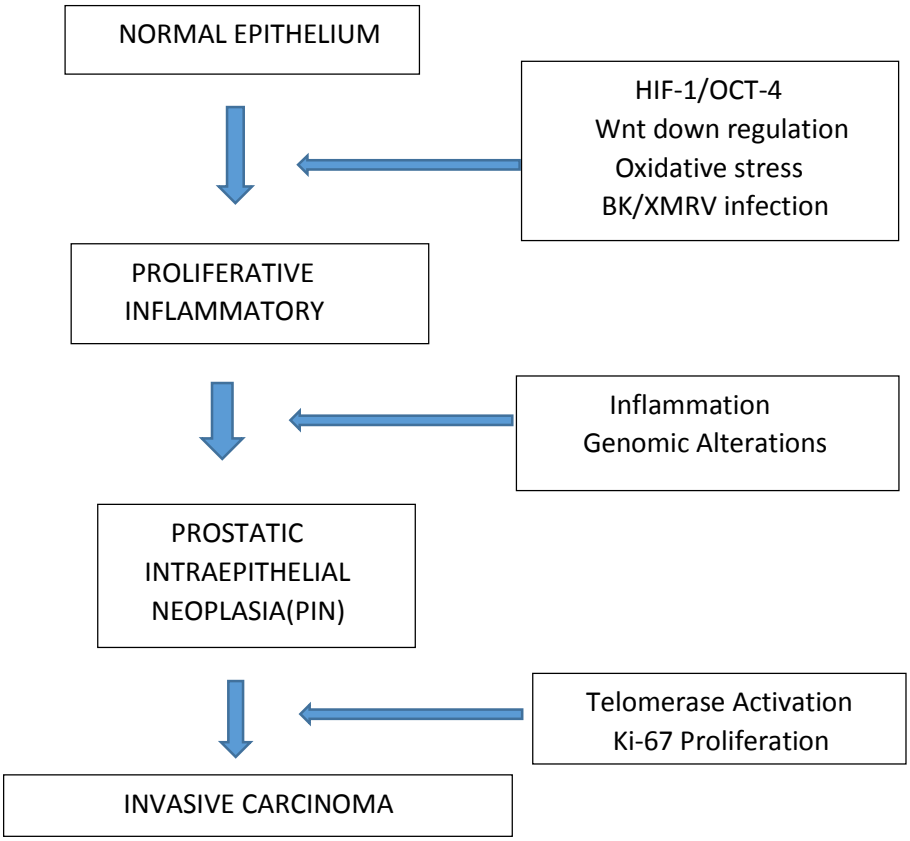


FIG 6: A model for prostate oncogenesis. The normal epithelium (under oxidative stress, Wnt down-regulation or human gammaretrovirus XMRV infection) have an increased proliferative potential and eventually lead to the appearance of the PIN. The high proliferative potential and telomerase activation determine the evolution from PIN to invasive, metastatic and treatment resistant carcinoma.

MORPHOLOGY OF PROSTATIC ADENOCARCINOMA

Carcinoma of prostate arises in the peripheral zone of the gland, classically in a posterior location, where it may be palpable on rectal examination. Charasterisctically on cross-section of the prostate the neoplastic tissue is gritty and firm.[2]

Histologically, most lesions are adenocarcinoma that produce well-defined, readily demonstrable gland patterns. The gland are typically smaller than benign glands and are lined by a single uniform layer of cuboidal or low columnar epithelium.In contrast to benign glands, prostate cancer glands are more crowded and characteristically lack branching and papillary infolding. The outer basal cell layer

typical of benign glands is absent. The cytoplasm of the tumour cells ranges from pale-clear to a distinctive amphophillic appearance. Nuclei are large and often contain one or more large nucleoli. There is some variation in nuclear size and shape, but in general pleomorphism is not maked.[2]

GRADING AND STAGING

Grading is of particular importance in prostatic cancer.[2]

RATIONALE FOR MODIFICATION OF THE GLEASON SYSTEM

The underlying principles of the Gleason grading system and its contributions to prostate cancer clinical management retain relevance and influence more than half a century from the time of its development. However, a number of new pathologic and clinical discoveries, changes in prostate cancer screening and detection, and development of new clinical and pathologic methodologies justify the need for revising the original grading system.[18]

A NEW CONTEMPORARY PROSTATE CANCER GRADING SYSTEM

Problems With the Current Gleason System

First, Gleason scores 2 to 5 are currently no longer assigned and certain patterns that Gleason defined as a score of 6 are now graded as 7, thus leading to contemporary Gleason score 6 cancers having a better prognosis than historic score 6 cancers.[18]

Second, in practice, the lowest score now assigned is 6, although it is on a scale of 2 to 10. This leads to a logical yet incorrect assumption on the part of patients that the cancer on biopsy is in the middle of the grade scale, compounding the fear of a cancer diagnosis, thus leading to an expectation that definite treatment is always necessary.[18]

Third, combining Gleason scores into a 3-tier grouping (6, 7, 8–10) is used most frequently for prognostic and therapeutic purposes, despite 3+ 4 = 7 versus 4+ 3 = 7 and 8 versus 9 to 10 having very different prognosis.[18]

Development of a New Grading System

As a result of the first two problems noted above, it has been questioned whether Gleason score 3 + 3 =6 should retain the designation of cancer or be relabeled as indolent lesion of epithelial origin to avoid fear and consequential overtreatment of a proportion of potentially indolent prostate cancers. From a pathologist's viewpoint, Gleason score 6 is still cancer, with many of the same morphologic and even molecular features of higher-grade cancer, a lack of a basal cell layer, and the potential to locally invade.[18]

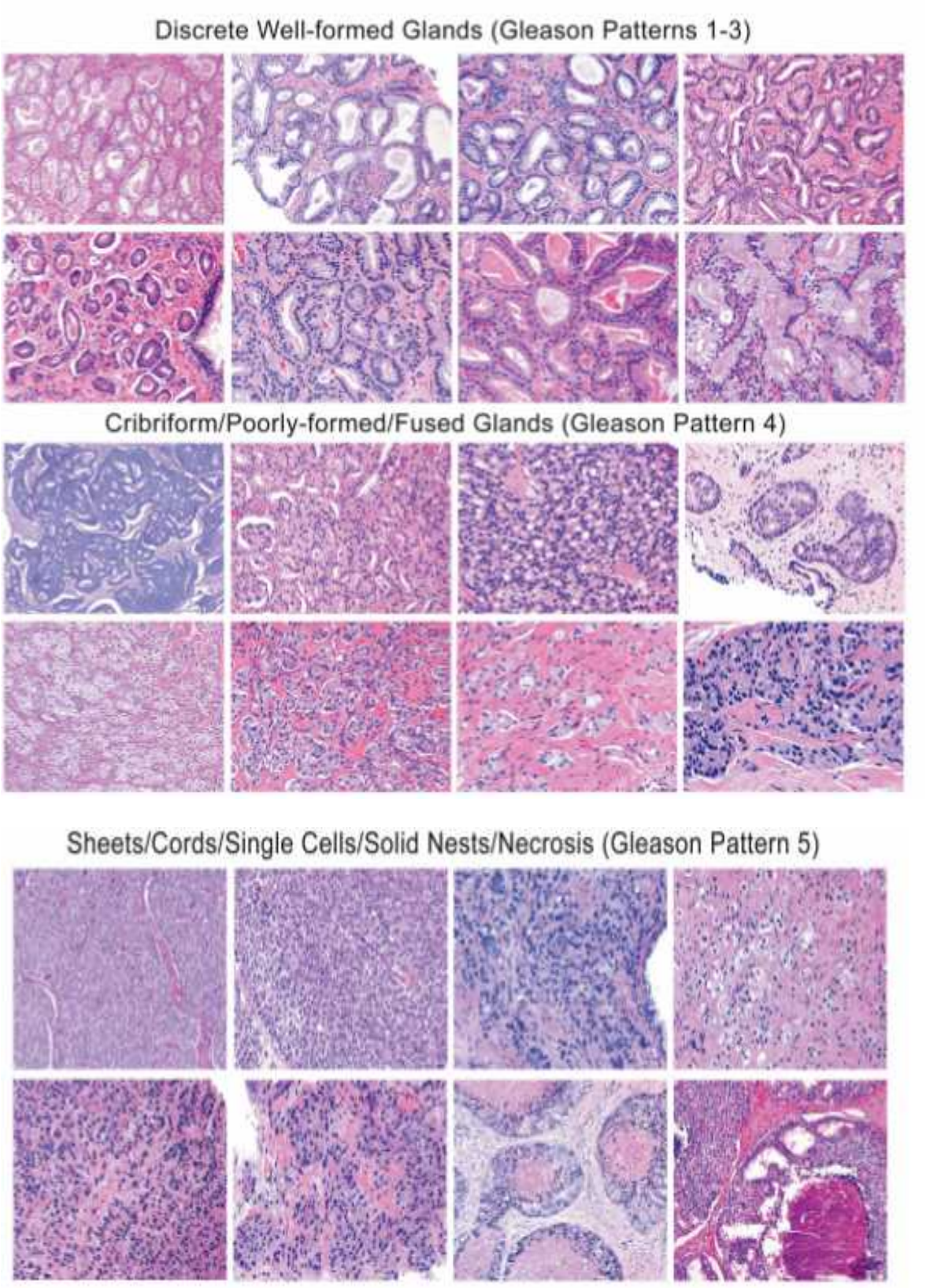
New Grading System Morphologic Patterns and Grade Group Pattern Composition[19]

Grade Group	Pattern Definition
Grade Group 1 (Gleason score ≤6)	Only individual, discrete, well-formed glands 5
Grade Group 2 (Gleason score 3+4 =7)	Predominantly well-formed glands with a lesser component of poorly formed/fused/ cribriform glands
Grade Group 3 (Gleason score 4+ 3 =7)	Predominantly poorly formed/fused/cribriform glands with a lesser component of wellformed glands[a]
Grade Group 4 (Gleason score 8)	Only poorly formed/fused/cribriform glands or Predominantly well-formed glands with a lesser component lacking glands.[b] or Predominantly lacking glands with a lesser component of well formed glands.[b]
Grade Group 5 (Gleason scores 9–10)	Lacks gland formation/necrosis with or 5 without poorly formed/fused/cribriform glands.[a 5]

a For cases with more than 95% poorly formed/fused/cribriform glands or lack of glands on a needle core or at radical prostatectomy, the component of less than 5% well-formed glands is not factored into the grade.

b Poorly formed/fused/cribriform glands can also be a more minor component.

A NEW CONTEMPORARY PROSTATE CANCER GRADING SYSTEM



Various Gland Patterns In Adenocarcinoma

The new grading system for prostate cancer has obvious benefits:

1. More accurate grade stratification than the current Gleason system
2. Simplified grading system of 5 as opposed to multiple possible scores depending on various Gleason pattern combinations
3. Lowest grade is 1 as opposed to current practice of Gleason score 6, with the potential to reduce overtreatment of indolent prostate cancer

The new grading system, using the above terminology, has been accepted by the 2016 World Health Organization (WHO).[19]

PROSTATIC INTRAEPITHELIAL LESION

For many years, atypical epithelial lesions of the prostate have been known to occur, but much refining of this knowledge has evolved during the last 2 decades. Initially 2 lesions, dysplasia of the prostate now known as prostatic intraepithelial neoplasia (PIN) and atypical adenomatous hyperplasia, were assumed to be precursors of carcinoma. Of these, PIN has remained as the only well-proven preneoplastic condition with clinical significance. Atypical adenomatous hyperplasia or adenosis is no longer considered a premalignant lesion but rather a benign small glandular process of the transition zone that simulates acinar adenocarcinoma.[20]

It is readily identified at low magnification by 3 important findings:

(1) the lining of the ductal structures is darker,

(2) it is also thicker than the surrounding normal ducts, and

(3) there may be a complex intraluminal pattern of growth.

