"DIAGNOSTIC UTILITY OF PSA FOR DETECTION OF PROSTATIC LESIONS"

By

DR. NIKITA BANSAL

Dissertation submitted to

SBKS MEDICAL INSTITUTE & RESEARCH CENTRE

SUMANDEEP VIDYAPEETH, PIPARIA, VADODARA

In partial fulfilment of the requirements for the degree of

M.D.

in

PATHOLOGY

Under the Guidance of

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SBKS MEDICAL INSTITUTE & RESEARCH CENTRE,

PIPARIA, VADODARA

YEAR 2015-2018

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ACKNOWLEDGEMENT

The writing of this dissertation has been one of the most significant academic challenges I have ever faced. It gave me great pleasure in preparing this dissertation and I take this opportunity to thank everyone who has made this possible.

First and foremost, I bow down to ***"The God"*** *for giving me energy, inspiration, courage to complete this task and for blessing me so abundantly, far beyond what I deserve.*

I am just wordless to express my deep sense of gratitude towards my P. G. Guide, ***Dr. Jasmin Jasani,*** *Professor of Pathology, S.B.K.S. M.I. & R.C. PIPARIA whose sagacious suggestions, immense interest in subject, keen evaluation and constructive criticism have promoted completeness to this work. His patience tutelage, objective critique and inspiring support at all times have made me able enough to bring this dissertation to its present status. He has always respected my individual thoughts and ideas too. His guidance helped me in all the time of research and writing of this dissertation. I could not have imagined having a better advisor and mentor for my M.D. study. There is much to thank you for, if only the words could suffice. But deep inside I know I can never repay you for the care you took to nurture me.* ***Sir, "I am really grateful to you for being there."***

I express my gratitude to my father, ***Dr Mahesh Bansal*** *and to my mother* ***Mrs. Sangeeta Bansal*** *for making me what I am today through their perseverance and constant struggle and for being inspiration of my life since my childhood. It is their love, prayer and sacrifices that made my education possible.*

*I also owe my deep sense of gratitude to my brother, **Dr. Ojas Bansal**, my sister in law **Dr. Prachi Bansal** for their love, care and constant support.*

*I completely feel myself lucky to have a husband like **Mr. Akash Agarwal** who is one to engrave confidence and faith in me. I express my deep gratitude for his understanding, encouragement, love and care.*

*I also express my gratitude to my father-in-law **Mr. Dinesh Agarwal** and mother-in-law **Mrs Sunita Agarwal** for their constant support and care.*

*I humbly acknowledge **Dr. R. K. Pasale**, Professor and Head of Pathology, who was most generous with his sage advice, valuable comments, guidance and motivation which helped a lot to shape my carrier and understanding pathology.*

*I express my sincere thanks to Hon. **Dr. Mansukh Shah**, President, Sumandeep Vidyapeeth, **Dr. Dixit Shah**, Executive Trustee, Sumandeep Vidyapeeth, **Dr. G. D. Mehta**, Hon. Chancellor, **Dr. (Col). V. P. Singh**, officiating Vice chancellor, and **Dr. Manoj M Sattigeri**, Registrar Sumandeep vidyapeeth for providing all the necessary facilities.*

*I am thankful to **Dr. G. V. Shah**, Dean, S.B.K.S. M.I. & R.C., Piparia, for providing facility at the institute to do this dissertation work. I am also obliged to **Dr. Rakesh Sareen** CEO & Medical Superintendent for letting me proceed with my study in the lab uninterrupted.*

*I am indebted to all my teaching staff **Dr. R.K Tandon**, Prof. of Pathology, **Dr. S. S. Goswami,** Prof. of Pathology. They were always ready to guide and solve queries with their critical suggestions and enormous knowledge whenever I was in problem. I am extremely thankful to **Dr. Kuntal Patel**, Asst. Prof. of Pathology*

***Dr. Rippal Bhimani**, Asst. Prof. of Pathology, **Dr. Jigna Patel**, Asst. Prof. of Pathology, **Dr. Sumit Bharadva**, Incharge of Blood bank, **Dr. Roshni** Asst. Prof. of Biochemistry, **Dr. Mihir** Asst. Prof. of Biochemistry **Dr. Jyoti**, Asst. Prof. of Pathology, **Dr. Devanshi,** tutor of Pathology and for their guidance, constant encouragement, altruistic cooperation and support throughout my post graduate study.*

I express my sincere thanks to the Member Secretary of Institutional Ethics Committee (Human) of Sumandeep Vidyapeeth for permission to carry out and providing facilities for the present study.

*I am lucky to have colleagues and close friends **Dr. Mansi**, **Dr.Nirmala, Dr.Tulsi, Dr. Aviral**, **Dr. Bhavya**, **Dr. Prashant**, **Dr. Monil**, **Dr. Nisarg**, **Dr.Shreya,** for the stimulating discussions , for all the fun we have had , sleepless nights we were working together in the last three years and for being with me whenever I needed. You were all my family to me in these years. I thank to my seniors **Dr. Disha, Dr**. **Priyanka**, **Dr. Aanchal, Dr. Annie, Dr. Denish**, **Dr. Mobeen**. Thank you all for helping me throughout my post graduate study and helping out wherever I needed.*

*I am also thankful to my enthusiastic juniors **Dr Nehal, Dr Vaibhavi, Dr Akanksha, Dr Krishna, Dr Meera, Dr Bhavik, Dr Jay, Dr Payal, Dr Sonu, Dr Hardik, Dr Shilpan, Dr Sahil** for their endeavouring performance.*

*I am very thankful to my most dear friends **Dr Khushbu Patel, Dr Nirmala, Dr. Akshita and Dr Sheetal** for their immense support.*

*I cannot forget to thank the technical staff **(Patel kaka, Mr. Yogesh, Mr. Vinod, Mrs. Jyoti, Mr. Navneet and Mr. Heera**, **Miss Kiranben, Mr. Soma,***

Mr. Poonam, Mrs Kinnari, Mrs Anita) *of the pathology department for their help and support.* ***Mr. Kanubhai Parmar*** *C/O Vishal Graphics for editing and manuscripting of my dissertation. Special thanks to all the patients included in the present study without whom this work would not have been possible. Thank you, one and all.*

Dr. Nikita Bansal

ABSTRACT

INTRODUCTION:

Prostatic carcinoma has become the most common type of cancer and second most common cause of death due to cancers in male patients. According to American cancer society, a man has 1 in 6 chance of developing prostate cancer during his lifetime. Extensive efforts have been made at primary and secondary level for preventions since curative treatments are limited to early stages of the disease, the availability of an efficient, easy to test, broadly acceptable, cost effective, method for diagnosis of prostatic cancer is essential.

There has been an ongoing research for a tumor marker more sensitive and specific than prostate acid phosphatase (ACP) for prostate cancer, since the levels of ACP are usually affected by iso-enzymes generated by other organs. This led to the discovery of some antigens that subsequently became known as prostate specific antigen (PSA). Now, PSA is recognized as the best tumor marker for prostate cancer.

Prostate specific antigen (PSA) is a kallikrein like serine protease produced entirely by the epithelial cells of prostate. Although increased PSA levels have been found to be closely related with prostate cancer, there can be different reasons for an elevated PSA level, including benign prostatic hyperplasia, prostatitis, prostatic trauma, and prostatic infarction.

The addition of measurement of serum PSA level to digital rectal Examination for early detection of prostate cancer, has improved the percentage of prostatic cancer detection over the last several years.

METHODS

A total number of 100 prostatic biopsies collected from january 2016 to january 2017 at DHIRAJ hospital, Piparia-vadodara. The tissues were fixed in 10% formalin and processed routinely. The PSA levels will be estimated in the Department of Biochemistry, Dhiraj hospital, piapria-gujarat. The PSA levels were estimated using the TOSOH- immunoassay AIA360, chemiluminescence system which estimates PSA by a sandwich assay utilizing a constant amount of 2 antibodies-labelled polyclonal sheep antibody and monoclonal mouse antibody.

They were graded into benign, inflammatory conditions and malignant lesions. Gleason`s microscopic grading was used to grade all the prostatic adenocarcinoma cases. Serum PSA levels were correlated in all the cases.

RESULTS

There were 90 TURP, 8 Needle biopsies and 2 prostatectomy specimens. Most of the patients were in sixth and seventh decade. Lesions encountered were benign prostatic hyperplasia / prostatitis 85%, LGPIN 7% and 8% malignant.

CONCLUSION

Benign Prostatic Hyperplasia was the common lesion encountered. Associated lesions like prostatitis BCH, CCCH, transitional metaplasia, granulomatous prostatitis, abscesses were encountered.

Among the malignant lesions adenocarcinoma was the common lesion seen in sixth decade and Gleason`s score 7 was the commonest. One of the case sent as metastatic TCC from bladder was confirmed histologically.

Serum PSA levels were elevated in few cases of benign lesions due to associated lesions like prostatitis, abscesses and granulomatous prostatitis. Many of the malignant cases showed very high levels of PSA.

KEYWORDS

Prostate specific antigen; Abscess; Adenocarcinoma of prostate; Gleason`s score; Granulomatous prostatitis; Leucocyte common antigen; Benign prostatic hyperplasia; Transitional cell carcinoma, Transurethral resection prostate.

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INTRODUCTION

"When hair becomes gray and scanty, when specks of earthy matter begin to be deposited in tunics of artery, and when a white zone is formed at the margin of the cornea, at this same period the prostate gland usually, might perhaps say invariably becomes increased in size."

- Sir Benjamin Brodie

Prostate gland occupies center stage in the lives of many elderly males. Because of its location at bladder neck, enlargement of the gland leads to problems related to urinary obstruction.[1] Incidence of prostatic disease, Benign prostatic hyperplasia (BPH) and carcinoma increases with age. Recently there has been a significant advance in understanding of various prostatic diseases.

Prostatitis, BPH and tumors are the three important lesions to be studied in detail as they are frequently encountered. Diagnosis of prostatitis is very necessary as they can be successfully treated with antibiotics. Benign prostatic hyperplasia is a hyper plastic process of stromal and epithelial elements of prostate. It is an extremely common problem in elderly men over the age 50.[1] Prostatic carcinoma is more common in India compared to other Asian Countries.[2] It is the 5th cause of cancer in men and 4th in cancer mortality in India. At some time in their lives approximately one in 22 Indian males will be struck by prostatic carcinoma and its incidence is increasing by 3.5% every year.[3] Etiology of prostatic carcinoma is largely unknown today rendering disease prevention difficult. Hereditary factors have a role.[4,5] The great differences in the incidence of clinically manifest 1 carcinoma indicate that the nutritional and environmental factors also may have an influence on the development and progression of the disease.[6] Diet rich in animal fats, red meat and diet poor in

fruits, vegetables are the likely culprit in prostatic carcinoma.[7] Low levels of dietary selenium, vitamin E and vitamin D also play a role.[8] Studies also reveal that there is no definite role of sexual activity, smoking, height, weight and alcohol consumption.[9]

Although can almost be considered as an aging process, the histological variations like different types of hyperplasias, low grade prostatic intraepithelial neoplasia (LGPIN) and high grade prostatic intraepithelial neoplasia (HGPIN) merits discussion.

Prostatic carcinoma also has to be given importance as its incidence is increasing owing to the westernization in Asian countries including India. This study comprises description of incidence of various lesions of prostate encountered at Dhiraj hospital, associated clinical manifestations, morphological changes and also serum Prostatic Specific Antigen (PSA) level correlations. It is all the more necessary to study prostatic diseases in the present situation as their incidence keeps growing due to extended male longevity past the 60s.[3]

AIMS AND OBJECTIVES

1. Correlation of levels of Prostate Specific Antigen in different prostatic pathologies.
2. To evaluate the validity of Prostate Specific Antigen in identifying patients, diagnosed clinically as prostatic cancer.
3. Correlate Prostate Specific Antigen levels with Gleason's grading of carcinoma.

REVIEW OF LITERATURE

The Prostate Gland- Location, Development, and Function:-

All men are at some risk of developing prostate cancer, but there are many men who do not have the correct knowledge about the location and function of this organ; that contributes significantly to male development, health, sexual function and general quality of life. The prostate gland is a secondary sexual and exocrine organ that is an integral part of the human male reproductive system. Prostate development begins before birth; but rapid growth occurs during puberty for the production of semen.

An enzyme: 5-alpha reductase converts testosterone into a more potent form- dihydrotestosterone that provides signals to promote prostate growth.

These androgens stimulate the prostate gland and it continues to grow until adulthood. A healthy prostate gland is of chestnut shape and is usually the size of a walnut. The prostate gland secretes a low alkaline fluid, that constitutes approximately 70% of the volume of the seminal fluid which helps in nourishement and protection of sperms during ejaculation.

Anatomy and Histology of Prostate gland-

Prostate gland is an accessory gland of the male reproductive system. Normal adult gland weighs 20 gms ± 6 gms and lies immediately below the base of bladder surrounding the proximal part of urethra. The length of anterior aspect is between 3 and 4 cms and its width between 3.5 and 5cms. Prostate is composed of approximately 70% glandular elements and 30% fibromuscular stroma. Prostate contains a number of individual glands composed of 30 to 50 lobules leading to 15-30 secretory ducts that open into urethra.