At high magnification, there is a cytologic triad including

(1) varying degrees of nuclear enlargement with nuclear stratification,

(2) hyperchromasia, and

(3) nucleolar prominence .

Prostatic intraepithelial neoplasia is usually multifocal and involves clusters of glandular structures or may involve a single gland either partially or completely.[20]

HISTOLOGICVARIANTS OF PIN: Several histologic variants of PIN have been reported in the literature.

These include (1) signet ring cell variant

(2) mucinous variant

(3) small cell neuroendocrine variant

(4) foamy variant

(5) inverted variant

(6) PIN with squamous differentiation

Prostatic intraepithelial neoplasia may display a spectrum of architectural patterns, from a simple flat epithelium to a complex cribriform pattern that may be difficult to distinguish from cribriform carcinoma. The 4 most common patterns of high grade PIN are the tufting pattern (87%), the micropapillary pattern (85%), the cribriform pattern (32%), and the flat pattern(28%).

All of these patterns are frequently observed in the same radical prostatectomy specimen.

Although it is important for diagnostic purposes to recognize these different patterns, it has been shown that there is no significant relationship between the pattern of HGPIN and the Gleason grade of carcinomas arising in the same specimen.

PIN DISTRIBUTION

Prostatic intraepithelial neoplasia is found predominantly in the peripheral zone of the prostate (75%–80%), rarely in the transition zone (10%–15%), and extremely rarely in the central zone (<5%). This distribution parallels the frequency of the zonal predilection for prostatic carcinoma. The frequency of HGPIN in needle biopsy series ranges from 5% to 16% and in transurethral resection of the prostate specimens between 2.3% and 4.2%.McNeal in 1969 mentioned the multifocality of this process, this observation has since been corroborated by others.

Diagnostic Criteria of Prostatic Intraepithelial Neoplasia (PIN)

Features	Low-Grade PIN (PIN 1)	High-Grade PIN (PIN 2, 3)
Architecture	Crowding, stratification, irregular spacing	More changes, 4 patterns (Tufting,micropapillary, cribriform, flat)
Nuclei	Slight enlargement, size variation	Definite enlargement, less size variation
Chromatin	Normal	Increased
Nucleoli	Rarely prominent	Frequently prominent

DIFFERENTIAL DIAGNOSIS OF PIN

Normal prostatic structures, metaplasias, benign epithelial proliferations, and malignant tumors may be confused with PIN. The normal prostatic structures that are frequently misinterpreted as PIN are normal central zone glands and ejaculatory duct/seminal vesicle epithelium.[20]

PROSTATITIS

Prostatitis, a histological diagnosis, that has evolved over the years to describe a clinical syndrome that was believed to be associated with prostatic inflammation.[21]

Epidemiology

Prostatitis is the most common urologic diagnosis in men younger than 50 years and the third most common urologic diagnosis in men older than 50 years after benign prostatic hyperplasia (BPH) and prostate cancer.[8]

Types

Prostatitis may be divided into several categories: acute and chronic bacterial prostatitis, chronic abacterial prostatitis, and granulomatous prostatitis.[2]

Histopathology

For the pathologist, prostatitis is defined as an increased number of inflammatory cells within the prostatic parenchyma. Prostatic inflammation may or may not be noted in patients with a diagnosis of prostatitis , BPH , or prostate cancer and is noted in autopsy series in as many as 44% of prostate tissue samples from men without any definitive prostate disease.

Consistently, fairly distinct although often coexisting patterns of chronic inflammation can be found in the prostate glands of patients with or without prostate disease. The most common pattern of inflammation is a lymphocytic infiltrate in the stroma immediately adjacent to the prostatic acini.[8]

The intensity of the inflammatory process varies considerably from only scattered lymphocytes to dense lymphoid nodules. Stromal lymphocytic infiltrates frequently coexist with periglandular inflammation. Sheets, clusters, and occasional nodules of lymphocytes and scattered plasma cells are seen within the fibromuscular stroma with no apparent relationship to the ducts and acini. Infiltrates of inflammatory cells restricted to the glandular epithelium and lumen are found in association with prostatitis and BPH. The intraepithelial inflammatory cells may be neutrophils, lymphocytes, macrophages, or all of these, whereas neutrophils and macrophages are typically found in the lumen.[8]

Granulomatous prostatitis presents a nonspecific and variable histologic pattern typified by heavy lobular, mixed, inflammatory infiltrates that include abundant histiocytes, lymphocytes and plasma cells. Small, discrete granulomas may be present, or the pattern may be typified by well-defined granulomas. Granulomatous prostatic inflammation is a common consequence of surgery or bacille Calmette-Guérin (BCG) therapy and a rare event in patients with systemic tuberculosis.[8]

Association of Clinical Prostatitis and BPH

BPH is a disease of ageing men .An estimated 42% of men 51 to 60 years of age have histological BPH. The incidence increases to over 70% in men 61 to 70 years of age and to almost 90% in those 81 to 90 years of age. The prevalence of Lower urinary tract symptoms (LUTS) associated with BPH parallels that of pathological BPH> 50% of men over 50 are believed to experience LUTS secondary to an enlarged prostate gland. Prostatitis has traditionally been considered a condition which inflicts younger men, but it is apparent that it is as common in older men.[21] Compared to men aged 51 and higher the odds of a documented prostatitis diagnosis is only 2-fold greater in younger men. Approximately 8% of men over 50 years of age report at least some mild prostatitis-like symptom in the past week compared to 11% of younger men.

Little attention has been given to the association, despite the high prevalence of both conditions in ageing men.[21]

Association of Inflammation and Clinical BPH

Histological inflammation can be demonstrated in the majority of BPH pathological Specimens.

Kramer and Marberger have recently outlined the current state of knowledge in regard to the influence of inflammation on the pathogenesis of BPH. Chronic inflammatory infiltrates, mainly composed of chronically activated T cells and macrophages frequently are associated with BPH nodules These infiltrating cells are responsible for the production of cytokines (IL-2 and IFNγ) which may support fibromuscular growth in BPH. Cytokines and chemokines, inflammatory mediators are believed to be important in the pathogenesis of prostate inflammation. Increased expression of IL-8 is noted in BPH tissue culture which by direct and indirect

mechanisms could promote proliferation of nonsenescent epithelial and stromal cells thus contributing to the increased tissue growth seen in BPH.

Inflammation in the prostate gland appears to more closely related to BPH than the clinical syndrome chronic prostatitis. [21]

PROSTATE SPECIFIC ANTIGEN

The prostate specific antigen test is one of the most important biochemical cancer tumor markers identified in the 20th century.[22] PSA has changed the practice of urologists and oncologists in the screening and detection of prostate cancer. To date, PSA is the tumor-associated antigen that has demonstrated the greatest impact on the early detection and the management of cancer patients [23].

During ejaculation, the prostate adds up to 40 g of a milky secretion to the ejaculate, in which prostate-specific antigen (PSA), a protein formed by the prostate gland, is present in high concentrations.[24]

Prostatic secretions are slightly acidic with a pH around 6.4. The acidity serves to neutralize vaginal alkalinity and prolong the lifespan of spermatozoa. PSA liquefies semen, promoting sperm motility, and serves to dissolve cervical mucus. PSA is present in low concentrations in the blood, but the concentration increases with prostate irritation, prostatic infection, and benign prostatic hyperplasia.[24]

PSA exists in the blood in two forms. Most PSA in blood is bound to serum proteins, some of which are inhibitors of the serine protease activity of PSA. Further, PSA is also present as free PSA. Total PSA is the sum of both bound and free PSA; however, free PSA is measured only if the total PSA is increased. PSA is primarily a tissue-specific marker. From an elevated PSA measurement, it is difficult to differentiate between a benign and malignant transformation of the prostate gland. To distinguish between these two transformations free PSA is useful. Free PSA is more

often formed from benign transformations while bound PSA tends to come from malignant transformations. Both tests (free and total PSA) have high accuracy and repeatability.[24]

Cancerous prostate tissue usually releases more PSA and more complexed PSA into the blood than normal, healthy tissue does. Thus, an increased PSA may indicate the presence of prostate carcinoma. The higher the PSA concentration in blood, the more likely one is to find tumors that have extended beyond the prostate gland.[24]

PSA is a glycoprotein produced predominantly, although not exclusively, by the prostate gland. PSA in blood may increase as a result of a variety of pathologic conditions of the prostate and may be a suitable marker for prostate carcinoma.

The reference range for serum PSA is 0–4 µg/L and is dependent on the method used. PSA is usually elevated in the presence of prostate carcinoma; however, many benign conditions also result in PSA elevation.

The most important reason to measure PSA in blood is to screen for prostate carcinoma in men over age 50. In addition to screening, PSA is measured to evaluate the success of treatment and progression of disease when a known prostate carcinoma is present. However, an increased value does not always indicate carcinoma since studies have shown that about 70% of men with PSA values from 4–10 µg/L are free of prostate cancer[24].

Causes other than prostate carcinoma that can lead to elevated PSA values include:

1. Adenomatous hyperplasia of prostate.
2. Inflammation of the prostate gland (prostatitis).
3. Prostate infarction.
4. PIN
5. Manipulations to the prostate gland or ejaculation

On the other hand, a normal value does not absolutely indicate that carcinoma is not present, since a considerable percentage of men with carcinoma of the prostate have serum PSA levels under 4 µg/L[24].

PSA is produced by both benign and malignant epithelial cells of the prostate. It is well documented that the presence of prostatic adenocarcinoma can cause elevation of serum PSA.

The mechanism by which PSA is released into the circulation is by disruption of the basement membrane caused by tumour invasion or other destructive membrane processes, such as inflammation or infarct.The basement membrane within PIN is intact. Therefore, it is reasonable to believe that PSA produced by neoplastic cells in PIN is not released into the serum at clinically significant levels.[25]

Jasani JH *et al* [4] in their study included 180 cases between age group of 48-76 years. Out of total 180 cases studied 56% cases were of BPH, followed by 32% cases of Adenocarcinoma.

PIN comprised of 7.22 % cases, prostatitis being 2.7% and TCC being the least 1.11 % The study showed maximum 86.2% Adenocarcinoma cases having PSA levels >10 ng/mL, 12 % cases with PSA level in the range of 4-10 ng/mL and 1.7% case within range of 0-4 ng/mL. 63.72% cases of BPH showed PSA levels in 0-4ng/mL range, 27.4% cases had PSA values in 4-10ng/mL range and 8.8% cases showed PSA values more than 10ng/mL.61.53% PIN cases had PSA values more than 10 ng/mL, 23.0% case had PSA 0-4 ng/mL and 15.3% had PSA range of 4-10 ng/mL. 60% cases of Prostatitis cases had PSA levels in 4-10 ng/mL while 40% showed PSA in the range of 0-4 ng/mL.

Rukhsana A *et al* [26] studied 60 patients of prostatic pathology.Most of the patients 50% were diagnosed with Benign Prostatic Hyperplasia (BPH). Higher levels of PSA (>20) were found in 57.1% of patients of BHP with chronic prostatitis. Out of the total number of patients with adenocarcinoma, 77.8% of the patients were having preoperative PSA levels greater than 20. In his study, the positive predictive value for increasing PSA levels was 8.3% for PSA <4 ng/mL, 16.6% for PSA >4 ng/mL, 24.2% for PSA >10 ng/mL and 83.3% for PSA >100 ng/mL

Wadgaonkar A *et al*[1] studied 80 prostate tissues and of these 15% were malignant, 1.25% showed low grade prostate intraepithelial neoplasia and the remaining 83.8% were BPH. The majority (11 cases) of the malignancies were adenocarcinomas, and one case was of transitional cell carcinoma and most frequent Gleason score was 7 (in 54.5%).The highest incidence of malignancies and hyperplasia occurred between 60 and 69 years of age. The mean serum PSA value in benign cases was 8.90 ng/mL (SD ± 12.77) and in malignant cases was 83.06 ng/mL (SD ± 80.36). Serum PSA in the range of 0-4 ng/mL was significantly associated with benign lesions and value more than 20 ng/mL was significantly associated with malignant lesions.

Albasri A *et al*[27] showed out of 417 prostate lesions reviewed, 82.3% were benign and 17.7% were malignant, giving a benign to malignant ratio of 4.6:1. Benign prostatic hyperplasia (both with and without inflammation) was the commonest prostatic lesion and accounted for 80.3% of all cases and 97.6% of all benign cases. The age range was 20 to 97 years with a mean of 69.2 years and a peak age group at 70-79 years. Seventy one cases of adenocarcinoma accounted for 95.9% of the total of 74 malignant tumors. It showed an age range of 44 to 95 years, a mean age of 70.9 years and peak prevalence in the 80-89 year age group. Gleason score seven was the

most frequent (39.4%) in occurrence. Most adenocarcinomas, 57.7%, were moderately differentiated (Gleason score of 5-7).

PSA values ranged widely between 16-1865 ng/ml with a mean of 363.4 ng/ml. Elevated PSA (>100 ng/mL) levels were found in 53 (81.6%) patients. There was a statistically significant positive correlation between serum PSA level and Gleason score (p=0.0304)

Barakzai MA *et al*[28] showed the mean age of patients was 66.9 ± 9.4 years (range: 52-100 years). The mean serum PSA was 97.1±119.4 ng/mL (range: 4-449 ng/mL).

Mean number of cores obtained per case was 7.8±0.9 (range: 4-9). Overall, 55.6% cases showed benign lesions and 44.4%, were malignant. Benign lesions consisted of adenomyomatous hyperplasia. Fourteen of benign cases (46.6%) showed significant inflammatory changes. Among malignant lesions, all cancers were of moderate to high Gleason grades and scores. Mild serum PSA rise was seen in 48.1% patients; among these, 73% cases showed benign lesions and 26.9%, were malignant. Moderate serum PSA rise was seen in 25.9% cases; among these 64.3% were benign and 35.7% malignant. 25.9% patients had serum PSA ≥ 50.1 ng/mL. Among these 85.7% had adenocarcinoma, 14.3% had hyperplasia, one of the later with active prostatitis.

Josephine *et al*[29] study featured Benign prostatic hyperplasia and Carcinoma of the prostate are increasingly frequent with advancing age. Among the 106 biopsies received, 74.52% cases were of Benign prostatic hyperplasia, 1.89% were Prostatic intraepithelial neoplasia and 23.58% were carcinoma of prostate. Prostatitis was the most common associated lesion in cases of benign prostatic hyperplasia presenting in 25.31% patients. Among the Carcinoma patients, 80% were of Adenocarcinoma of

prostate and 20% cases were Small cell carcinoma of prostate. Both Benign prostatic hyperplasia and Carcinoma prostate were common in the seventh decade. Most common clinical presentation was difficulty in micturition. Most common histological type of Carcinoma prostate was Adenocarcinoma. Serum PSA estimation was done in 49 cases of prostate biopsies. Elevations of serum PSA levels were noted in both BPH and Carcinoma prostate patients.Eight cases of BPH, had serum PSA values in the range of 0-4 ng/mL. Six cases of Carcinoma prostate ,had serum PSA values in the range of >80 ng/mL.

Amarneel S *et al*[30] study included 64 cases, out of which 43 cases were benign and 21 cases were malignant. Maximum numbers of benign and malignant lesions were in the age group of 60 – 69 years. Most of the malignant cases 85.71% had PSA level above 20 ng/mL. Histological grade III carcinomas were restricted to PSA levels of 50 ng/mL and above, while grade I was restricted to PSA level of less than 10 ng/mL and grade II carcinomas did not have any correlation with specific PSA levels.

Kim LH *et al*[25] in his study of Prevalence Of High-Grade Prostatic Intraepithelial Neoplasia and its relationship to serum prostate specific antigen showed The mean serum PSA in men with PIN without evidence of prostatic adenocarcinoma was 1.9 ng/mL (SD=2.026). The incidence of isolated high-grade PIN was 63%. They observed that the presence of high-grade PIN does not result in a significant elevation of serum PSA.

MATERIALS AND METHODS

- A cross-sectional study was carried out in the histopathology laboratory of Department of Pathology in collaboration with Department of Urology and Department of Biochemistry BLDEU's Shri B.M. Patil Medical College, Hospital and Research centre, Bijapur from 1st December 2014 to 30th June 2016.
- **Inclusion criteria**: Patients presenting with clinical signs and symptoms of bladder outlet obstruction and undergoing transurethral resection of prostate (TURP)//biopsy were included in the study group.

Methods of collection of data.

1. This is a prospective study of lesions of prostate and their correlation with serum PSA levels.
2. The present study included 60 prostate specimens (Transurethral resection of prostate/Needle Biopsy) from patients for histopathological examination and their serum PSA levels, coming to the Department of Pathology, Shri B.M. Patil Medical college, Vijayapur during the period from 1st December 2014 to 30th June 2016.
3. The specimen were received in 10% formalin. Prostatic tissue was grossly examined first and findings were noted. Attempts were made to process the tissue in entirely. Tissue was submitted till 4 cases were filled, and one additional cassette for each 10 gram of tissue was submiited. When specimen was large, the TURP chips showing soft or rubbery, and yellow grey in colour were chosen for processing.
4. The sections were cut at 3-5 micron thickness and were stained by haematoxylin and eosin stain.

Harris Hematoxylin and Eosin Stain(Regressive Stain)

Harris Haematoxylin

Haematoxylin Crystals	5.0 gm
Alcohol 10%	50.0 ml
Ammonium or potassium alum	100.0 gm
Distill water	1000.0 ml
Mercuric oxide(red)	2.5 gm

Dissolve haematoxylin in alcohol and alum in water with aid of heat.Remove from heat and add mercuric oxide slowly. Reheat until solution becomes dark purple. Remove from heat and plunge vessel into a basin of cold water until itis cool. Add 2-4 ml of glacial acetic acid per 100 ml of solution and the stain is ready for use.

Acid Alcohol

Alcohol 70%	1000.0ml
Hydrochloric acid concentrated	010.0ml

1% Stock Alcohol eosin

Eosin Y, water soluble	1.0 ml
Distill water	20.0 ml
Alcohol 95%	80.0 ml

Working eosin solution

Eosin solution	1 part
Alcohol, 80%	3 parts

Just before use, add 0.5 ml of glacial acetic acid to each 100ml of stain and stir.

Staining Procedure

- Remove paraffin wax with xylene- 5 minutes.
- Treat with absolute alcohol- 2 min.
- Immerse in 90% alcohol- 2 min.
- Immerse in 70% alcohol- 2 min.
- Immerse in 50% alcohol- 2 min.
- Immerse in water- 5 min.
- Immerse in hematoxylin- 5 to 10 min.
- 1% acid alcohol- 3 to 5 dips
- Immerse in running tap water for blueing- 10 min.
- Immerse in 1% eosin- 1 min.
- Wash in water.
- Dehydrate and clear in xylene.
- Mount in DPX

Results:

Nuclei	-	Blue black
Cytoplasm	-	Varying shades of pink
Muscle fibres	-	Deep pink red
Erythrocytes	-	Orange red
Fibrin	-	Deep pink

5. Histopathological examination was carried out and the lesions were classified into neoplastic and non-neoplastic on microscopy.
6. All the lesions were correlated with pre-operative serum PSA levels.

Estimation of total serum PSA values:

Blood samples for total Serum PSA estimation were collected on ambuatory basis i.e. at the time of admission by venipucture. The blood was sent to Biochemistry laboratoty of BLDEU Medical College Hospital & Research Centre in a plain bulb. Serum was separated and was processed for PSA levels.

Method Of Measurement

VIDAS TPSA is an automated quantitative test for use on the VIDAS family instruments, for the quantitative measurements of prostate specific antigen (PSA) Levels in human serum or plasma(lithium heparin or EDTA) were measured, using the ELFA Technique(Enzyme Linked Fluorescent Assay).

PRINCIPLE

The assay principle combines a two step enzyme immunoassay sandwich method with a final Fluorescent detection(ELFA).The solid phase Receptable(SPR) serves as the solid phase as well as the pipetting device. Reagents for the assay were ready to use and pre-dispensed in the sealed reagent strips.All of the assay steps were preformed automatically by the instrument. The reaction medium was cycled in and out of the SPR several times.

The sample was cycled in and out of the SPR several times. This operation enables the antibody fixed onto the interior wall of the SPR to capture the prostate specific antigen present in the sample. Unbound components were eliminated during the washing step. Alkaline phosphatase- labelled antibody was then incubated in the SPR where it binds with the prostate specific antigen. Unbound conjugate was then eliminated during the washing steps.

During the final detection step, the substrate (4-Methy-umbelliferyl phosphate) was cycled in and out of the SPR. The conjugate enzyme catalyzes the

hydrolysis of this substrate into a fluorescent product(4-Methy-umbelliferone), the fluorescence of which was measured at 450nm.The intensity of the fluorescence was proportional to the concentration of prostate specific antigen present in the sample.

At the end results were automatically calculated by the instrument in relation to the calibration curve stored in memory , and then printed out.

The SPR

The SPR was coated during production with monoclonal antibody anti-PSA antibodies. Each SPR was identified by the code TPSA.

PROCEDURE

1. Required reagents(Control C1, Standard S1 and Diluent R1) were removed from the refrigerator and were allowed to come at room temperature.
2. One 'TPSA' strip and one 'TPSA' SPR for each sample, control to be tested was used.
3. The test was identified by the 'TPSA' code on the instrument, and the control by C1 respectively.
4. Control and samples were mixed using a vortex type mixer(for serum or plasma separated from the pellet)
5. Control and sample test portion was 200ul for this test.
6. 'TPSA' SPRs and 'TPSA' strips were inserted into the instrument.
7. Assay steps were automatically performed by the instrument.
8. Assays were completed within approximately 60 minutes.
9. Used SPRs and strips were disposed.

Sample Size:

With Benign prostatic hyperplasia (BPH) PSA level [MEAN±SD]

is 4.86±3.03[4]at 99% confidence interval and ±1 margin of error, the sample size was 58≅60

$n = Z\alpha^2 X \sigma^2/d^2$

Zα=Z value at α level=99%

σ^2= Standard deviation of BPH=3.03

d= margin of error = ±1

Statistical analysis:

Data was presented using:

- Drawings
- Mean± SD

RESULTS

Table 1: Distribution of cases according to histopathological diagnosis

Histopathological Impression	N	%
Adenocarcinoma	16	26.7
BPH	28	46.7
BPH with Prostatitis	13	21.7
PIN	3	5.0
Total	60	100

Figure 7: Bar Diagram showing Distribution of cases according to histopathological diagnosis

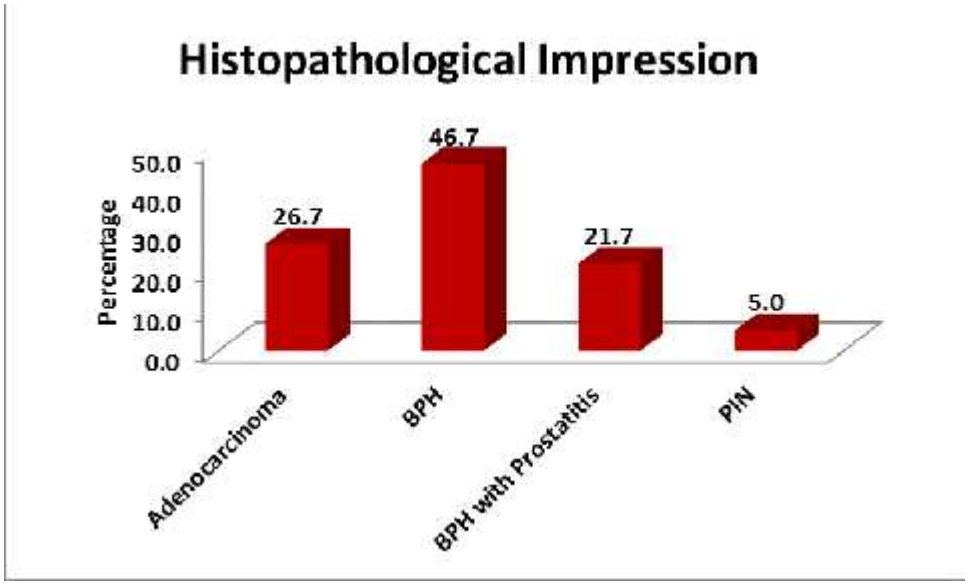


Table1.&Fig.7 shows the most common prostatic lesion was Benign Prostatic Hyperplasia (BPH) followed by Adenocarcinoma, BPH associated with Prostatitis and Prostatic Intraepithelial Neoplasia (PIN) respectively.