The prostate gland is located between the urinary bladder and the penis; and is anterior to rectum. The urethra crosses through the central part of the prostate gland. Refer to figure 1. The prostate gland comprises of both muscular and glandular parts.

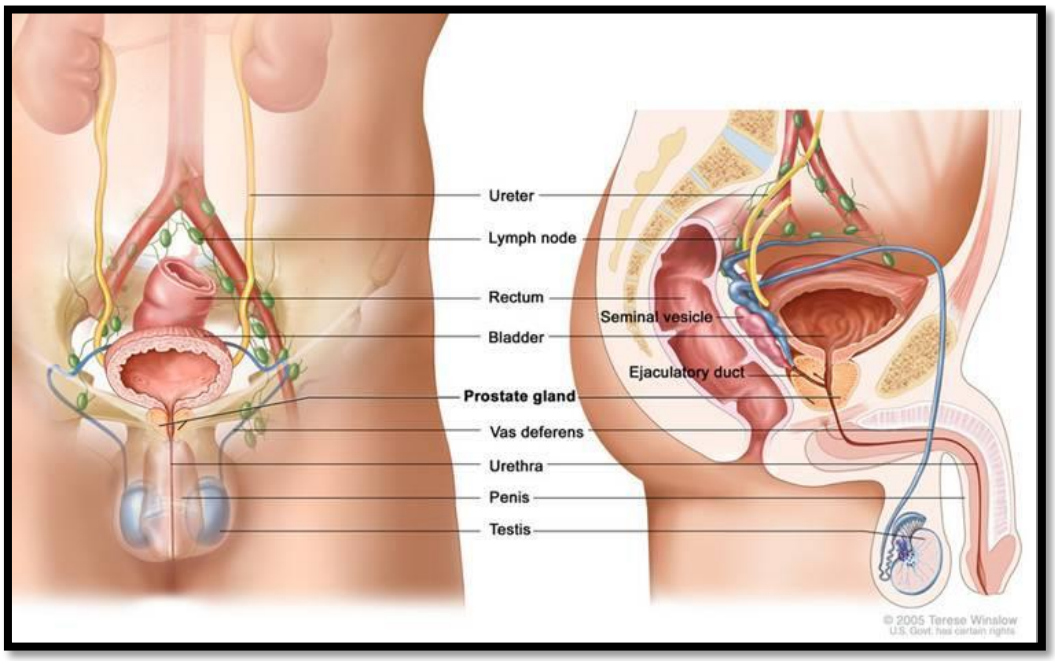


Figure 1- Human Male Genitourinary Tract and Pelvic Area: Anatomy

Prostate was believed to be a lobular structure for many years. Prior to 1906, when Home described the middle lobe, prostate was considered to be composed of only 2 lateral lobes. Later the existence of 5 prostatic lobes was proposed – 2 lateral lobes, an anterior lobe, posterior lobe and middle based on embryonic finding.[10]

The anterior lobe is also known as the isthmus of the prostate gland, is the narrow middle area of the prostate gland that lies anterior to the urethra.

This anterior lobe is mostly non-glandular and is made up of fibromuscular tissue. The median lobe is cone-shaped portion within the gland and is located between the urethra and the two ejaculatory ducts. The lateral lobes are located along the right and left sides of the prostatic urethra and constitute the largest mass of the prostate gland

and are continuous toward the posterior lobe. The posterior lobe is the part of lateral lobes which can be palpated through the rectum; during digital rectal examination. It is situated inferior to the ejaculatory ducts and is posterior to the urethra.

Prostate is composed of 4 distinct zones-

(a) Anterior fibromuscular stroma: stroma occupies 1/3$^{r\,d}$ of the prostate and consists of very few glands and smooth muscle tissue.

(b) Peripheral zone comprising of 70% of prostate and common site of PIN and carcinoma,

(c) Central zone comprising 25% of prostate and surrounds ejaculatory ducts,

(d) Transition zone comprising 5% of prostate and is the site for BPH

The glands of prostate are tubuloalveolar and lined with cuboidal or columnar epithelium. Scattered neuroendocrine cells of unknown function is found between the secretory cells. Beneath the epithelial cells flattened basal cells line each acinus and are believed to be stem cells for secretory epithelium. Each acinus is surrounded by a thin layer of stromal smooth muscle and connective tissue.

Embryonic Development

The prostate first appears and starts its development from urogenital sinus during the third month of fetal growth and its development is directed primarily by dihydro testosterone, which is produced from metabolic conversion of fetal testosterone through the action of enzyme 5 α reductase. The prostate forms acini and collecting ducts by arborization that branches into urethra and may be visualized as similar to a small tree with the growth occurring on tips as ducts extend and branch during development.

At birth the majority of prostatic acini are lined by squamous epithelium and metaplastic epithelial cells that have scattered secretory activity and lead to cyst formation. Pubertal maturation period starting about age 11 or 12 yrs is characterized by general development of pseudostratified epithelium with basal and secretory cells in all parts of gland and increase in diameter of lumen of ducts. Formation of mature acini starts at about 15-16 yrs. The prostate reaches its mature morphologic and functional structure by age 18-20 yrs and retains this organization for approximately 10 yrs. Around age 30 yrs initial signs of structural and functional disintegration occur and gland gradually loses its functionally organized structure.

Thus, prostate is derived from a composite area of urogenital sinus requiring androgen during organogenesis. It undergoes different phases of androgen responsivity perinatally and during puberty.[11]

Prostate Function

The primary function of the prostate gland is to store a part of the seminal fluid and assist ejaculation during sexual activity. The smooth muscles in the prostate help in expulsion of the semen during ejaculation. The slightly alkaline fluid produced by the prostate constitutes upto 25% of seminal fluid and aids sperm motility and viability. The vaginal tract is acidic, therefore the alkalinity of the semen neutralizes the environment and allows the sperms to stay viable. A major constituent of prostatic secretion is prostate specific antigen (PSA), along with citrate (18.7 mg/ml), zinc (488 µg/ml), spermine (243 mg/ml) and cholesterol (78 mg/ml).

PSA

PSA is a glycoprotein produced by the prostate acinar cells and is unique to the prostate gland[12].The known function is to liquefy semen after ejaculation in order to facilitate the transport of spermatozoa along the female reproductary tract. . PSA may be complexed to serum proteins, when it is known as "complexed PSA" or it can be free, known as "free PSA". Both, free PSA and complexed PSA are combined to give measure of the total PSA. Although, PSA is present in high concentrations in seminal fluid(0.5 to 2.0 mg/mL), it has much lower concentration in the blood; almost 1000 times lower. Although the variations in concentration are independent of other proteins, it is sensitive to changes in serum testosterone levels[13]. Normal ranges are age specific which are used to identify elevated levels of PSA, however these ranges vary according to the assay used. Blood level of PSA has been shown to correlate the risk of prostatic cancer.

PSA was first demonstrated is prostatic tissues, then in seminal plasma, purified from prostatic tissue and finally measured in serum of men. PSA in serum was demonstrated to be a clinically important assay for the monitoring of prostatic carcinoma.**[14]** PSA was widely used as a clinical marker for prostate cancer by 1988.**[14]**Serum PSA levels increases proportionately with advancing clinical stage.**[15]** Studies have shown that serial increases in serum PSA, increases the incidence of occult carcinoma.

As benign prostatic lesions can also be responsible for increase in PSA levels, an adjusted value called PSA density, is sometimes used. In such cases, the serum PSA value is divided by the prostate volume. The main purpose of this test is that it helps in decision making for prostate biopsies. However, a transrectal ultrasound (TRUS) is required for the measurement of prostate volume, but it causes discomfort to the

patient and it is costly[16]. Free PSA can be measured by a blood test and is usually lower in prostate cancer patients, however the reasons for this are unclear [17].In patients with free PSA of less than 15%, have a higher risk of prostate cancer, yet in patients with 25% or higher free PSA, the risk significantly reduces [17].

PSA increases with age, so cut off values are age dependent. There are also different reference ranges for different ethnicities [18]. Although these reference ranges are easy to use, they can fail to detect high grade prostate cancer in older men [19].

Several modifications in the estimation of serum PSA are developed.

These include :

(a) PSA density: Which is the ratio between the serum PSA value and volume of prostate gland.

(b) PSA velocity: The rate of change of PSA and the value that distinguishes between men with and without prostatic carcinoma is 0.75ng/ml per year.

(c) The age specific reference ranges, which is 2.5ng/ml for men of 40-49 yrs of age, 3.5ng/ml for men of 50-59yrs of age, 4.5ng/ml for men of 60-69 yrs years of age and 6.5ng/ml for men of 70-79yrs of age.

Studies have revealed that immunoreactive PSA exits in 2 forms, a major fraction bound to α1 anti-chymotrypsin and a minor free fraction. The percentage of free PSA (free PSA/total PSA x100) is lower in prostatic carcinoma than in BPH It helps in discriminating benign and malignant lesion when total PSA level is in “gray zone” of 4 to 10ng/ml. In a study it was found that normal prostate had a higher percent of free PSA (27.7%), than those with BPH(20.1%), HGPIN (20.8%) and percentage was lowest in prostatic carcinoma. [20]

Prostatic acid phosphatase (PAP) a glycoprotein was previously used for detection and monitoring of patients with prostatic carcinoma, however its sensitivity is low and serum PSA has largely supplanted serum PAP. [21]

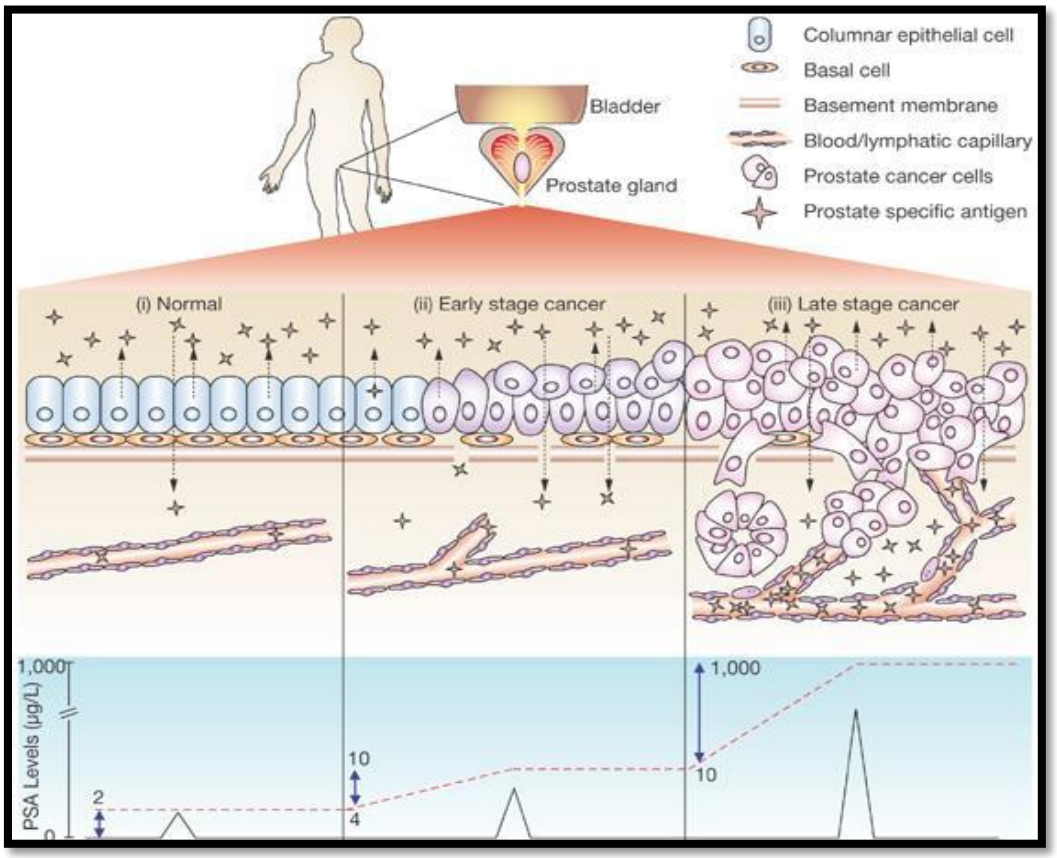


Figure 2. Prostate cancer invasion and tissue destruction as a measure of PSA elevation.

Pathology of Prostate

BENIGN PROSTATIC HYPERPLASIA

BPH involves overgrowth of epithelium and fibro muscular stroma of transition zone and periurethral area. It results in varying degrees of urinary obstruction sometimes requiring surgical intervention.