Table 2: Detailed histopathological diagnosis

Histopathological Diagnosis		**N**	**%**
Adenocarcinoma	Grade group I (GLEASON SCORE≤6)	8	50
	Grade group II (GLEASON SCORE 3+4)	2	12.5
	Grade group III (GLEASON SCORE4+3)	1	6.25
	Grade group IV (GLEASON SCORE 8)	1	6.25
	Grade group V (GLEASON SCORE 9-10)	4	25
	Total	16	100
BPH	BPH	25	89.3
	BPH with Cystitis Cystica	1	3.6
	BPH with Prostatic abscess	1	3.6
	BPH with Prostatic Infarct and Squamous Metaplasia.	1	3.6
	Total	28	100
BPH with Prostatitis	BPH with Acute on Chronic Prostatitis	1	7.7
	BPH with Acute Prostatitis	2	15.4
	BPH with Chronic Prostatitis	9	69.2
	BPH with Granulomatous Prostatitis	1	7.7
	Total	13	100
PIN	Focal Low Grade PIN with BPH	1	33.3
	Low Grade PIN with BPH	1	33.3
	Low Grade PIN	1	33.3
	Total	3	100

Table 3: Distribution of cases according to age and histopathological diagnosis

Age(Yrs)	Adenocarcinoma		BPH		BPH with Prostatitis		PIN		p value
	N	%	N	%	N	%	N	%	
41-50	0	0.0%	0	0.0%	1	7.7%	0	0.0%	
51-60	2	12.5%	7	25.0%	0	0.0%	0	0.0%	
61-70	6	37.5%	13	46.4%	9	69.2%	2	66.7%	0.049
71-80	5	31.3%	7	25.0%	3	23.1%	1	33.3%	(sig)
>80	3	18.8%	1	3.6%	0	0.0%	0	0.0%	
Total	16	100.0%	28	100.0%	13	100.0%	3	100.0%	

Figure 8: Bar Diagram showing Distribution of cases according to age and histopathological diagnosis.

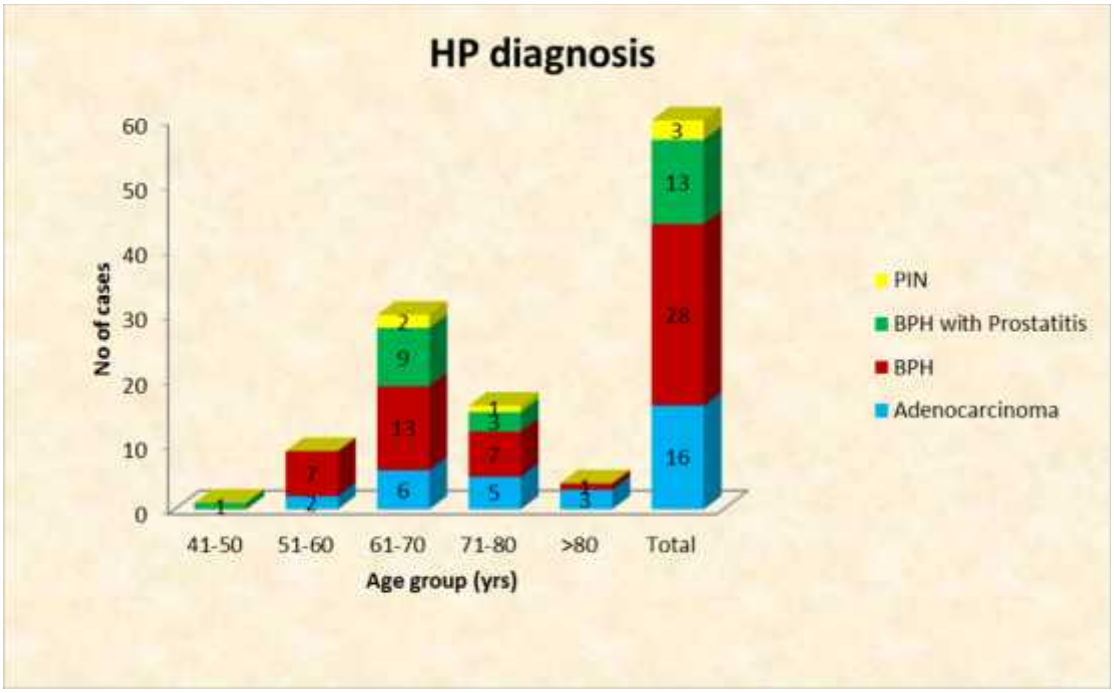
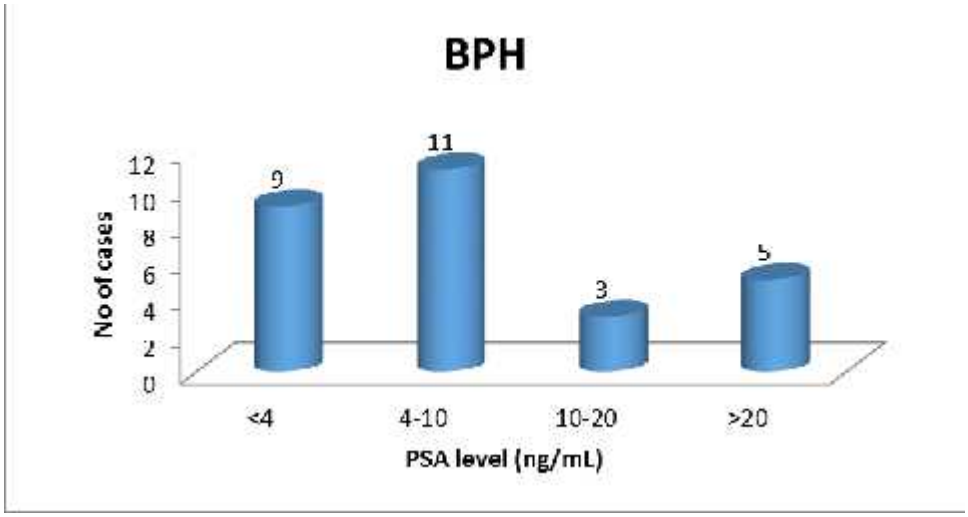


Table 3 and Fig 8 shows both BPH & Adenocarcinoma were more common in 61-70 years of age group followed by 71-80 years. While BPH was also common in 51-60 years of age group. The association of the various lesions was statistically significant(p value 0.049) with increasing age.

Table 4: Serum PSA levels (ng/mL) in BPH cases

PSA level (ng/ml)	N	%
<4	9	32.1
4-10	11	39.3
10-20	3	10.7
>20	5	17.9
Total	28	100.0
Mean±SD	13.4±20.7	
Range	0.7 - 100	

Figure 9: Bar Diagram showing Serum PSA levels (ng/mL) in BPH cases.



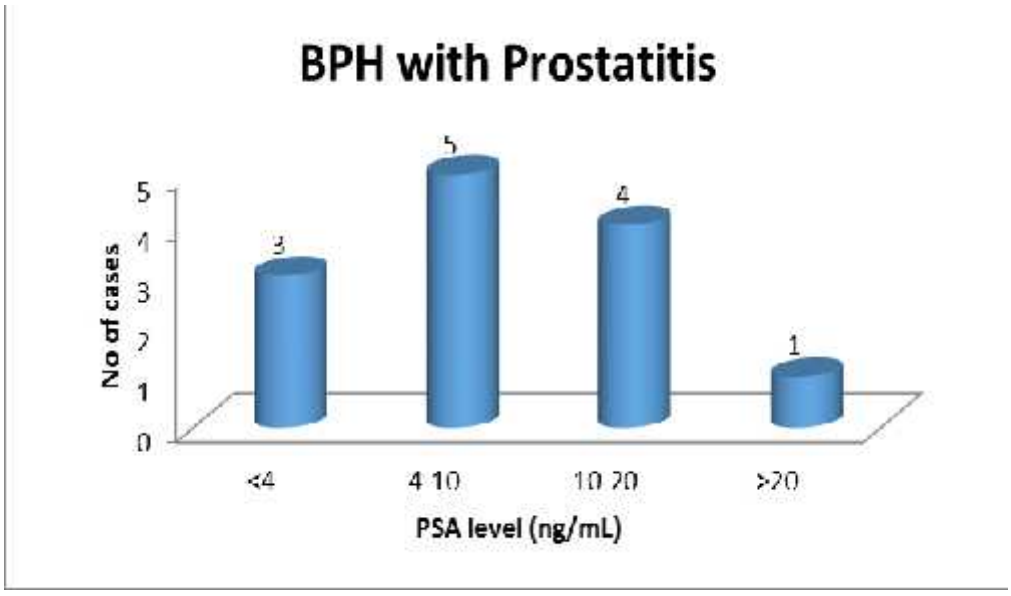
11 cases had serum PSA level in range of 4-10 ng/ml followed by 9 cases with PSA levels of <4 ng/mL. 3 cases had Serum PSA levels in the range of 10-20 ng/mL and 5 cases had PSA levels more than 20 ng/mL.

Mean±SD PSA values for diagnosis of BPH was 13.4±20.7.

Table 5: Serum PSA levels (ng/mL) in BPH with Prostatitis cases

PSA level (ng/mL)	N	%
<4	3	23.1
4-10	5	38.5
10-20	4	30.8
>20	1	7.7
Total	13	100.0
Mean±SD	10.2±8.6	
Range	0.5 - 33.4	

Figure 10: Bar Diagram showing Serum PSA levels (ng/mL) in BPH with prostatitis cases.