The tissue resected for BPH is quite heterogeneous and that the nodules are composed of varying proportion of both epithelial and stromal components. The relative proportions of epithelium and stroma are related to development of symptomatic BPH with higher percentage of symptomatic BPH. [22] Inflammation induced release of platelet derived growth factor (PDGF) is a possible, contributing factor in development of BPH. [23]

Epidemiology

BPH is extremely common accounting for approximately 4,00,000 partial prostatectomies annually, the most common form of surgery in American men. In India the incidence of benign prostatic hyperplasia is estimated to be 92.97%.[24] The age specific prevalence is remarkably similar in populations through out the world. There is rapid increase in prevalence of BPH beginning in the 4th decade of life and culminating in 100% prevalence in 9th decade. [25]

Risk factors

Advanced age and an intact androgen supply are the only undisputed risk factors for BPH. It does not occur in men castrated before puberty. The risk is lower in patients with androgen resistance or deficiencies. Anti-androgens, gonadotropin releasing hormone agonists and 5 alpha reductase inhibitors also reduce the symptoms. Most epidemiologic studies of environmental and life style risk factors have yielded

equivocal results, including studies of medical history, sexual history, smoking, alcohol use, socio economic status and occupational exposure. [25]

Pathogenesis

The development of BPH includes 3 pathologic changes:

a) Nodule formation

b) Diffuse enlargement of transition zone and periurethral tissue

c) Enlargement of nodules.

Pathology

Grossly it is characterized by nodules of varying sizes, which are soft or firm, rubbery and grayish white in colour weighing between 60 to 100 gms. The cut section is nodular. Degenerative changes include calcification and infarction. [25]

Microscopy

The earliest change is stromal proliferation, which contains more smooth muscle and less elastic tissue than normal stroma. The glands are dilated or even cystic often contain an inspissated secretion corpora amylacea. Epithelium is flat or columnar sometimes facing each other in same gland (functional polarization). The epithelium is thrown in to numerous papillary buds and infoldings. The cells have pale cytoplasm and regular central nuclei. Aggregates of lymphocytes are often found within the stroma. In majority of instances, the nodules are adenofibromyomatous nodules, which contain all elements. Small areas of hemorrhagic necrosis surrounded by reactive change in residual epithelium at the margins (squamous metaplasia or transitional metaplasia) may be seen within the nodules. [25]

Variants of hyperplasia

1) Post-atrophic hyperplasia

This is characterized by benign proliferating luminal cells with scanty clear cytoplasm in an atrophic background. The cells often show mild cytologic atypia and luminal mucin may be identified. [25]

2) Basal cell hyperplasia

This is characterized by proliferation of basal cells of more than two cells thick and protrudes into the gland lumen, retaining the overlying secretory luminal epithelium. The hyperplastic basal cells are usually larger than normal, are elongated (spindled) basal cells and is often accompanied by nuclear enlargement.[12]

3) Cribriform hyperplasia

This includes clear cell cribriform hyperplasia and consists of nodule composed of glands arranged in distinctive cribriform pattern. The cells usually have pale-clear cytoplasm and small uniform nuclei with inconspicuous nucleoli. [26]

4) Sclerosing adenosis

It shows striking myoepithelial metaplasia of basal cell compartment as well as a exuberant stroma composed of fibroblasts and loose ground substance. [27]

Associated benign lesions

1) Atrophy

This is characterized by small-distorted glands with a flattened epithelium, hyperchromatic nuclei and stromal fibrosis. It is idiopathic and its prevalence increases with advancing age.

2) Atypical basal cell Hyperplasia

This is basal cell hyperplasia in which nucleoli are prominent. [28]

3) Basal cell adenoma

This consists of large round circumscribed nodule or nodules that contain uniformly spaced aggregates of hyperplastic basal cells varying from small solid nests to cystically dilated glands.

4) Adenoid basal cell tumor

Consists of basaloid cell nests of varying sizes that infiltrate the stroma. The cell nests are often large, round to angular. The peripheral basaloid cells have elongated nuclei and often show palisading. There is prominent cell crowding.

5) Atypical adenomatous hyperplasia (Adenosis)

This is localized and circumscribed proliferation of small glands within the prostate that may be mistaken for carcinoma.

6) Stromal Hyperplasia with atypia

This is characterized by stromal nodules that occur in setting of BPH but show increased cellularity and nuclear atypia. These appear as solid stromal nodules or as atypical cells interspersed within benign glands. Stromal nuclei are large hyperchromatic, rarely multinucleated or vacuolated and contain inconspicuous nucleoli. There are no mitoses and necrosis. Stromal hyperplasia with atypia has no malignant potential and the atypical cells are considered to be degenerative.

7) Phyllodes Tumor

This is a rare neoplasm of adults. It is a fibroadenoma that shows increased cellularity and cytologic atypia, reminiscent of phyllodes tumor of breast. The glandular

epithelium is distorted and lines slit like spaces surrounded by a variably cellular proliferative stroma composed of fibroblasts and smooth muscle cells.[29,30]

Association of BPH and prostate cancer

Both show a parallel increase in prevalence with increasing age according to the results of autopsy studies, although cancer lags by 15-20 yrs. Both require androgens for growth and development to occur and both may respond to androgen deprivation treatment. Most cancers arise with in prostate together with BPH Cancer is found incidentally in a significant number (10%) of TURP specimens. BPH may be related to prostate cancer arising in transition zone, perhaps in association with certain forms of hyperplasia, but BPH is not a pre-malignant lesion or a precursor of cancer.

Infarct

Infarct of prostate occurs predominantly in large prostates that exhibit Benign prostatic hyperplasia. It is found to be present in 18% to 25% cases. The size and number of infarcts are directly related to degree of prostatic hyperplasia. The mechanism of infarct is unknown, but may be related to the presence of prostatic infection or trauma resulting from an indwelling catheter, cystitis or prostatitis all of which may result in thrombosis of intraprostatic portion of urethral arteries. [25]

Grossly, infarcts vary in size from a few millimeters up to five centimeters. They are speckled grayish yellow and often contain streaks of blood. The peripheral margins are sharp and hemorrhagic.

Microscopically, there are sharply specific areas of ischemic coagulative necrosis which involve the stroma and few glands. Prominent squamous metaplasia is often seen in the ducts bordering a infarct. This metaplastic change is confined to the expanded ducts, keratinizes only rarely, and does not extend to the surrounding

prostatic tissue. Infarct may cause serum elevation of PSA levels, removal of infarcted area return the levels to normal.

Prostatic Inflammation

The spectrum of prostatitis encompasses a multitude of inflammatory diseases of prostate. These varied forms of prostatitis show marked differences in treatment and clinical outcome and therefore require accurate diagnosis. Patchy acute and chronic inflammatory infiltrate is present in the prostate of most adult men and is considered a normal finding. But when the inflammation is severe and extensive or clinically apparent the term prostatitis is warranted. It is associated with increased serum PSA levels, which return to normal levels following treatment.

1) Acute Bacterial Prostatitis

Acute bacterial prostatitis presents with sudden fever, chills and irritative voiding symptoms. The prostate is swollen, tender and warm. The bacteria responsible for acute prostatitis are Escherichia Coli (80%) other enterobacteriacea such as pseudomonas, serratia, klebsiella (10-15%) and enterococci (5-10%). [40]

Microscopically there are sheets of neutrophils in and around prostatic ducts and acini with desquamated epithelium and cellular debris. Stroma is edematous and hemorrhagic and contains variable numbers of lymphocytes, plasma cells and macrophages. Microabscesses are frequently seen. Diagnosis is based on findings yielded by urine culture and biopsy is contraindicated.

Prostatic Abscess

A rare complication of acute bacterial prostatitis occurring most commonly in immunocompromised patients. Predisposing factors include urethral instrumentation and use of indwelling catheters. Patients present with prostatic enlargement, fever and retention of urine. A fluctuant mass is occasionally palpated by rectal examination.

Prostatic abscess can be caused by aerobic and anaerobic bacteria.

2) Chronic Prostatitis

The spectrum includes chronic bacterial, chronic abacterial and granulomatous prostatitis. Chronic prostatitis presents with variable clinical features and include frequency, urgency, dysuria, pain in perineum, lower back and testis. Digital rectal examination varies from normal to tender and boggy. Microscopically charecterised by aggregates of lymphocytes, plasma cells and macrophages within the prostatic stroma.

The epithelium displays reactive atypia with occasional prominent nucleoli. The histologic findings in combination with clinical manifestations are characteristic of chronic prostatitis. Bacterial and abacterial chronic prostatitis mimic each other clinically and histologically but differentiated by presence or absence of bacteria on culture. Usually gram-positive bacteria are found in cultures of prostatic fluid.

a) Chronic bacterial prostatitis

Most cases are due to E.Coli infection. In patients with prostatic calculi, and relapsing urinary tract infection (UTI), the stones serve as a nidus of infection, with bacteria embedded in mineral matrix.

b) Chronic abacterial (idiopathic) prostatitis

This is more common than bacterial prostatitis. Cultures of urine and expressed prostatic secretion yield negative results. This form of prostatitis has a prolonged indolent course characterized by relapses and remissions.

3) Granulomatous prostatitis

It is a group of morphologically distinct chronic prostatitis caused by a wide variety of inciting agents, including infections, tissue disruption after biopsy and inflammation. It accounts for approximately 1% of benign inflammatory conditions of prostate. Most of the patients have a history of UTI, it is probably caused by blockade of prostatic ducts and stasis of secretions. Epithelium is destroyed and cellular debris, bacterial toxins and prostatic secretions sperm, semen escape into stroma eliciting a intense localized inflammatory response.

Grossly the gland is firm to stony hard. Cut section shows obliteration or architecture with formation of yellow granular nodules. Microscopically large nodular aggregate of histiocytes, epitheloid cells, lymphocytes and plasma cells are seen. Caseation necrosis is absent.

a) Idiopathic (non-specific) granulomatous prostatitis

This makes up the majority of cases. The granulomas are usually non-caseating and associated with parenchymal loss, marked fibrosis and more number of eosinophils in stroma.

Xanthoma- Xanthoma is characterized by a localized collection of cholesterol laden histiocytes.

It is a a rare form of idiopathic granulomatous prostatitis.

b) Infectious granulomatous prostatitis

Numerous microorganisms can induce granulomatous prostatitis, including bacteria (Mycobacterium tuberculosis, Brucellosis), fungi (Cryptococcus and Blastomycosis), parasite (Schistosoma haematobium) and virus (Herpes zoster).

c) Iatrogenic granulomatous prostatitis: This can be caused by surgery, radiation therapy and Bacille Calmette-Guerin (BCG) therapy for bladder cancer.[31]

i) Post-surgical Granulomatous Prostatitis

ii) Post-radiation granulomatous prostatitis

iii) BCG-Induced granulomatous prostatitis

Malakoplakia

This is a granulomatous disease attributable to defective intracellular lysosomal digestion of bacteria. Patients present with obstructive symptoms including frequency, urgency, dysuria, nocturia and fever. This occurs in men over 50 years of age with systemic illnesses and other debilitating conditions. Digital rectal examination reveals diffuse induration suggestive of prostatic carcinoma. E. coli is commonly isolated from urine cultures. Grossly, prostatic malakoplakia is characterized by discrete and confluent soft yellow brown plaques, with central umbilication or ulceration and peripheral hyperemia.

Microscopically, the prostatic architecture is effaced by dense sheet-like aggregates of histiocytes (Van-Hansemann cells) admixed with lymphocytes and plasma cells. Intracellular and extracellular Michaelis-Gutmann bodies are seen, appearing as sharply demarcated spherical structures with concentric "owl's eyes" measuring 5 to 10 μm in diameter. These stain with Periodic acid Schiff (PAS) (polysaccharides),

Alizarin red-S (Calcium), Prussian blue (iron), and Von Kossa (anionic component of calcium ions). Gram stain, acid-fast stain and fungal stains are negative.

d) Systemic Granulomatous Disease

These include

i) Allergic (eosinophilic) granulomatous prostatitis

ii) Sarcoidosis

iii) Rheumatoid Nodules

Prostatic inflammation and carcinogenesis: Chronic or recurrent inflammation plays a role in development of carcinoma. Inflammatory cells elaborate numerous microbicidal oxidant that cause cellular or genomic damage to prostate giving rise to cells of PIN and carcinoma. [7]

Prostatic calculi

Prostatic calculi are seen in about 7% of prostates with Benign prostatic hyperplasia. They should be distinguished from those found in the prostatic urethra, which may have their origin in the bladder, ureter or renal pelvis. The corpora amylacea seen in the glands with Benign prostatic hyperplasia may act as the nucleus for stone formation as a result of improper drainage, infection of the acini and calcium deposition. Blood clots, epithelial detritus, and bacteria are also present in the stone nucleus. The main inorganic elements are phosphated salts (calcium, magnesium, aminomagnesium, potassium), calcium carbonate and calcium oxalate. Because of their extreme hardness, large prostatic calculi may be mistaken for carcinoma on digital rectal examination. They are radio-opaque and can be easily detected by radiographic examination.