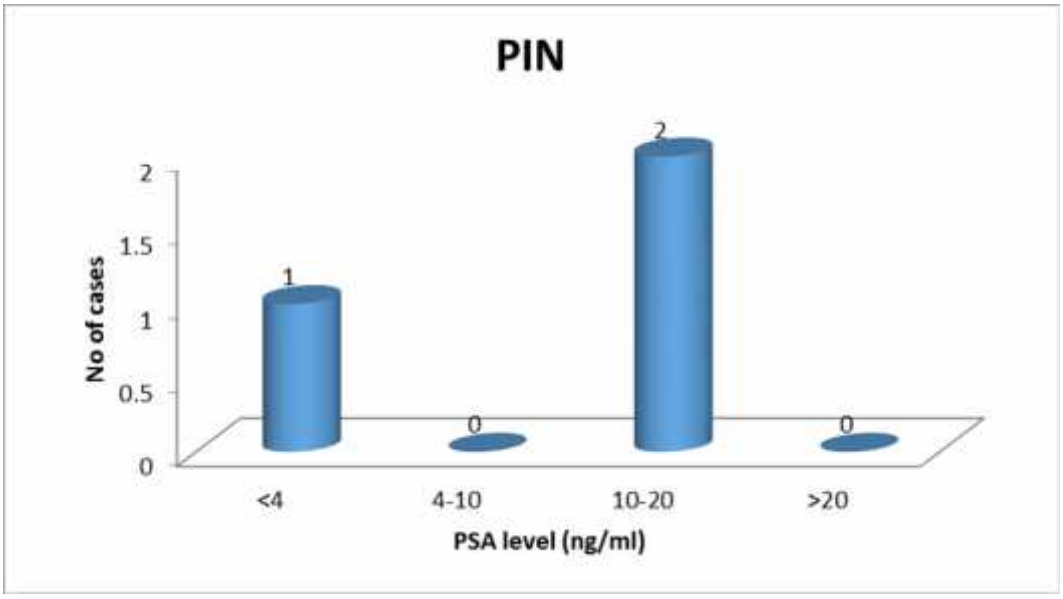
BPH with prostatitis cases i.e Out of total 13 cases 9 cases had serum PSA levels in 4-20 ng/mL range followed by Serum PSA levels < 4ng/mL in 3 cases. One case had PSA levels more than 20 ng/mL.

Mean±SD PSA values for diagnosis of BPH with prostatitis was 10.2±8.6.

Table 6: Serum PSA levels (ng/mL) in PIN cases

PSA level (ng/ml)	N	%
<4	1	33.3
4-10	0	0.0
10-20	2	66.7
>20	0	0.0
Total	3	100.0
Mean±SD	10.5±9.4	
Range	0.9 - 19.6	

Figure 11: Bar Diagram showing Serum PSA levels (ng/mL) in PIN cases



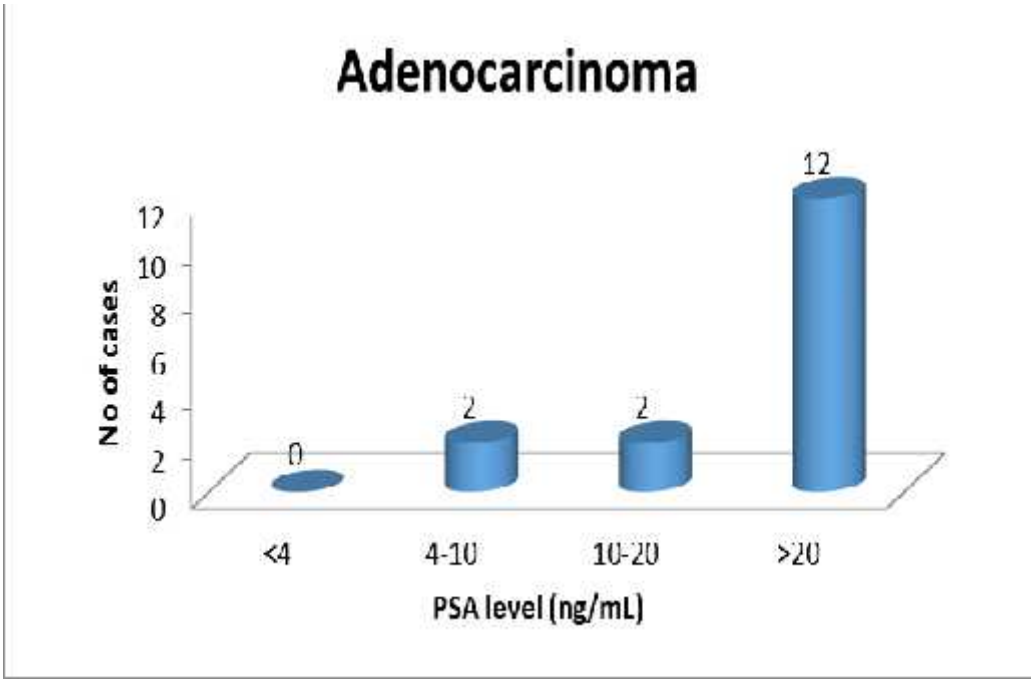
While 2 cases of PIN had Serum PSA in the range 10-20 ng/ml one had PSA values less than 4 ng/mL.

Mean PSA ±SD value for PIN was 10.5±9.4.

Table 7: Serum PSA levels (ng/mL) in Adenocarcinoma cases

PSA level (ng/mL)	N	%
<4	0	0.0
4-10	2	12.5
10-20	2	12.5
>20	12	75.0
Total	16	100.0
Mean±SD	55.6±36.5	
Range	4.6 – 100	

Figure 12: Bar Diagram showing Serum PSA levels (ng/mL) in Adenocarcinoma cases



12 cases had Serum PSA levels >20 ng/mL followed by 2 cases each in the range of 4-10 and 10-20 ng/mL.

Mean ±SD PSA value for Adenocarcinoma was 55.6±36.5.

Table 8: Distribution of adenocarcinoma cases by Gleason Grade

Gleason Grade	N	%
Grade group I (≤6)	8	50
Grade group II (3+4)	2	12.5
Grade group III (4+3)	1	6.25
Grade group IV (8)	1	6.25
Grade group V (9-10)	4	25
Total	16	100

Figure13: Bar Diagram showing Distribution of adenocarcinoma cases by Gleason Grade

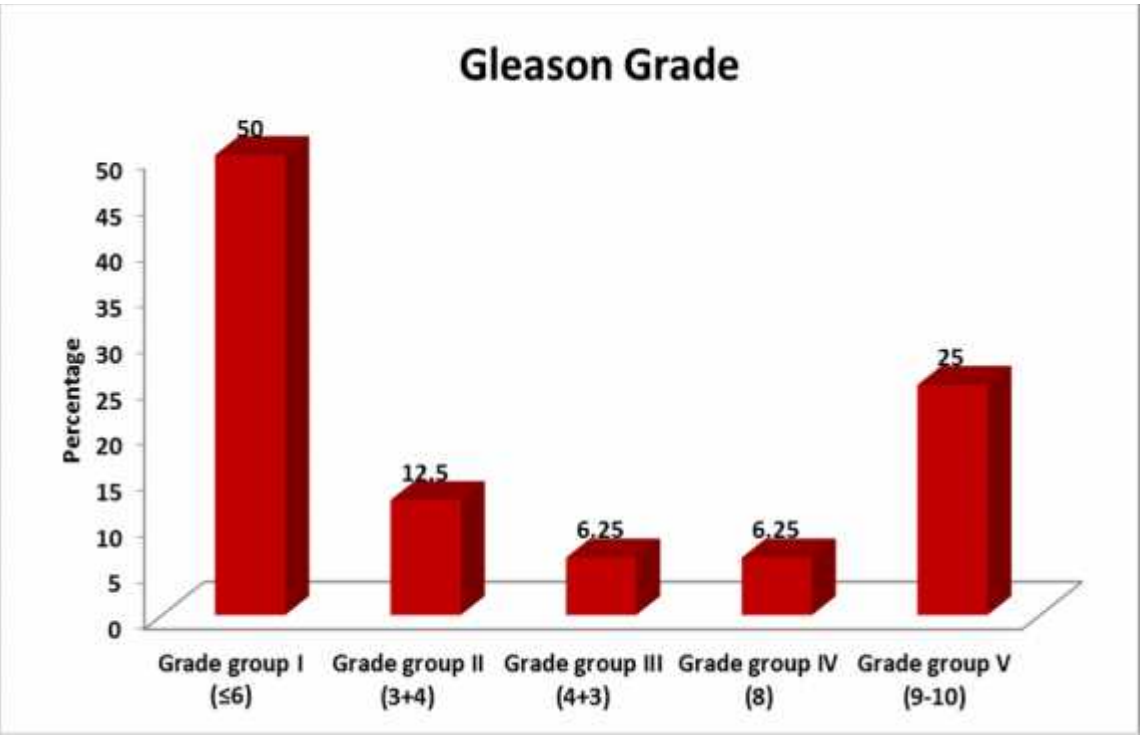
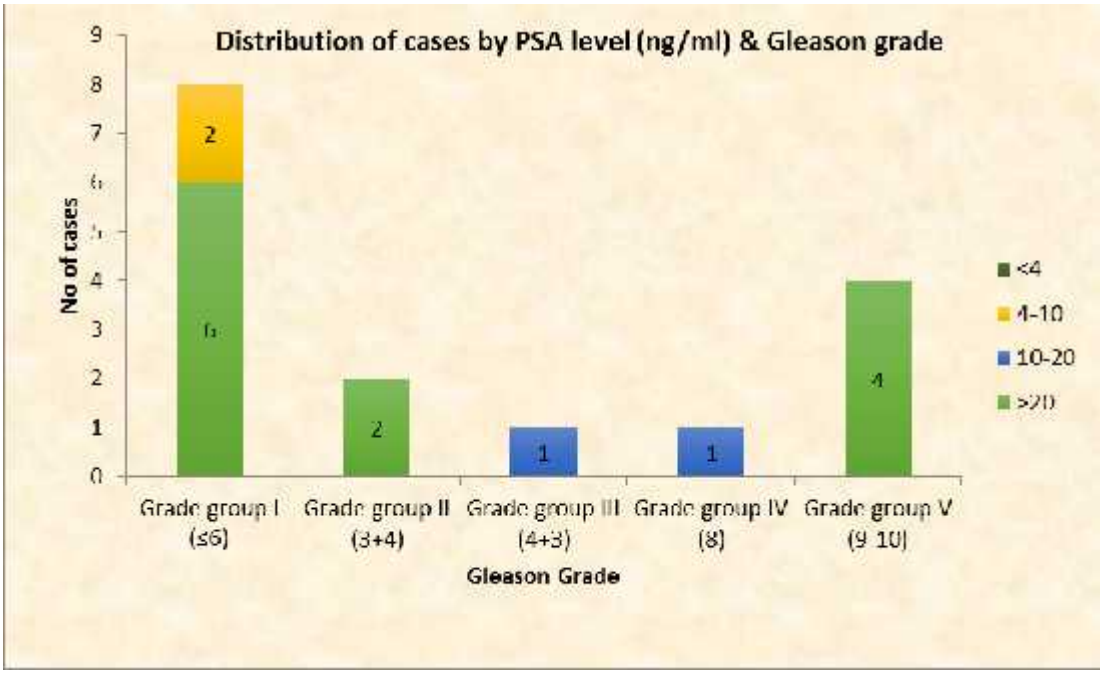


Table 9: Serum PSA levels (ng/ml) in various Gleason Grades of adenocarcinoma

PSA level (ng/ml)	Grade group I (Gleasons score≤6)		Grade group II (Gleasons score 3+4)		Grade group III (Gleasons score 4+3)		Grade group IV (Gleasons score 8)		Grade group V (Gleasons score 9-10)	
	N	%	N	%	N	%	N	%	N	%
<4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
4-10	2	25.0	0	0.0	0	0.0	0	0.0	0	0.0
10-20	0	0.0	0	0.0	1	100.0	1	100.0	0	0.0
>20	6	75.0	2	100.0	0	0.0	0	0.0	4	100.0
Total	8	100.0	2	100.0	1	100.0	1	100.0	4	100.0
Mean±SD	46.4±37.3		79.0±29.6		11.4±NA		17.1±NA		82.8±19.9	
Range	4.6-100.0		58-100.0		11.4-11.4		17.1-17.1		65-100.0	
ANOVA p value	0.181									

Out of 16 cases of adenocarcinoma Maximum cases of adenocarcinoma (8) fell in group I followed by (4) in group V. Group II had (2) cases while group III & IV had (1) case each.

Figure14: Bar Diagram showing Serum PSA levels (ng/ml) by Gleason Grade



GROSS IMAGE

FIG 1A GROSS:Transuretheral Resection of Prostate(TURP) chips

FIG 2A Needle Core Biopsy

PHOTOMICROGRAPHS

(TURP & BIOPSY SPECIMENS)

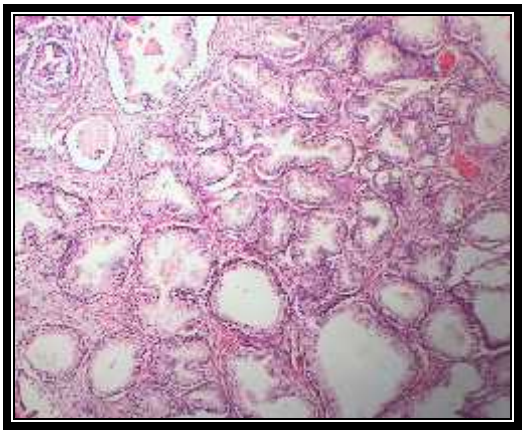


FIG 3A.Benign Prostatic Hyperplasia: Hyperplasia of glandular component with double layer of columnar epithelium surrounded by fibromuscular stroma. (H&E 100X)

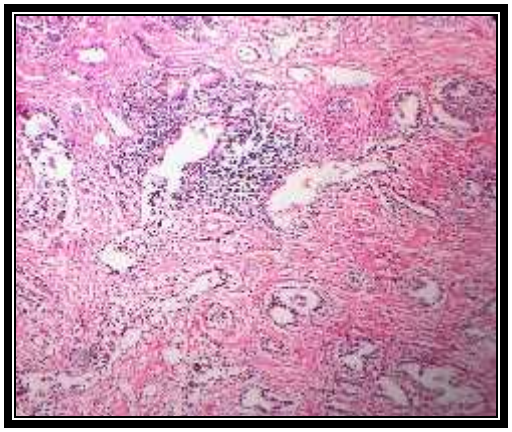


FIG 4A. Benign Prostatic Hyperplasia with Chronic Prostatitis: Lymphoid aggregate along with hypeplastic glands (H&E 100X)

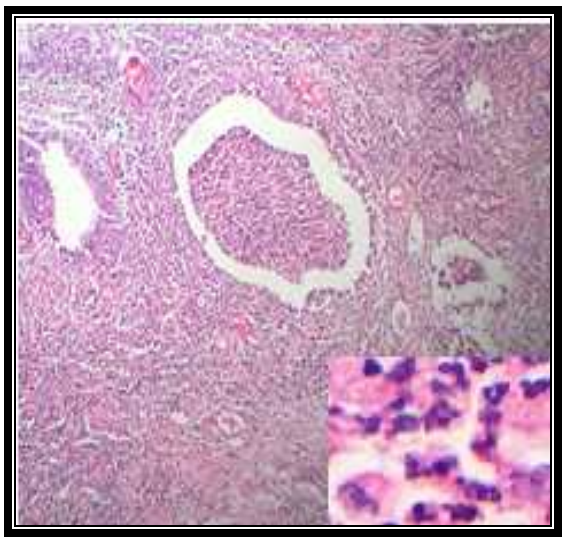


FIG 5A. Benign Prostatic Hyperplasia with Acute Prostatitis. (H & E 100X)
Inset: High power view(400X) of the gland filled with Neutrophils

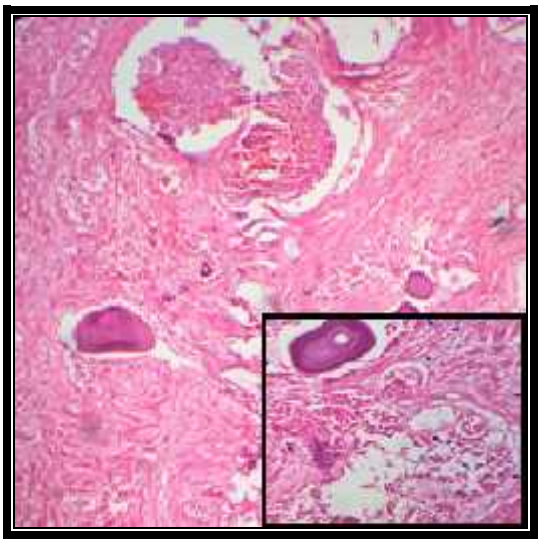


FIG 6A. Benign Prostatic Hyperplasia with Infarct. (H&E 100X).
Inset: Coagulative necrosis of the gland.

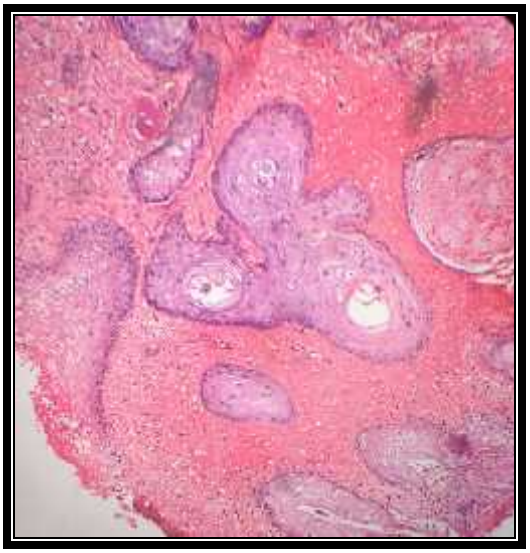


FIG 7A: Benign Prostatic Hyperplasia with squamous metaplasia with infarct(H&E 100X)

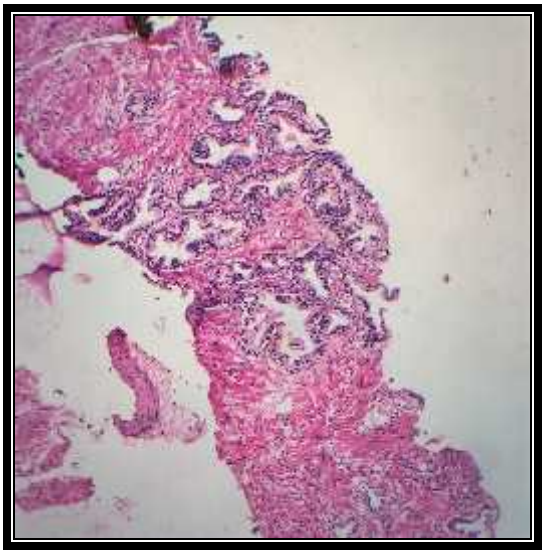


FIG 8A **Prostate Biopsy** Specimen showing Benign Prostatic Hyperplasia (H&E 40X)

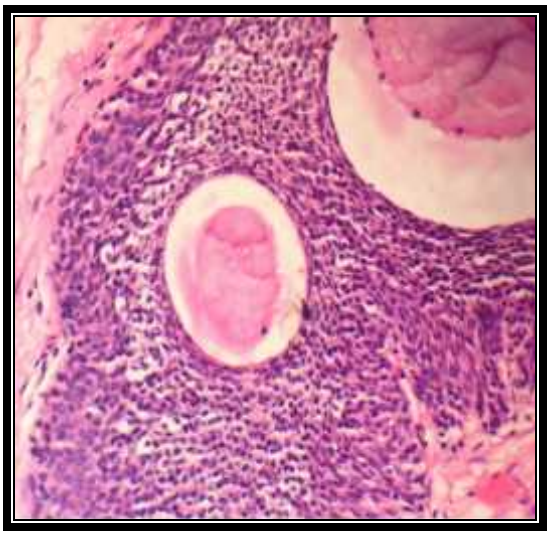


FIG 9A Incomplete Basal cell hyperplasia in prostate gland showing peripheral palisading. (H&E 100X)

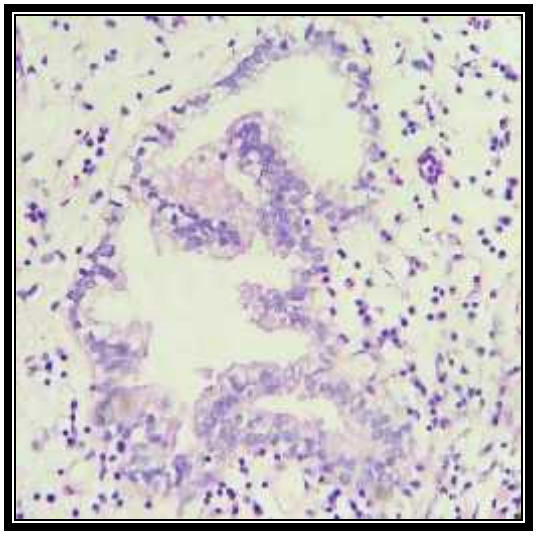


FIG 10A: Low grade Prostatic Intraepithelial Neoplasia (PIN)(H&E 100X)

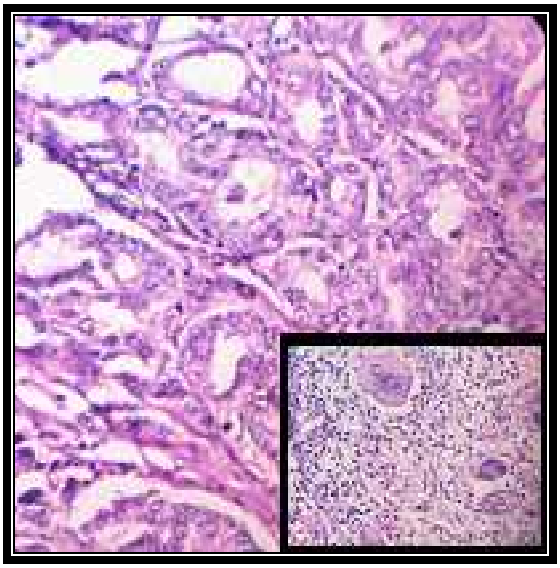


FIG 11A: Adenocarcinoma of Prostate showing well formed glands with granulomatous prostatitis with giant cells, epitheloid cells (INSET) .ZN Stain for Acid Fast Bacilli- Negative.
(Gleason ≤6) GROUP 1(H&E 100X)

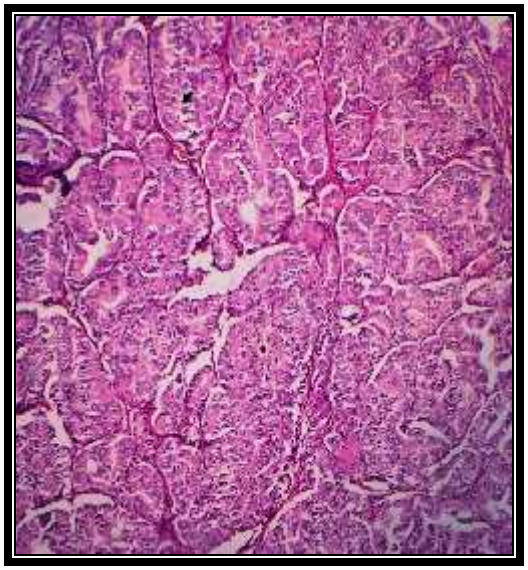


FIG 12A Adenocarcinoma of prostate with individual, discrete, well-formed glands. (Gleason ≤6) GROUP 1 (H&E 100X)

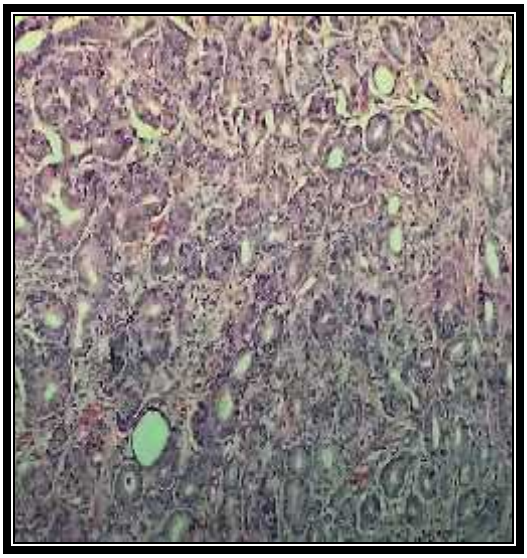


FIG 13A: Adenocarcinoma Of Prostate with majority of well formed glands with glands appearing fused [lesser component] in the upper left corner.(Gleason3+4)
GROUP 2(H&E 100X).