PROSTATIC INTRAEPITHELIAL NEOPLASIA (PIN)

Definition: It is a neoplastic transformation of lining epithelium of prostatic ducts and acini. The process is confined within the epithelium. [32]

The term prostatic intraepithelial neoplasia (PIN) was adopted by Bostwick and Brawer (1989) to include all forms of atypical and malignant lesions of epithelial cells confined to the lumens of duct/acinar system as well as similar lesions accompanied by microinvasion. PIN is subdivided into 3 grades: PIN-I, II and III,described by Mc Neal and Bostwick. The Bethesda workshop participants proposed a two-tier system comprising low grade (PIN1) and high grade (PIN 2 and 3). [33]

PIN consists of dysplasia and proliferation of the normal luminal cell layer lining the prostatic ducts and acini.

Diagnostic Criteria

McNeal and Bostwick (1986) described the diagnostic criteria for PIN. [25]

Table 1- Diagnostic criteria for PIN:

Features	Low grade PIN (formerly PIN-I)	High grade PIN (formerly PIN 2 and 3)
1. Architecture	Epithelial cell crowding, stratification with irregular spacing	Similar to low grade PIN; more stratification and crowding
2. Cytology **a. Nuclei**	Enlarged with considerable size variation.	Enlarged; some size and shape variation
b. Chromatin	Normal	Increased density and clumping
c. Nucleoli	Rarely prominent	Occasionally to frequently large and prominent similar to invasive carcinoma.
3. Basal cell layer	Intact	May show some disruption
4. Basement membrane Intact	Intact	Intact

LGPIN

The cells within ducts and acini are heaped up, crowded and irregularly spaced and there is variation in nuclear size. Elongated hyperchromatic nuclei and nucleoli are sometime seen but not prominent. Mc Neal summarizes that there is not a sharp line of demarcation between LGPIN and mild degrees of deviation from normal histology.[34]

HGPIN

It exhibits features similar to LGPIN but cell crowding and stratification is more pronounced and there is less variability in nuclear size but prominent nucleoli is diagnostic. It displays four architectural patterns; tufting, micropapillary, cribrifom and flat.

Evidence For The Association Of Prostatic Intraepithelial Neoplasia An Prostatic Carcinoma

1. Histology: Similar cyto-architectural features.

2. Location: Both are multifocal with predominant peripheral zone distribution.

3. Correlation with proliferative activity: Both have more than 3 times the proliferative activity of benign glands.

4. Loss of the basal cell layer: PIN-III has loss of basal cell layer similar to invasive carcinoma.

5. Increased frequency of PIN, in the presence of carcinoma: Higher grades of PIN are associated with a statistically significant increase in the frequency of invasive carcinoma.

6. Increased severity of PIN in the presence of carcinoma: Higher grades of PIN are associated with a statistically significant increase in the frequency of invasive carcinoma.

7. Immunophenotype: Both are immunoreactive for cytokeratins 14, 15, 16 and 19 unlike nodular hyperplasia. Both show Ulex Europaeus-1 Lectin binding unlike normal epithelium and benign prostatic hyperplasia. Both show loss of vimentin immunoreactivity 24 unlike benign prostatic hyperplasia. Both show loss of blood group A,B unlike normal epithelium.

8. Age: Incidence and extent of both lesion increase with patient age. [35]

CLINICOPATHOLOGICAL EVALUATION OF PIN

On identification HGPIN on biopsy

1) All the tissue should be processed and serially sectioned
2) Basal cell specific anti-keratin monoclonal antibody (34βE12) stains should be done.
3) Transrectal ultrasound with biopsy should be done.
4) Serum prostate specific antigen levels should be monitored.
5) Repeat PSA, Trans rectal ultrasound guided biopsy at 3-month intervals for the first two years and repeated yearly thereafter for life should be done. [35]

Carcinoma of the Prostate

Epidemiology

Prostatic carcinoma is the sixth most common malignancy in the world (in terms of number of new cases). It represents 9.7% of cancers in men (15.3% in developed countries and 4.3% in developing countries). [36] It is the second most common cause of cancer death in men. It is predominantly a disease of elderly men over 50 years.

Prostate cancer is one of the few sites of cancer where the difference in incidence rates between that in India and Western countries is enormous. Incidence rates in India are less than one-tenth of the rates seen in the United States, but there is a rising trend. The epidemiological studies for prostate cancer in India are few and are mostly based on different hospital findings. Cancer of the prostate is primarily a disease of elderly men. About three-quarters of cases worldwide occur in men 65 years or more.[37] Yeole[38] showed increasing trends in prostate cancer incidence rates in five population-based cancer registries (Mumbai, Chennai, Bengaluru, New Delhi, and Bhopal) in the past 20 years. Jain *et al*[39]reviewed data from 25 cancer registries from 2009 to 2011. Prostate was the second leading site of cancer for four PBCRs, namely New Delhi, Kolkata, Nagpur, and Thiruvananthapuram. Prostate cancer incidence is relatively low in some states such as Gujarat and Madhya Pradesh, but lowest in the North-East regions of India. The incidence rates of this cancer are constantly and rapidly increasing, and the cancer projection data show that the number of cases will become alarmingly doubled by 2020. Past smoking and current alcohol consumption significantly increase the risk of prostate cancer, which was shown in a population-based case–control study on prostate cancer in New Delhi by Tyagi *et al*.[40]In a similar study of 123 prostate cancer cases by Ganesh *et al*., advanced age, body mass index, and hypertension emerged as risk factors for prostate cancer.[41]

Location

Cancers detected by TURP specimens arise predominantly within the transition zone. 8% of contemporary TURP specimens disclose carcinoma. When TURP is done without clinical suspicion of carcinoma prostate cancer is incidentally detected in approximately 8-10% of specimens. [42]

WHO Histological classification of tumors of prostate

Epithelial tumors

1) Glandular neoplasms

- Adenocarcinoma (acinar)
- Atrophic
- Psuedohyperplastic
- Foamy
- Colloid
- Signet ring
- Oncocytic
- Lymphoepithelioma like carcinoma with spindle cell differentiation (carcinosarcoma, sarcomatoid carcinoma)
- PIN
- PIN Grade III (PIN III)
- Ductal adenocarcinoma
- Cribriform
- Papillary
- Solid

2) **Urothelial tumors**

- Urothelial carcinoma

3**) Squamous tumors**

- Adenosquamous carcinoma
- Squamous cell carcinoma

4) **Basal cell tumors**

- Basal cell adenoma
- Basal cell carcinoma

5) Neuroendocrine tumors

- Endocrine differentiation with in adenocarcinoma
- Carcinoid tumor
- Small cell carcinoma
- Paraganglioma
- Neuroblastoma

6) Prostatic stromal tumors

- Stromal tumor of uncertain malignant potential
- Stromal sarcoma

7) Mesenchymal tumors

- Leiomyosarcoma
- Rhabdomyosarcoma
- Chondrosarcoma
- Angiosarcoma
- Malignant fibrous histiocytoma
- Malignant peripheral nerve sheath tumor
- Haemangioma
- Chondroma
- Leiomyoma
- Granular cell tumor
- Hemangiopericytoma
- Solitary fibrous tumor

8) Hematolymphoid tumors

- Lymphoma
- Leukaemia

9) Miscellaneous tumors

- Cystadenoma
- Nephroblastoma (Wilm's tumor)
- Rhabdoid tumor
- Germ cell tumors
- Yolk sac tumor
- Seminoma
- Embryonal carcinoma and teratoma
- Choriocarcinoma
- Clear cell adenocarcinoma
- Melanoma

10) Metastatic tumors

Grading and staging

Tumor staging

When a patient is diagnosed with a prostatic tumor, the cancer should be staged to determine whether it has spread beyond the prostate or not. Staging gives a better view about the risk of further disease spread; so that a correct treatment option is selected. The TNM stage was developed by the **American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC)**[43].

It is used to evaluate the extent of the primary tumor (T), the affected regional lymph nodes (N) and if it has spread or metastasized (M).

There are four stages:

In stage I : only a small part of the prostate is cancerous most of the cells are normal and the gland feels normal.

In stage II : a lump can be felt in the prostate to the examining finger and a larger part of the prostate is affected.

In stage III : the tumor has spread beyond the prostate

In stage IV : it has spread to lymph nodes or nearby organs. A more detailed view can be found in Table-2.

Table no. 2: TNMStaging of Prostate Cancer

Primary Tumor (T):			
		TX	Primary tumor cannot be assessed
		T0	No evidence of primary tumor
		Ta	Non invasive papillary carcinoma
		Tis	Carcinoma in situ: "flat tumor"
		T1	Tumor invades sub epithelial cells
		T2	Tumor invades muscle **T2a-** Tumor invades superficial muscle, (inner half); **T2b-** Tumor invades deep muscle, (outer half);
		T3	Tumor invades perivesical tissue **T3a-** Microscopically **T3b-** Macroscopically
		T4	Tumor invades prostate
			T4a- Tumor invades prostate **T4b-** Tumor invades pelvic wall or abdominal wall
Regional Nodes (N):	**Lymph**	**NX**	Regional lymph nodes cannot be assessed,.
		N0	No regional lymph node metastasis Metastasis in a single lymph node 2cm or less in greatest
		N1	dimension. Metastasis in a single lymph node 2cm but no more than
		N2	5cm in greatest dimension Multiple lymph nodes, none more than 5cm in greatest Dimension Metastasis in a lymph node no more than 5cm in
		N3	greatest dimension,
Distant (M):	**Metastasis**	**MX**	Distant metastatis cannot be assessed
		M0	No distant metastatis.
		M1	Distant metastatis

Tumor Grading

GLEASON`S MICROSCOPIC GRADING SYSTEM OF PROSTATIC CARCINOMA

Tumors are graded for better predictions of tumor prognosis. The Gleason Grading System for prostatic carcinoma, is most commonly used, where cancer scoring is done according to their microscopic appearances. When the biopsy specimen is received, some of the prostatic tissue is obtained and prepared by fixing and H&E staining of the slides. 2 different grade scores are assigned to the 2 most common tumor patterns, and these scores are added together for a total Gleason's score. Gleason's score ranges from 1 to 5, where 5 has the poorest prognosis and Gleason's score range from 2 to 10. The Gleason's patterns are detailed Table no. 3. For the primary grade, pathologists identify which pattern corresponds with at least 50% of the tumor and the secondary grade represents the minority of the tumor.

The prognosis for prostate cancer can be variable. More aggressive tumors, with Gleason sum 8, 9 or 10, can lead to death in a short space of time, however lower grades, with Gleason sum of 6 or lower, may not see any clinical consequences [23]. Albertsen *et al* conducted a series of studies on a cohort of 767 untreated cancer patients. Men with tumors of Gleason sum 5 had between 6% to 11% cancer mortality at 20 years. Patients with tumors with a higher Gleason sum had up to 70% (Gleason score 7 or 8) and 87% (Gleason score 10) rates of death from prostate cancer, with very few of the entire cohort surviving more than 15 years after diagnosis.[44,45]

Even after 40 yrs after the inception of the Gleason grading system it remains one of the most powerful prognostic predictors in prostate cancer.[46]

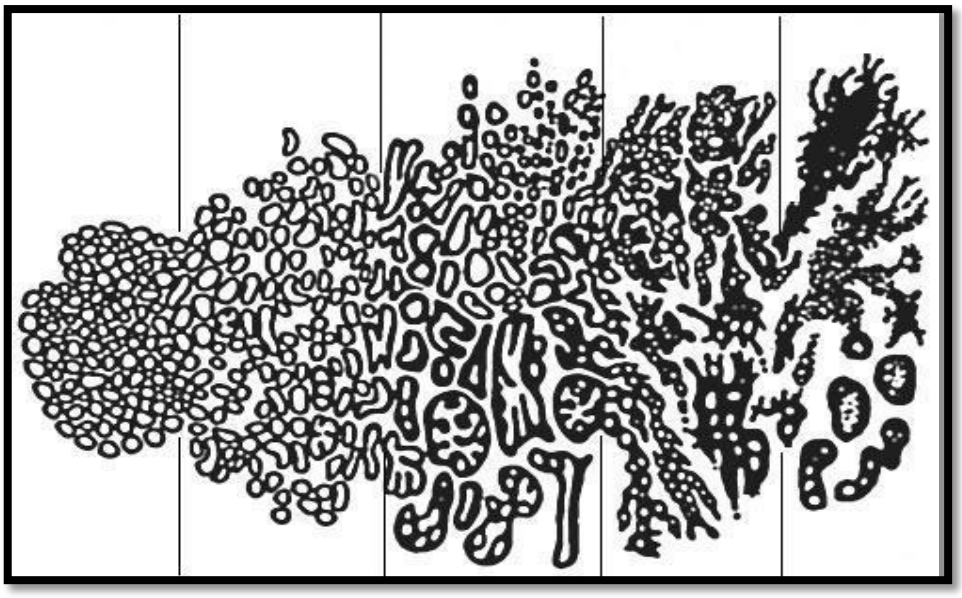


Figure 3. Gleason Grading System: Showing Microscopic Appearance of Cancer cells

Table no. 3 - Gleason Patterns

Pattern 1:	**Circumscribed nodule of closely packed glands but separate, uniform, rounded to oval, medium sized acini (larger glands than pattern 3).**
Pattern 2:	Similar to pattern 1 but fairly circumscribed but at the edge of the tumor nodule there may be some infiltration. Glands are more loosely arranged and not as uniform as Gleason pattern 1.
Pattern 3:	Presence of discrete units of glands Glands are typically smaller-than seen in Gleason pattern 1 or 2; Infiltrates in and amongst non- neoplastic prostate acini. Marked variation in size and shape. Smoothly circumscribed small cribriform nodules of tumor
Pattern 4:	Fused microacinar glands Ill- defined glands with poorly formed glandular lumina Large cribriform glands Cribriform glands with an irregular border Hypernephromatoid
Pattern 5:	The tissue does not have recognizable glands. There are often just solid sheets, cords or single cells throughout the surrounding tissue. Comedo carcinoma with central necrosis surrounded by papillary, cribriform, or solid masses

WHO Histopathological Grading [47] :

GX	**Grade cannot be assessed**			
G1	Well differentiated tumor (Gleason score 2- 4)			
G2	Moderately differentiated tumor (Gleason score 5 - 6)			
G3- 4	Poorly differentiated tumor/undifferentiated (Gleason score 7-10).			
Stage grouping :				
Stage- I	T1a	No	Mo	G1
Stage- II	T1a	No	Mo	G2,3- 4
	T1b,c	No	Mo	Any G
	T1,T2	No	Mo	Any G
Stage- III	T3	No	Mo	Any G
Stage- IV	T4	No	Mo	Any G
	Any T	N1	Mo	Any G
	Any T	Any N	M1	Any G

The ten year cancer-specific survival rate for all stages of cancer is about 51% with an estimated cure rate of 32%.