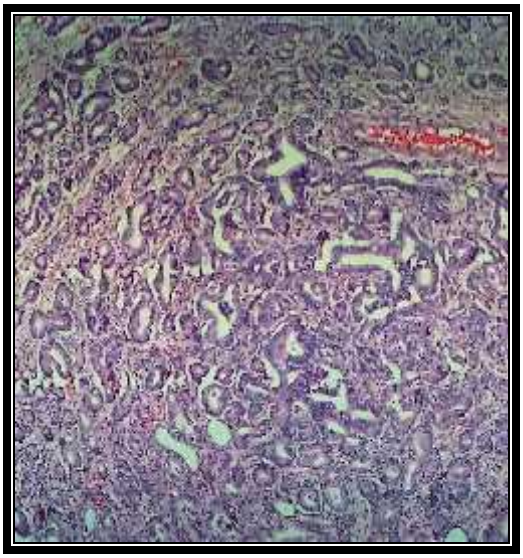


FIG 14A. Adenocarcinoma Of Prostate with majority of fused glands with a focus of well formed glands[lesser component] appearing in the upper left corner.(Gleason4+3)
GROUP 3 (H&E 100X).

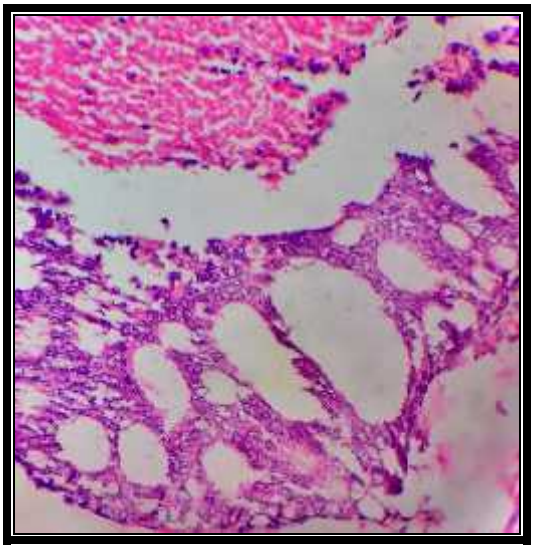


FIG 15A Adenocarcinoma with glands in cribriform pattern and focal area showing necrosis (UPPER PART).(Gleason 4+5)
GROUP 5(H&E 100X)

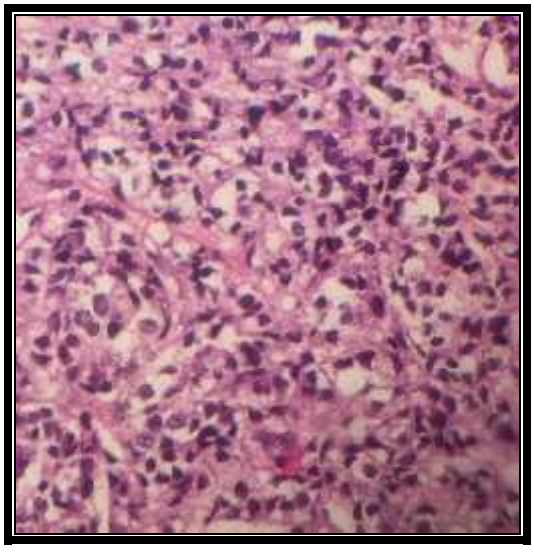


FIG 16A Adenocarcinoma with ill/poorly formed glands with clear cell change and signet ring cells. Gleason(4+4)
GROUP 4 (H&E 400X)

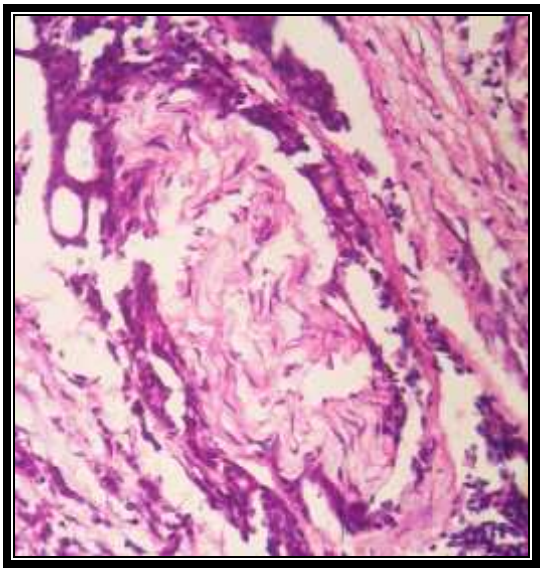


FIG 17A Adenocarcinoma showing perineural invasion. Gleason (5+3) GROUP 4 (H&E 100X)

FIG18A 1. Prostatic Biopsy with High Grade Adenocarcinoma. Gleason 10
GROUP 5(H&E 100X)

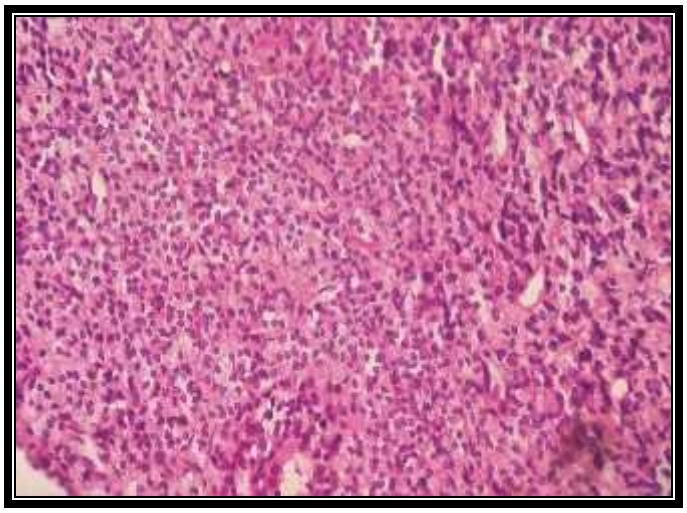


FIG18A 2. High power view show Tumor arranged in solid sheets, single cells
(Gleason 5+5) GROUP 5(H&E 400X)

DISCUSSION

The prostate gland is the largest accessory reproductive organ in males. It being an exocrine gland,majority of the seminal fluid is derived from here. Owing to its strategic location at the bladder neck, urinary obstruction is one of the major and most common symptoms in lesions related to it.[31]

Predominant lesions include benign prostatic hyperplasia (BPH) and carcinoma show an increasing trend with increasing age.

Age Specific Distribution of Various Lesions

Present study showed majority of the lesions were in the age group of 61-70 years comprising of 50% cases followed by 71-80 years of age group comprising of 26.7% cases. In our study youngest patient was 50 year old having BPH with chronic prostatitis while the eldest patient was 95 years old having adenocarcinoma.

Age distribution of cases in the present study was similar to the study conducted by Amarneel S *et al*[30] in which maximun number of benign and malignant cases were in the age group of 60-69 years.

These results were also comparable with the study done by Khatib W *et al*[31] in which both BPH and adenocarcinoma was most commonly found in the 6-8th decade. PIN was commonly encountered in the 6-7th decade in the present study in concordance with study conducted by Khatib W *et al*.[31]

Table10 Procedure Done for Various Prostatic Lesions

PROCEDURE	Wadgaonkar *et al*[1]	Josephine *et al*[29]	Khatib W *et al*[31]	Present Study
TURP specimen	69	62	72	58
Needle Biopsies	06	44	10	02
Prostatectomy Specimens	05	00	06	00

In our study, prostatic chips from TURP procedure comprised the majority of samples received i.e 58 followed by 2 needle core biopsies which was comparable to study conducted by Wadgaonkar *et al*[1], Josephine *et al*[29] and Khatib W *et al*[31].

According to study done by Chandanwade SP *et al*[32],TURP is most commonest procedure performed for prostatic lesions when compared with en block removal of prostate in India.

Table No. 11 Comparison of distribution of various lesions with other studies

Sr. No	HP Diagnosis	Jasani *et al*[4]	Arora K *et al*[33]	Azmi A. Haroun *et al*[34]	Jevan B *et al*[35]	Present Study
1	BPH	56%	85.8%	64.48%	83%	28(46.7%)
2	ADENO CA	32%	8.35%	27.1%	17%	16(26.7%)
3	PIN	7.2%	4.48%	-	-	01(1.6%)
4	BPH WITH PIN	-	-	-	-	02(3.3%)
5	TCC	1.1%	0.32%	-	-	-
6	PROSTATITIS	2.7%	0.64%	8.4%	-	-
7	BPH WITH PROSTATITIS (Acute,Chronic &Granulomatous)	-	-	-	-	13(21.7%)

Of the 60 cases studied in the present study, 28(46.7%) cases were of BPH, 16 (26.7%) cases were malignant which was comparable in order of frequency of BPH and malignant lesions found in studies conducted by Jasani *et al*[4] ,Arora K *et al*[33],Azmi A *et al*[34] and Jevan B *et al* [35].

In the present study 21.7%(13 cases) of BPH were associated with Prostatitis which was in concordance with the study conducted by Abdel-Meguid *et al*[36] who found prevalence of prostatic inflammation with BPH in about 20.1% cases.

Out of 13 cases of BPH with prostatitis, 69.2% (9) cases had chronic prostatitis,15.2%(2) cases had acute inflammation, 7.6%(1) case had acute on chronic inflammation and 7.6% (1) was of granulomatous prostatitis

1.6%(1) had low grade PIN and 3.3%(2) of BPH associated with PIN were noted in our study.A cases of BPH also showed incomplete basal cell hyperplasia with central lumina.

One case of BPH associated with cystitis cystica and prostatic abscess was seen. One case of BPH associated with squamous metaplasia and infarct which is a rare presentation was present and was not reported in other studies.

Table No.12 Comparative table showing correlation of serum PSA levels and BPH

PSA(ng/mL)	**Benign Prostatic Hyperplasia**				
	Jasani B *et al*[4]	**Arora K *et al*[33]**	**Khan IA *et al*[37]**	**Sharma P *et al*[38]**	**Present study**
0-4 ng/mL	63.7%	71.6%	-	-	9(32.1%)
4-10 ng/mL	27.4%	22.6%	85%	87.6%	11(39.2%)
>10 ng/mL	8.8%	3%	15%	12.4%	8(28.5%)

Majority of the cases in the present study had serum PSA levels in the range of 4-10 ng/mL which was comparable to studies conducted by Khan IA *et al*[37] and Sharma P *et al.* [38]

While in studies conducted by Jasani *et al*[4] and Kshitiji *et al*[33] , maximum number of cases had serum PSA levels in the range of 0-4 ng/mL.

Serum PSA levels in other Benign lesions:

Present study showed 38.5% (5) cases of BPH associated with prostatitis having serum PSA levels in the range of 10-20 ng/mL, 30.8%(4)cases in the range of 4-10 ng/mL, 23.1%(3) cases had values less than 4 ng/mL and 7.7%(1) case had >20 ng/mL.

One case each of BPH associated with cystitis cystica, infarct with squamous metaplasia and prostatic abscess showed PSA values as 100 ng/mL,37 ng/mL and < 4ng/mL respectively.