Patients with a well differentiated tumor, Gleason total score 2-4 have no clinically progressive cancer, where as one-third of patients with high grade lesions Gleason total score 7-10 will progress into locally invasive or metastatic disease.

Patients with less than 5% cancer do not have progressive cancer and do not require therapy, but patients with more than 5% cancer, about one-third of the patients progress to clinically manifest disease. If the tumor is unifocal, the chances of

progressive cancer is less, but the patient with more than 2 foci do progress to clinically manifest disease.

Prognosis

According to college of American Pathologists (1999) prognostic parameters are divided into:

A) Proven to be of prognostic importance and useful in clinical patient management

1. Preoperative serum PSA level
2. TNM stage grouping
3. Histologic grade as Gleason score
4. Surgical margin status

B) Extensively studied but whose importance remains to be validated :

1) Tumor volume
2) Histologic type
3) DNA ploidy

C) Not sufficiently studied to demonstrate their prognostic value:

1) Perineural invasion
2) Neuroendocrine differentiation
3) Microvessel density
4) Nuclear roundness
5) Chromatin texture
6) Other karyometric factors
7) Proliferation markers
8) PSA derivates
9) Other factors (oncogenes, tumor suppressor genes, apoptosis genes)

Immunohistochemical Features

The two immunocytochemical markers for prostatic epithelium are Prostate specific antigen (PSA) and Prostatic acid phosphatase (PAP).

Prostate specific membrane antigen (PSMA) a membrane bound glycoprotein is expressed in all types of prostatic adenocarcinoma.

P504 S is an ∝-methyl COA racemase is highly sensitive in adenocarcinoma. Prostatic cancer cells are immunoreactive for androgen and progesterone receptors.

Prostatic carcinoma cells are also positive for low molecular weight cytokeratins, Leu 7, Epithelial membrane antigen, carcinoembryonic antigen, B 72.3, cathepsin D, glycoprotein A-80, PTH-related protein and gastric acid proteinase gastricin.[48]

There are atleast 3 separate useful immunostains for basal cells 34βE12,P63 and CK 5/6 all of which are negative markers for cancer (that is when they stain positively the abnormal acinar focus is negative for cancer).[49]

MATERIALS AND METHODS

The present study included prostatic tissue specimen received in the pathology laboratory at Dhiraj hospital, piparia- vadodara from January 2016 to January 2017. Clinical data were noted from the case records, which included the age presenting symptoms , serum PSA levels and histopathological diagnosis.

Sample were collected after fulfilling the inclusion and exclusion criteria.

INCLUSION CRITERIA

1. Men of age group 35-90 yrs.
2. All Prostatic biopsies obtained from urology department through transurethral resection, needle biopsy or complete prostate resection.

EXCLUSION CRITERIA

1. Men less than 35 yrs of age.
2. Inadequate prostatic biopsies for histopathology reporting·

The specimens thus obtained were fixed in 10% formalin after detailed and careful examination. In case of TURP, approximately 5gm of tissue was processed in one cassette and embedded. The entire tissue was processed in case of TURP and needle biopsy and in cases of prostatectomy representative bits were processed. Then sections 4 to 6 microns thick were prepared. These were stained routinely with hematoxylin and eosin.

PROCEDURE FOR HAEMATOXYLIN & EOSIN STAINING:

- Sections were dewaxed in 2 jars of xylene, each for 2 min.
- Xylene was removed by keeping slides in 2 jars of absolute alcohol, each for 2 mins.
- Treatment with descending grades of alcohol.
- In 90% alcohol for 1 min.
- In 70% alcohol for 1 min
- Rinsed in water
- Sections were stained in Harris Haematoxylin for 2-5 min.
- It was followed by washing in running water till sections turned blue.
- Sections were decolourised with 1% acid alcohol solution.
- Again washed in running water for 5-15 min
- Counterstained with water soluble eosin for 2 min
- Washed rapidly in water
- Dehydrated in several changes of 70%, 80%, 90% and absolute alcohol.
- Cleared in xylene & mounted in DPX
- Results: Nucleus stained blue
- Cytoplasm stained pink.
- The slides were then examined.

Other special stains like Alcian blue pH 1, periodic acid schiff (PAS) and Ziehl Neelson were performed wherever necessary. The procedure followed for tissue processing and staining technique are those given in "Cellular Pathology technique" by CFA Culling. [50]

The PSA levels were estimated using the TOSOH- immunoassay AIA360, chemiluminescence system which estimates PSA by a sandwich assay utilizing a constant amount of 2 antibodies-labelled polyclonal sheep antibody and monoclonal mouse antibody. The prostate specific antigen level in serum is estimated. These values were correlated with prostatic volume and histopathological diagnosis.

PRINCIPLE & METHOD OF PSA TEST:

The ST AIA-PACK PA is a two-site immune enzymometric assay, which is performed entirely in the ST AIA-PACK. Amount of PSA level present in the test sample is bound with monoclonal antibody immobilized on a magnetic solid phase and enzyme labeled monoclonal antibody in the ST AIA-PACK. The magnetic beads are then washed to remove unbound enzyme labelled monoclonal antibody and are then incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4MUP). The amount of enzyme-labeled monoclonal antibody that binds to the beads is directly proportional to the PSA concentration in the test sample. A standard curve is constructed, and unknown sample concentrations are calculated using this curve.

The range of PSA determination using this equipment is 0.1-100ng/ml. Lesions were graded into non-neoplastic and neoplastic lesions. The cases of prostatic adenocarcinoma were graded using Gleason microscopic grading.

The clinical and histological data so obtained were analyzed and compared with other similar studies.

STATISTICAL METHODS

Chi-square and Fisher exact test have been used to test the proportions in association of lesions with Age, Clinical symptoms and Serum PSA values.

1) **Chi-Square Test:**

$\chi = \sum (Oi-Ei)^2 / Ei$, Where Oi is observed frequency and Ei is Expected frequency

2) **Fisher Exact Test**:

Fisher Exact Test statistic= $\sum_p = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{n!} \frac{1}{\sum a!b!c!d!}$

	Class 1	Class 2	Total
Sample 1	a	b	a+b
Sample 2	c	d	c+d
Total	a+c	b+d	n

Statistical software

The statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS AND OBSERVATION

The present study deals with evaluation of various histological lesions in prostatic specimens and their PSA levels. During the period of present study, 100 prostatic specimens were analysed in the Department of Pathology, SBKS Medical College, Piparia,Vadodara.

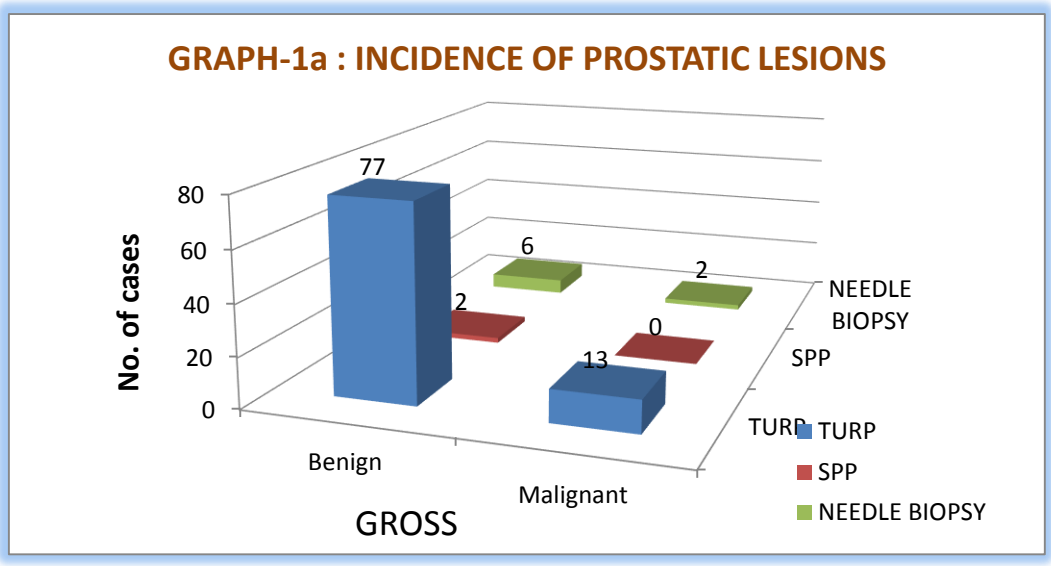
Prostatic lesions :

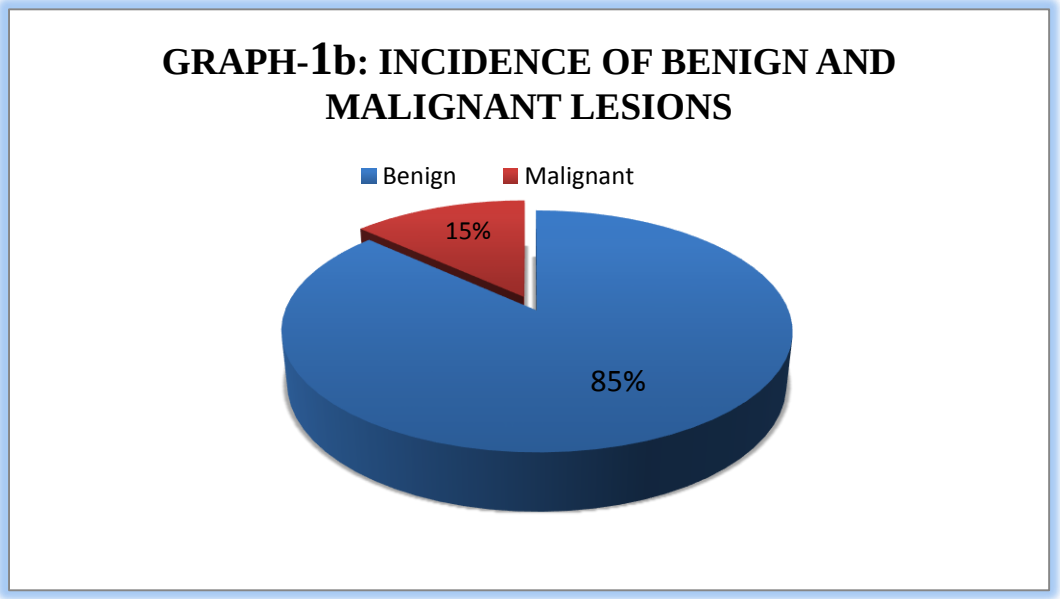
Out of 100 prostatic specimens received, 85 cases were benign lesions and prostatic malignancy was diagnosed in 15 cases. Incidence of benign lesions was 85% and malignant lesions 15% in this study.

Among the benign lesions, TURP was done in 77 cases, needle biopsy was done in 06 cases and suprapubic prostatectomy (SPP) in 02 cases. Malignant lesions were diagnosed in 13 TURP and 02 needle biopsy specimens.

TABLE -4 : INCIDENCE OF PROSTATIC LESIONS

Gross	Benign lesions	Malignant lesions	Total
TURP	77 (90.6%)	13 (86.6%)	90 (90%)
SPP	02 (2.3%)	00 (00%)	02 (2%)
NEEDLE BIOPSY	06 (7.1%)	02 (13.4%)	08 (8%)
Total	85 (85%)	15 (15%)	100 (100%)





Age :

Among 85 benign lesions, majority of the benign cases belonged to the age group of 61- 70 years. Youngest case was 41 years and oldest was 85 years. The mean age group ±SD for benign lesions is 66.4±8.6 years.