As the serum PSA levels in benign lesions showed a wide variation from <4 ng/mL to as high as 100 ng/mL, hence serum PSA values are not significant in diagnosis of these benign lesions of prostate.This was consistent with the studies conducted by Baida R *et al* [39]

Table No. 13 Comparative table showing correlation of serum PSA levels and Prostatic malignancy

PSA LEVELS(ng/mL)	**Amarneel S *et al*[30]**	**Zivkovic S[40]**	**Our study**
0-3.9	0	1(2.5%)	0
4.9-9.9	1(4.76%)	11(27.5%)	2(12.5%)
10-19.9	6(9.52%)	7(17.5%)	2(12.5%)
>20	18(85.7%)	21(52.25%)	12(75%)

Present study tried to evaluate the prognostic importance of preoperative serum PSA levels with adenocarcinoma of prostate. Out of total 16 malignant cases ,75%(12) of the cases had serum PSA values more than 20 ng/mL which is in concordance with the study conducted by Amarneel *et al*[30] and Zivkovic S *et al*[40] . In

the study done by Amarneel *et al*[30],out of total 25 malignant cases 85.7%(18) of malignant cases had serum PSA levels >20 ng/mL.

In Zivkovic S *et al*[40] study out of the 40 malignant cases, 52.25%(21) showed serum PSA values >20 ng/mL. Wadgaonkar *et al*[1] also found majority (66.7%) of malignant cases with severely elevated serum PSA levels above 20 ng/mL.

Present study had 12.5% (2) malignant cases with serum PSA levels in the range of 4.9-9.9 ng/mL. which was comparable with the study done by Amarneel *et al*[30] who found 4.76% (1) case in that range.

Both the present study and study by Amarneel *et al* [30] had no malignant cases with serum PSA levels in the normal range of 0-4 ng/mL.

Table 9: PSA level (ng/mL) in various Gleason Grades (New Grading System) of adenocarcinoma

PSA level (ng/mL)	Grade group I (Gleasons score≤6)		Grade group II (Gleasons score 3+4)		Grade group III (Gleasons score 4+3)		Grade group IV (Gleasons score 8)		Grade group V (Gleasons score 9-10)	
	N	%	N	%	N	%	N	%	N	%
<4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
4-10	2	25.0	0	0.0	0	0.0	0	0.0	0	0.0
10-20	0	0.0	0	0.0	1	100.0	1	100.0	0	0.0
>20	6	75.0	2	100.0	0	0.0	0	0.0	4	100.0
Total	8	100.0	2	100.0	1	100.0	1	100.0	4	100.0
Mean±SD	46.4±37.3		79.0±29.6		11.4±NA		17.1±NA		82.8±19.9	
Range	4.6-100.0		58-100.0		11.4-11.4		17.1-17.1		65-100.0	
ANOVA p value	0.181									

Present study showed that there was no statistically significant (p value 0.181)correlation between serum PSA value and increasing Gleason score.

Majority of the benign lesions had serum prostate specific antigen (PSA) levels 4-10 ng/mL .

Almost all cases of adenocarcinoma showed prostate specific antigen (PSA) levels > 20 ng/mL indicating significant association of serum prostate specific antigen (PSA) levels with malignancy in prostate and thus often it helps in distinguishing between the benign and malignant lesions of prostate.

Normal range of prostate specific antigen (PSA) levels is 0-4 ng/mL . Prostate specific antigen (PSA) is the best marker for adenocarcinoma and for patients who present with obstructive symptoms and have nodules on digital rectal examination . Though generally it is considered that very high prostate specific antigen (PSA) levels is diagnostic of malignancy, cases have also been reported in which the serum PSA levels were within intermediate limits of 4-10 ng/mL, but were diagnosed as malignancies, thus PSA has high sensitivity but low specificity.

CONCLUSION

1. Prostate is one of the most commonly affected organ in the males associated with significant morbidity. Though benign lesions mostly comprised of benign prostatic hyperplasia (BPH) , the morbidity associated with this has lead to increased awareness regarding treatment protocols.
2. Prostatic adenocarcinoma is showing an increasing trend in India. Hence, the need to understand better the tumour biology and behaviour in the Indian context.
3. Significantly elevated serum PSA levels >20 ng/mL is a reliable tumour marker and can lead to diagnosis of clinically significant cancer at an early and potentially curable stage, and thus a better predictor of prostate cancer and distinguishing between benign and malignant lesions most of the times.But not all prostate cancers are associated with elevated serum PSA levels. Thus it does not attain a diagnostic status due to its low specificity and high sensitivity.
4. To over come the ovelapping values of serum PSA levels between benign and malignant lesions, free PSA levels, PSA density, PSA velocity may be considered to improve the sensitivity and specificty of PSA.

SUMMARY

- Present study was conducted as a cross-sectional study from December 2014 to June 2016 to study the age distribution ,various types of prostatic lesions and their correlation with serum PSA levels.
- Total 60 samples of various prostatic specimens in the form of TURP/Biopsy were studied.Pre-operative PSA levels of patients undergoing TURP/Prostatic needle biopsy were estimated by Enzyme Linked Fluorescent Assay technique.
- TURP/Biopsy specimens were processed after overnight fixation and were stained with H&E.
- Subsequently microscopic examination was done and lesions were classified as benign and malignant.These benign and malignant lesions were correlated with pre-operative serum PSA levels.
- Benign and Malignant lesions were common in the age group of 61-70 years followed by 71-80 years.
- Majority of the lesions studied were benign followed by adenocarcinoma of prostate.In majority of benign lesions, PSA levels were in the range of 4-10 ng/mL ,while in majority of malignant cases, it was >20 ng/mL suggesting that values >20 ng/mL was significantly associated with malignant lesions, thus a better predictive tumor marker for carcinoma prostate when preceded by a careful digital rectal examination in a patient of prostatism.

LIMITATIONS OF THE STUDY

Present study tried to correlate the levels of total serum PSA levels in various prostatic lesions. Evaluation of parameters like free PSA , PSA density, PSA velocity were not included in the present study.Inclusion of above mentioned parameters can improve the sensitivity and specificity of PSA.

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41.ANNEXURE-I

ETHICAL CLEARANCE

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-11-2014 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "correlation of Serum prostate Specific antigen (PSA) levels in various lesions of prostate".

—x—x—x—

Name of P.G. student Dr. Nikhil Mehrotra
Dept of Pathology

Name of Guide/Co-investigator Dr Girija S. Patil
Associate professor of pathology.

for
DR.TEJASWINI VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE-II

B.L.D.E.UNIVERSITY , SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER ,BIJAPUR-586103

INFORMED CONSENT FORM FOR DISSERTATION/REASEARCH

I, the undersigned, _____ S/O D/O W/O _____, aged _____ years, ordinarily resident of _____ do hereby state/declare that Dr _____ of _____Hospital has examined me thoroughly on _____ at _____ (place) and it has been explained to me in my own language _____that I am suffering from _____disease (condition) and this disease/condition mimic following diseases _____Further Doctor **Nikhil Mehrotra** informed me that he/she is conducting dissertation/research titled Correlation of serum PSA levels in various lesions of prostate under the guidance of **Dr Girija S. Patil** requesting my participation in the study. Apart from routine treatment procedure of, the pre-operative observations will be utilized for the study as reference data.

Further doctor has informed me that my participation in this study help in evaluation of the results of the study which is useful reference to treatment of other similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also inform me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept

secret and not assessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt _____under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of patient:

Signature of doctor:

Witness: 1.

2.

Date:

Place

ANNEXURE III

PROFORMA FOR STUDY:

Demographic Details:

1: Name: 2: Age: 3: Religion:

4: Occupation:

5: Residence:

6: Lab No./Ward No:

7: Chief complaints:

8: History of present illness:

9: Past history:

10: Family history:

11: General physical examination**:**

Pallor : Icterus :

Built : Nourishment :

12: Vitals :

PULSE : BP : RR :

TEMP : WEIGHT :

- Systemic examination:

  1. Cardiovascular system

  2. Respiratory system

  3. Central Nervous System

4. Per Abdomen Examination

- Clinical diagnosis:
- Findings of digital rectal examination
- Investigations:
- Pre-Operative Serum PSA level: ng/mL

- HISTOPATHOLOGICAL DIAGNOSIS:

KEY TO MASTER CHART

PSA	Prostate Specific Antigen
HP	Histopathology
BPH	Benign Prostatic Hypeplasia
PIN	Prostatic Intraepithelial Neoplasia

MASTER CHART

Sr No.	Age	HISTOPATHOLOGICAL IMPRESSION	PSA(ng/ml)
1	67	BPH	19.2
2	65	BPH	0.7
3	56	BPH	8.22
4	80	BPH	8.33
5	75	BPH	8.01
6	62	BPH	2.92
7	70	BPH	7.29
8	68	BPH	48.02
9	60	BPH	3.86
10	70	BPH	14.88
11	60	BPH	21.4
12	65	BPH	19
13	74	BPH	20
14	70	BPH	0.8
15	60	BPH	0.8

16	80	BPH	1.2
17	68	BPH	2.3
18	60	BPH	5
19	70	BPH	4.9
20	73	BPH	1.8
21	81	BPH WITH PROSTATIC ABSCESS	3
22	64	BPH	4.6
23	60	BPH	4
24	61	BPH	5
25	80	BPH	6.7
26	75	BPH WITH CHRONIC PROSTATITIS	4.9
27	76	BPH WITH CHRONIC PROSTATITIS	6
28	70	BPH WITH CHRONIC PROSTATITIS	33.4
29	65	BPH WITH CHRONIC PROSTATITIS	8.2
30	65	BPH WITH CHRONIC PROSTATITIS	17
31	80	BPH WITH CHRONIC PROSTATITIS	8.8
32	62	BPH WITH CHRONIC PROSTATITIS	9.38

33	70	BPH WITH CHRONIC PROSTATITIS	2.8
34	50	BPH WITH CHRONIC PROSTATITIS	13.4
35	63	BPH WITH PIN	0.9
36	65	LOW GRADE PIN	11
37	64	BPH WITH CYSTITIS CYSTICA	100
38	78	ADENOCARCINOMA(GLEASON GRADE 5+4)	100
39	70	ADENOCARCINOMA(GLEASON GRADE 3+3)	4.6
40	80	ADENOCARCINOMA(GLEASON GRADE2+3)	100
41	65	ADENOCARCINOMA(GLEASON GRADE3+4)	100
42	95	ADENOCARCINOMA(GLEASON GRADE4+5)	100
43	65	ADENOCARCINOMA(GLEASON GRADE4+3)	11.4
44	55	ADENOCARCINOMA(GLEASON GRADE2+2)	93.14
45	63	ADENOCARCINOMA(GLEASON GRADE3+3)	6.21
46	76	BPH(NEEDLE BIOPSY)	4.7
47	78	ADENOCARCINOMA(GLEASON GRADE 5+5)Needle biopsy	65
48	60	ADENOCARCINOMA(GLEASON GRADE3+3)	32
49	75	ADENOCARCINOMA(GLEASON GRADE4+4)	17.1

50	83	ADENOCARCINOMA(GLEASON GRADE3+4)	58
51	68	ADENOCARCINOMA with GRANULOMATOUS PROSTATITIS(GLEASON GRADE2+2)	30.6
52	76	ADENOCARCINOMA(GLEASON GRADE2+3)	72.1
53	65	ADENOCARCINOMA(GLEASON GRADE4+5)	66
54	81	ADENOCARCINOMA(GLEASON GRADE2+3)	32.7
55	80	BPH WITH FOCAL LOW GRADE PIN	19.6
56	65	BPH WITH ACUTE PROSTATITIS	11.2
57	60	BPH WITH INFARCT & SQUAMOUS METAPLASIA	37
58	65	BPH WITH ACUTE ON CHRONIC PROSTATITIS	0.5
59	65	BPH WITH ACUTE PROSTATITIS	2
60	65	BPH WITH GRANUMATOUS PROSTATITIS	15