Among 15 malignant lesions, majority of the cases were seen in age group of 61- 70 years. Youngest person was 48 years and oldest person was 85 years old in this category. The mean age group ±SD for malignant lesions is 70.2±8.7 years.

When age groups of benign and malignant lesions were compared, P=0.07, which is not significant.

TABLE -5 : AGE INCIDENCE OF VARIOUS PROSTATIC LESIONS

Age (years)	Benign lesions	Malignant lesions		Total
41- 50	6 (7.08%)	1(6.66%)	7	(7%)
51- 60	18 (21.17%)	3 (20%)	21	(21%)
61- 70	38 (44.70%)	7 (46.68%)	45	(45%)
71- 80	18 (21.17%)	3 (20%)	21	(21%)
81- 90	5 (5.88%)	1 (6.66%)	6	(6%)
Total	85 (100%)	15(100%)	100 (100%)	

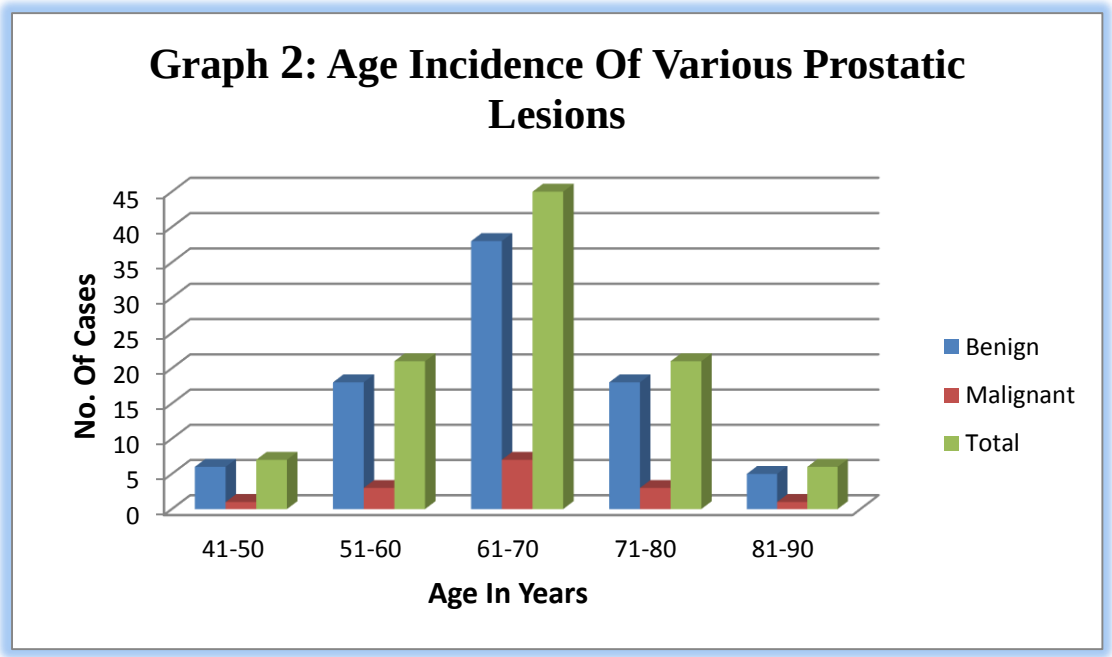
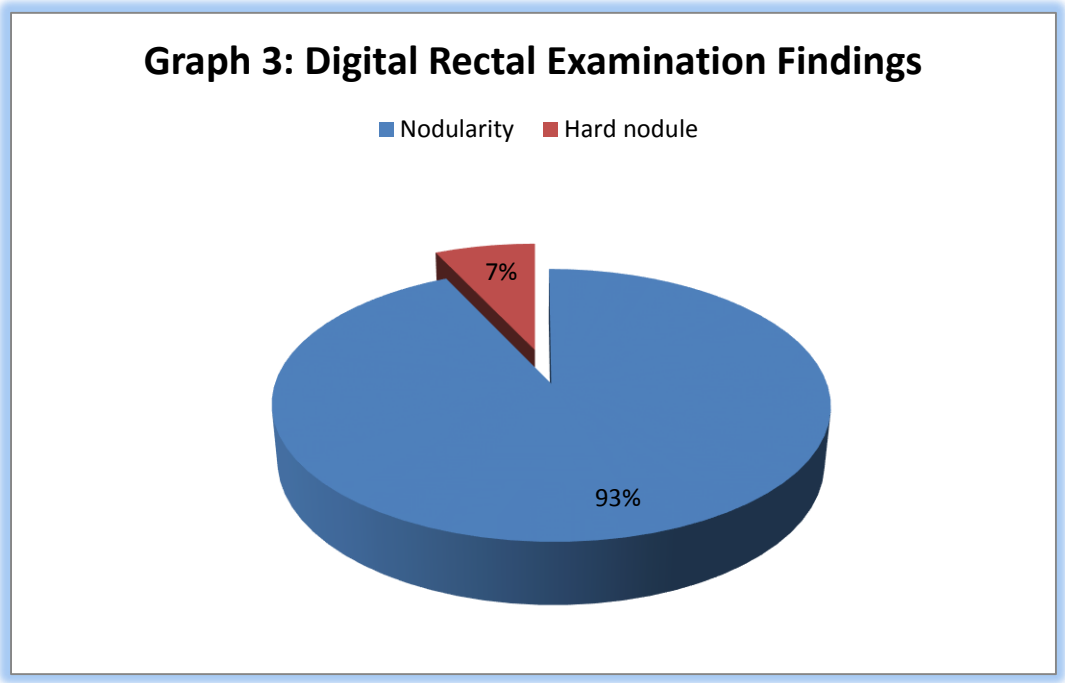


Table 6- Digital rectal examination findings

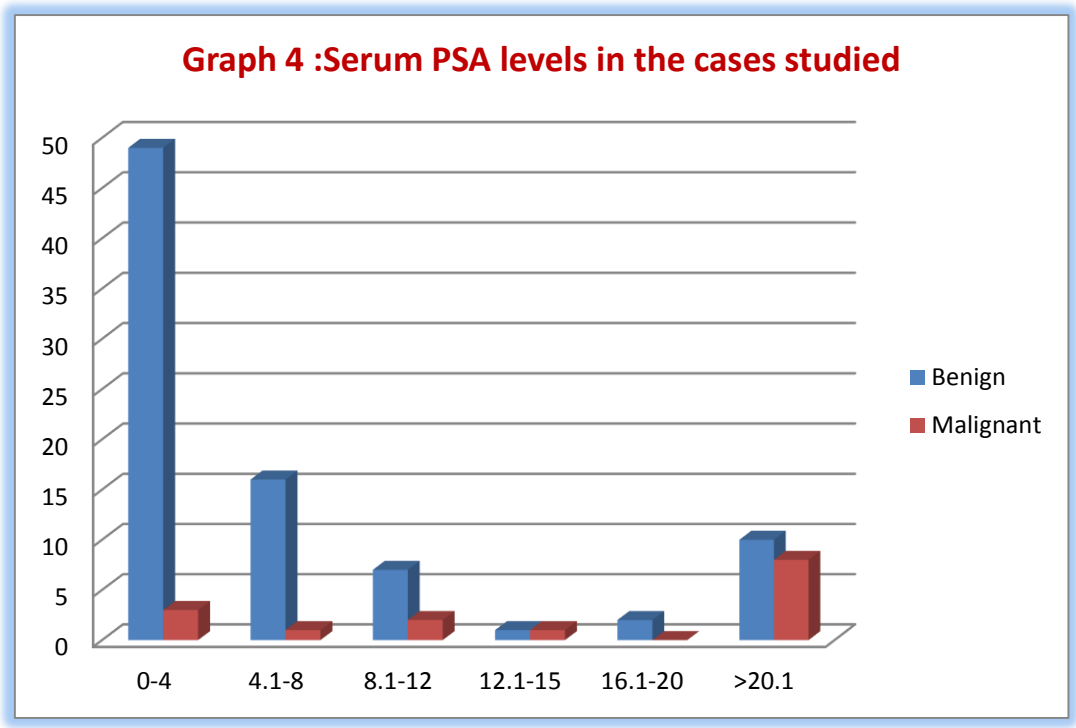
Digital rectal examination findings	
Nodularity	93
Hard Nodule	07



Clinically digital rectal examination findings showed nodularity in 93 cases and presence of hard nodule in 07 cases. When both benign and malignant cases were compared, hard nodule was significantly associated with malignant cases.

Table 7- Serum PSA levels in the cases studied

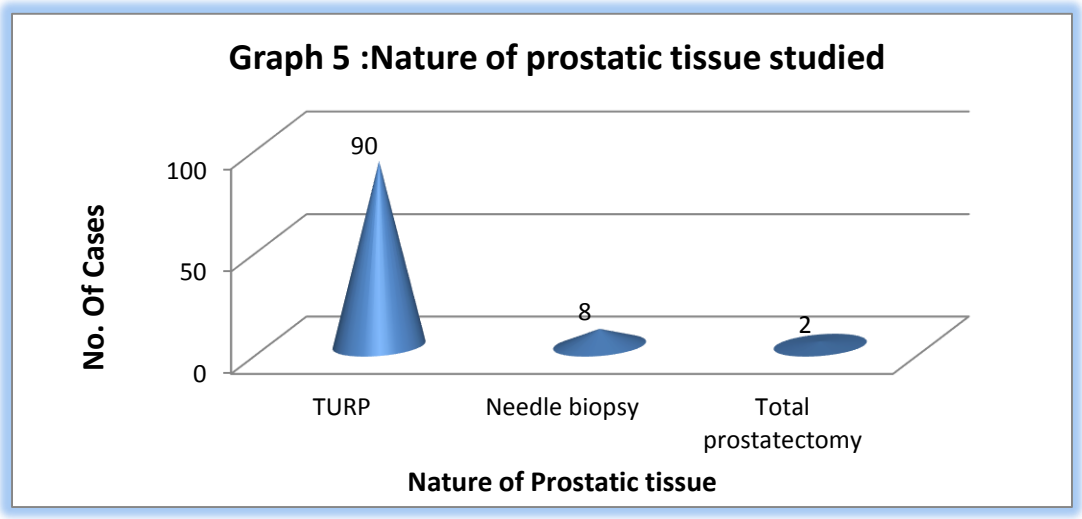
PSA values (ng/ml)	Benign	Malignant
0-4	49	3
4.1-8	16	1
8.1-12	7	2
12.1-15	1	1
16.1-20	02	0
>20.1	10	8
Total	85	15
Inference	PSA values with >20.1 are 8.21 times more likely to be malignant with p=0.001	



Among 85 benign lesions, majority of the benign cases had PSA level in the range of 0-4. Minimum PSA level seen was 0.21. Among 15 malignant lesions, majority of cases had PSA level >20.1. Maximun PSA level seen was 98.

Table 8- Nature of prostatic tissue studied

Nature of Tissue	No. of Cases
TURP chips	90
Needle Biopsy	8
Total Prostatectomy	2
Total	100



Out of total 100 specimens received; 90 were TURP specimens, 8 needle biopsies and 2 total prostatectomy specimens. Maximum specimens received were TURP (Transurethral resection prostate).

Gleason's score :

All of these 15 malignant cases were graded using Gleason's scoring system. Primary grade is assigned to dominant pattern and secondary grade to the subdominant pattern. The two numeric grades are added to obtain the combined Gleason's score. In tumors with one pattern of arrangement, the number is doubled.

Gleason score of 7 was the commonest pattern seen in 4 cases (57.14%). Gleason score of 8 was seen in 2 cases (28.57%) and Gleason score of 9 was seen in 1 case (14.29%) each. The earlier patterns of Gleason's score were not seen in the study.

TABLE -9 : Incidence Of Carcinoma With Reference To Gleason's Score

Gleason's score	No.of cases	%
7	4	57.14
8	2	28.57
9	1	14.29
10	0	0
Total	7	100%

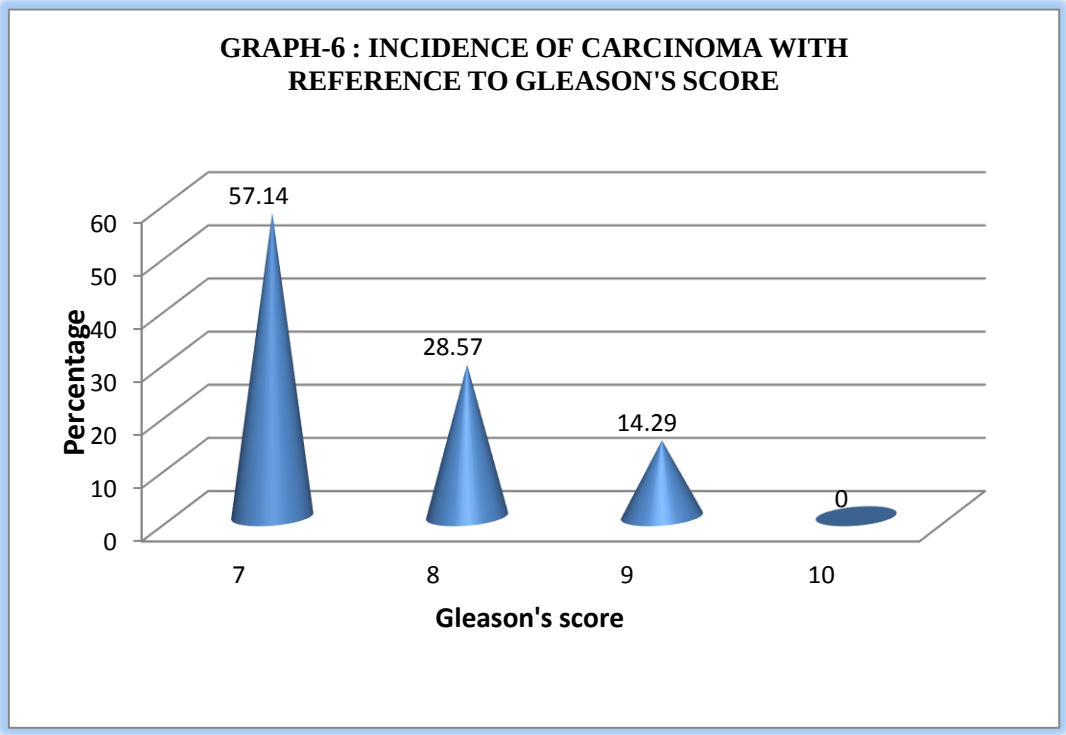
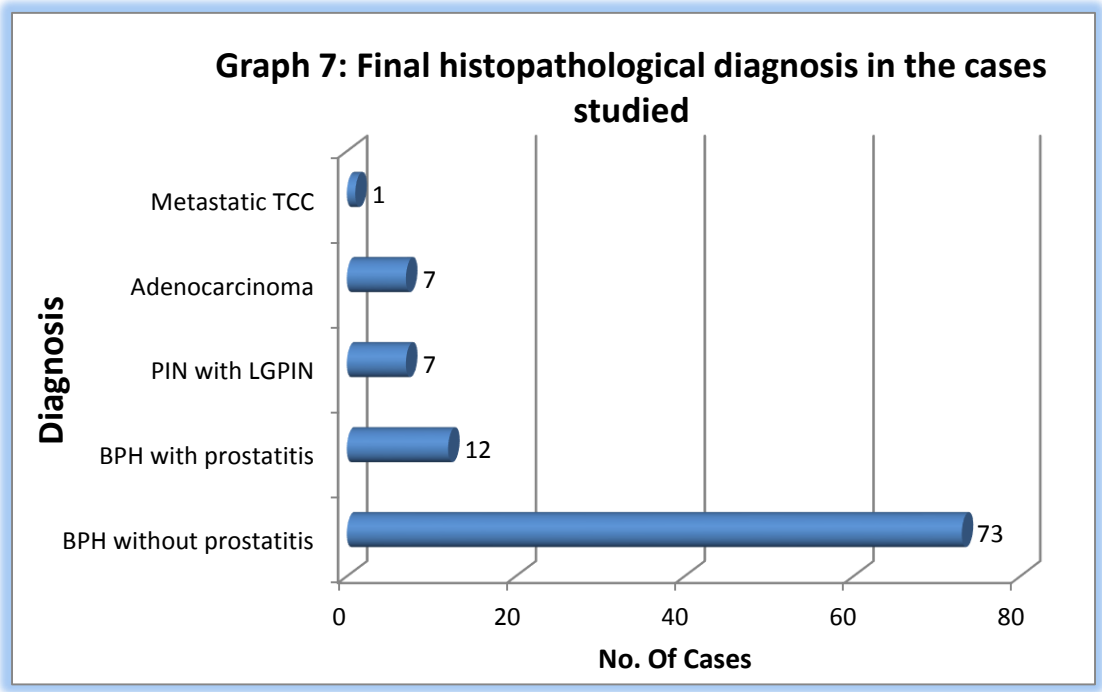


TABLE -10 : Final Histopathological Diagnosis In The Cases Studied

Final histopathological diagnosis	No. Of cases	%
1) BPH		
a) Without Prostatitis	73	73%
b) With Prostatitis	12	12%
2) PIN		
a) LGPIN	7	7%
3) Adenocarcinoma	7	7%
4) Metastatic TCC (from Urinary bladder)	1	1%



Among the 100 cases studied, 73 cases were BPH without prostatitis and 12 cases were with prostatitis, together constituting 85% of total cases. Malignant cases (15) constituted 15% .

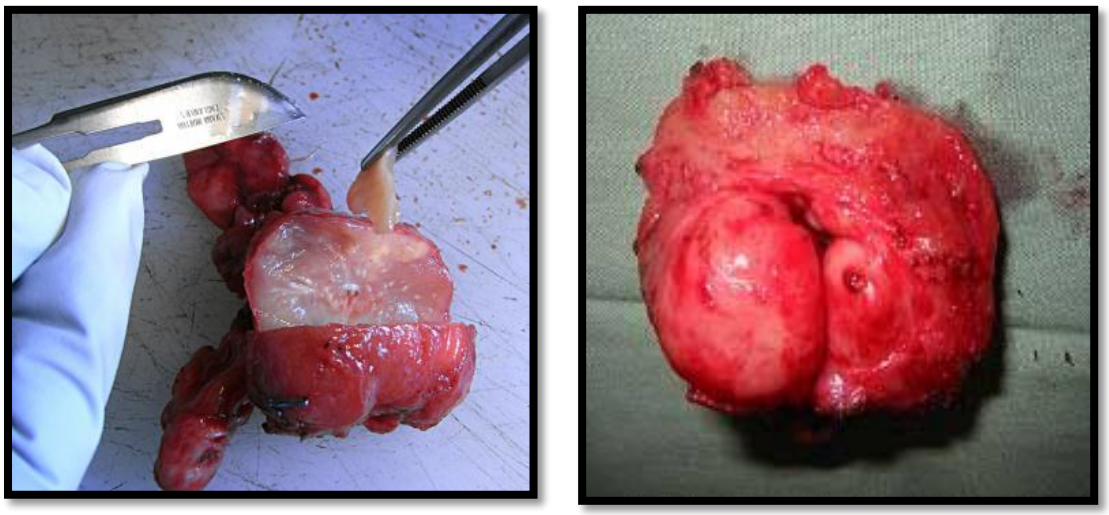


Figure 4: Gross appearance of prostatectomy specimens

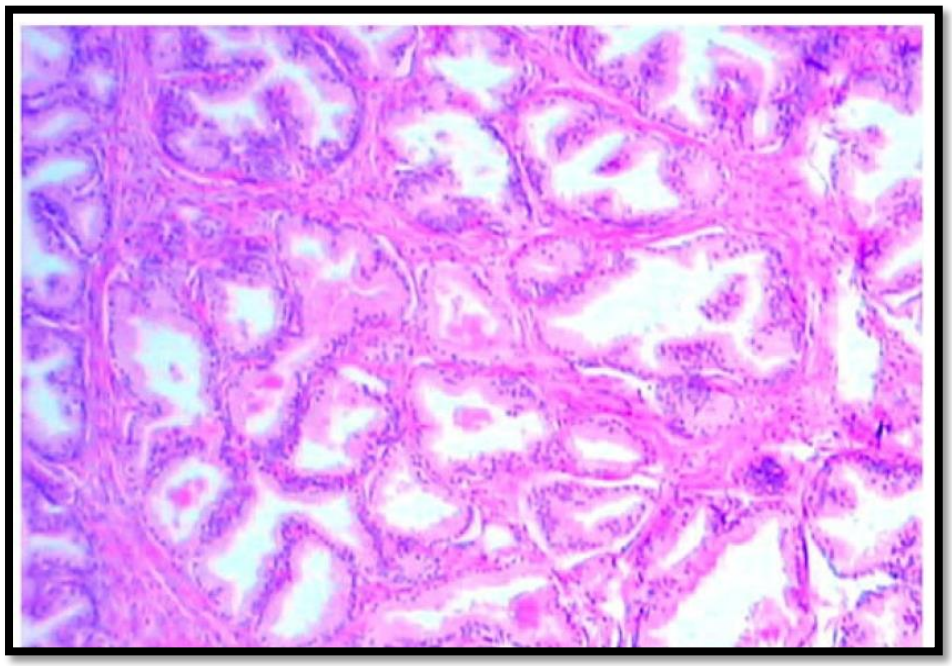


Figure 5: Benign prostatic hyperplasia showing hyperplastic glandular and stromal components (H&E, 100x)

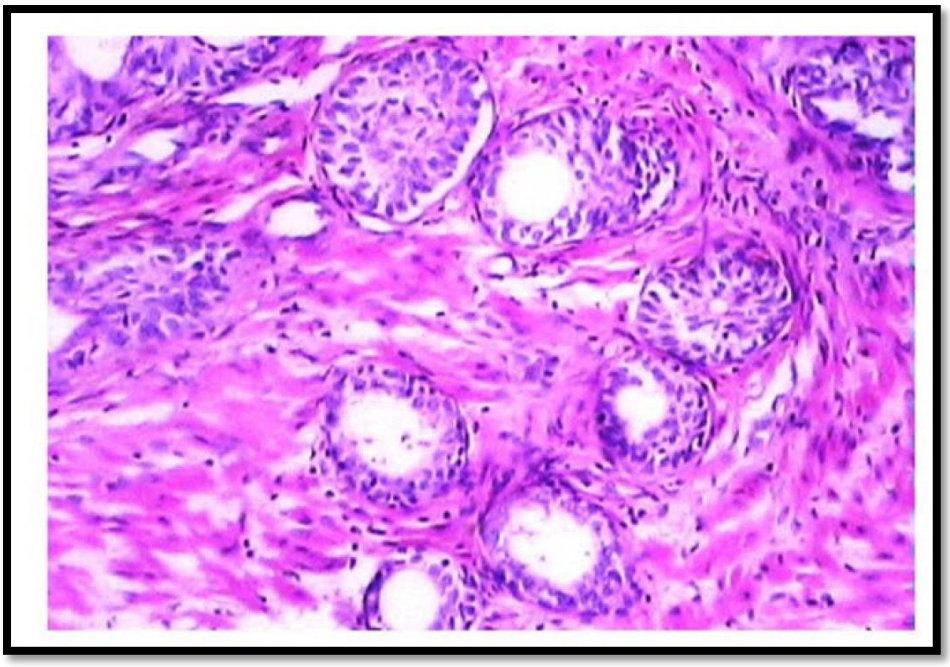


Figure 6: Basal cell hyperplasia, showing glands filled with small darkly staining basal cells with peripheral palisading (H&E, 100x)

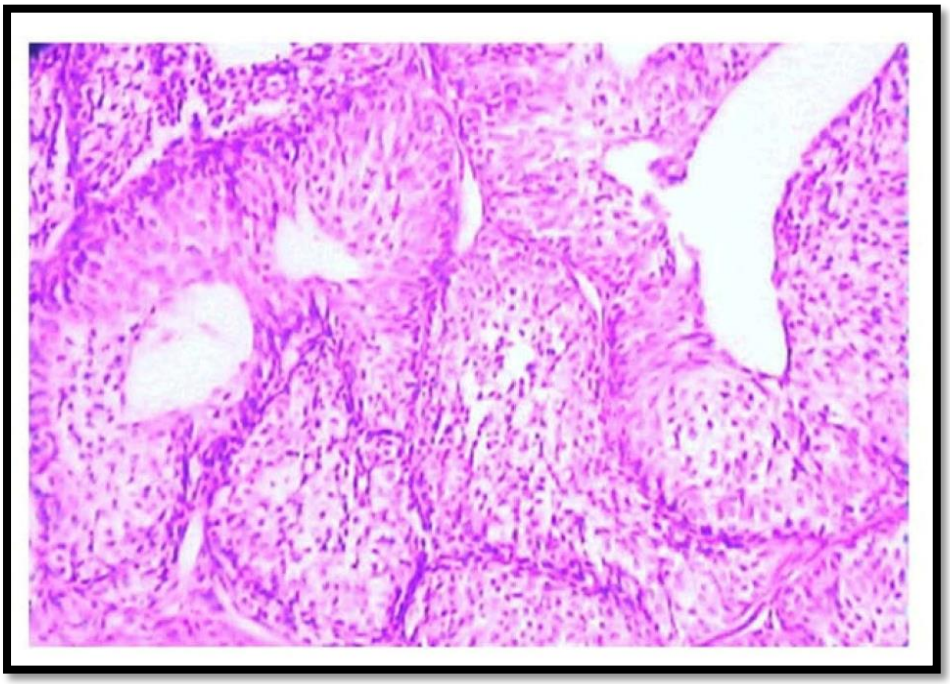


Figure 7: Clear cell cribriform hyperplasia, showing glands composed of cells with abundant clear cytoplasm (H&E, 100x)

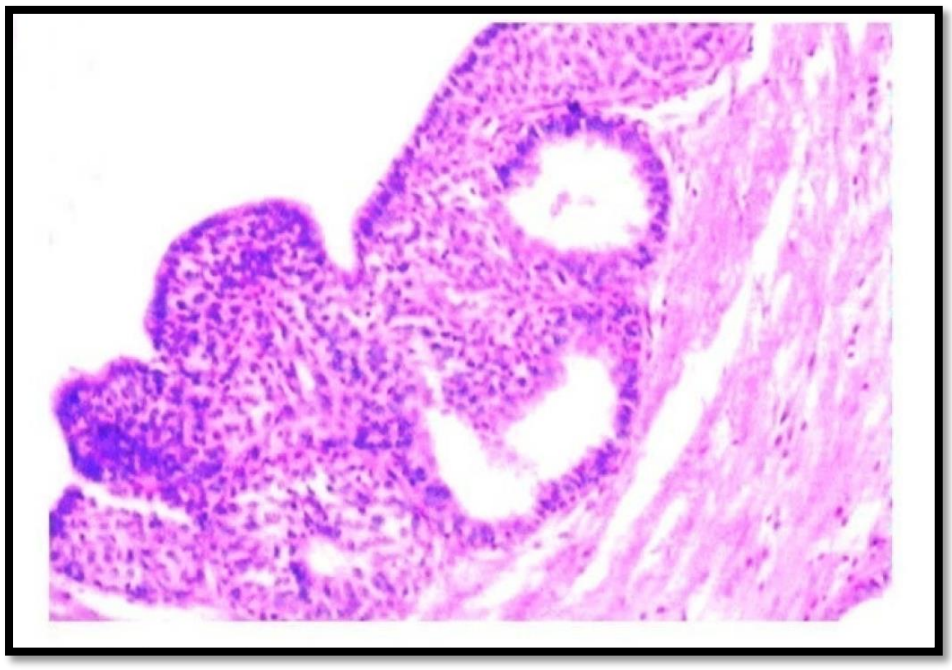


Figure 8: Transitional metaplasia in a case of nodular hyperplasia (H&E, 100x)

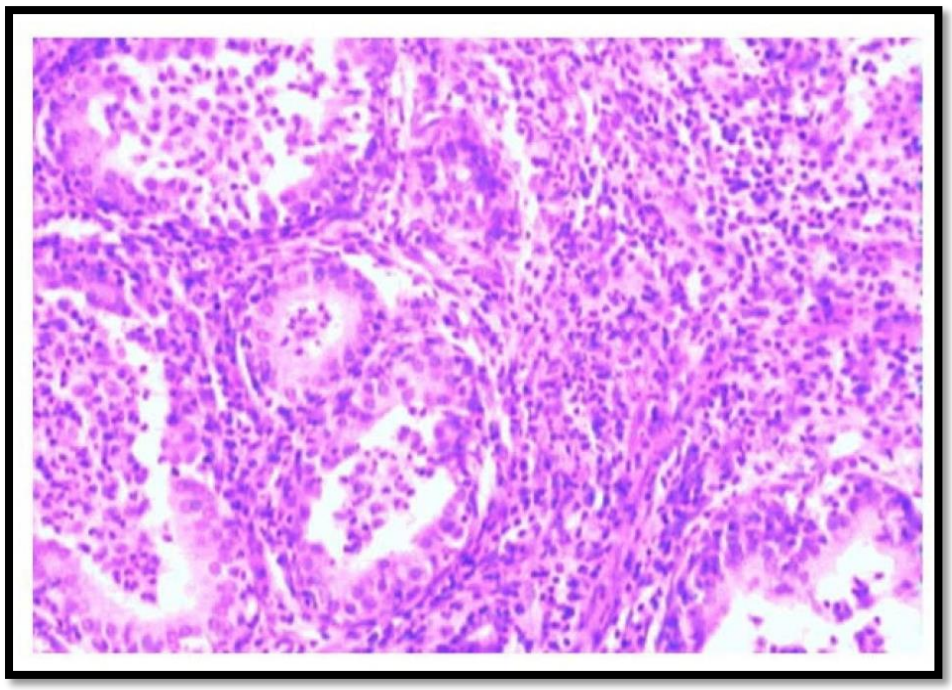


Figure 9: Prostatic abscess showing sheets of neutrophils in and around the acini (H&E, 100x)

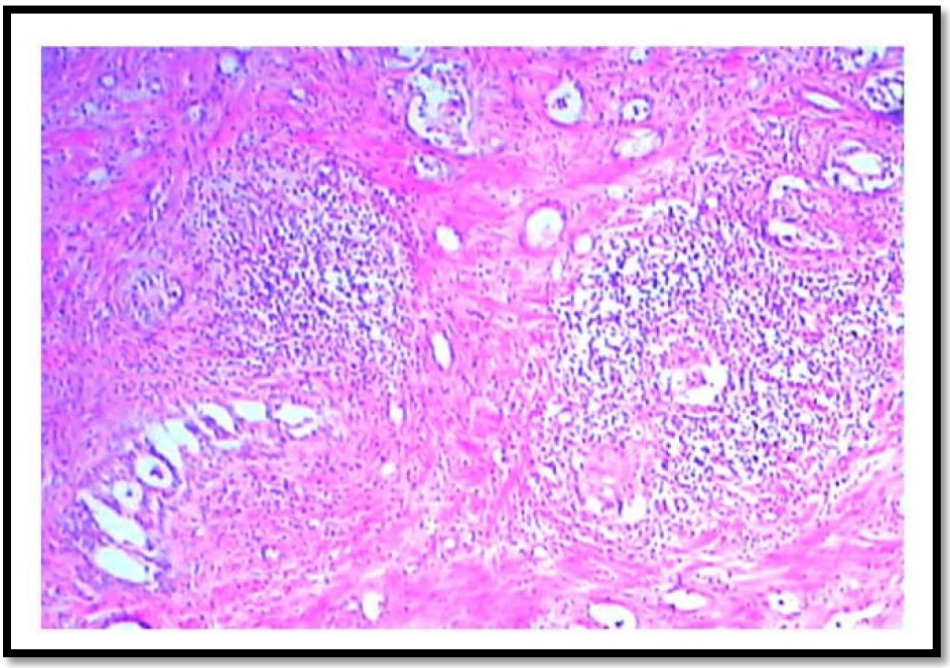


Figure 10: Chronic prostatitis showing infiltration of lymphocytes, plasma cells and histiocytes in the stroma (H&E, 100x)

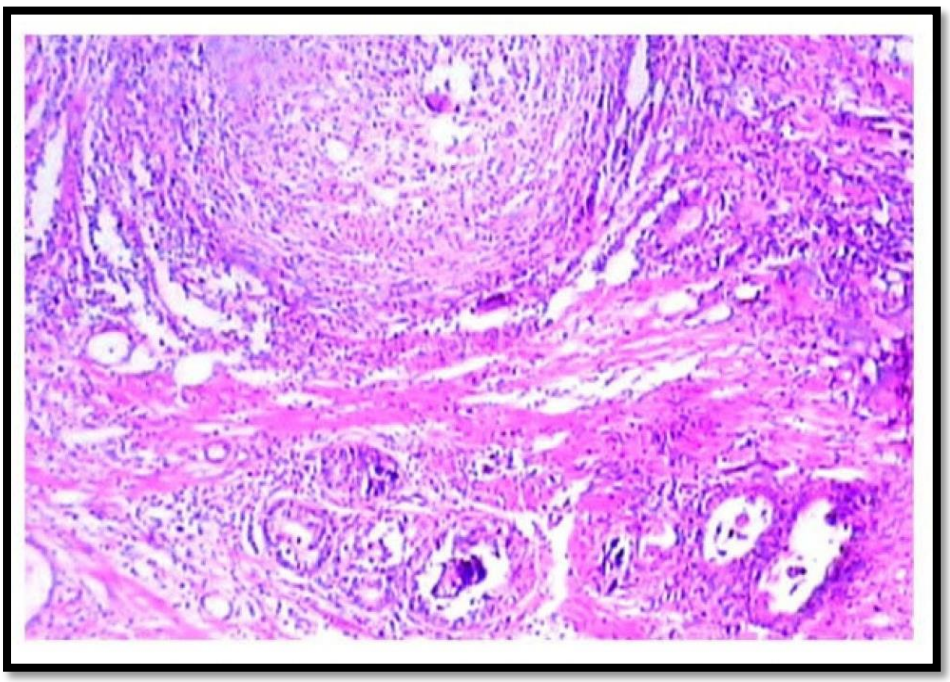


Figure 11: Granulomatous prostatitis showing well formed epitheloid granuloma with a giant cell (H&E, 100x)

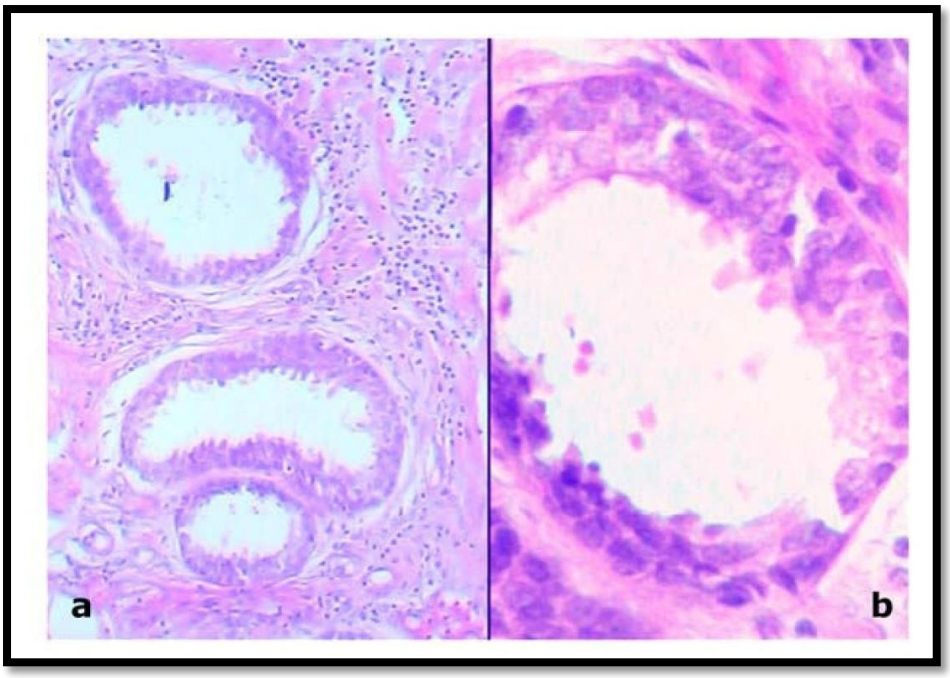


Figure 12: Low grade PIN showing epithelial crowding and stratification with anisonucleosis a) (H&E, 100x) b) (H&E, 400x)

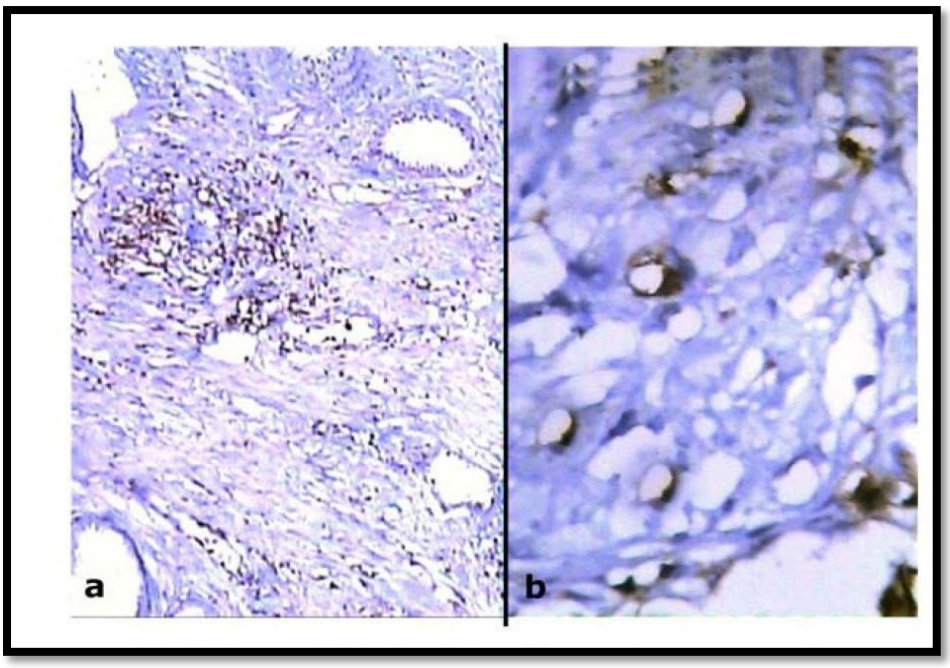


Figure 13: Immunohistochemistry of leucocyte common antigen for the above case showing membrane positivity a) (H&E, 100x) b) (H&E, 400x)

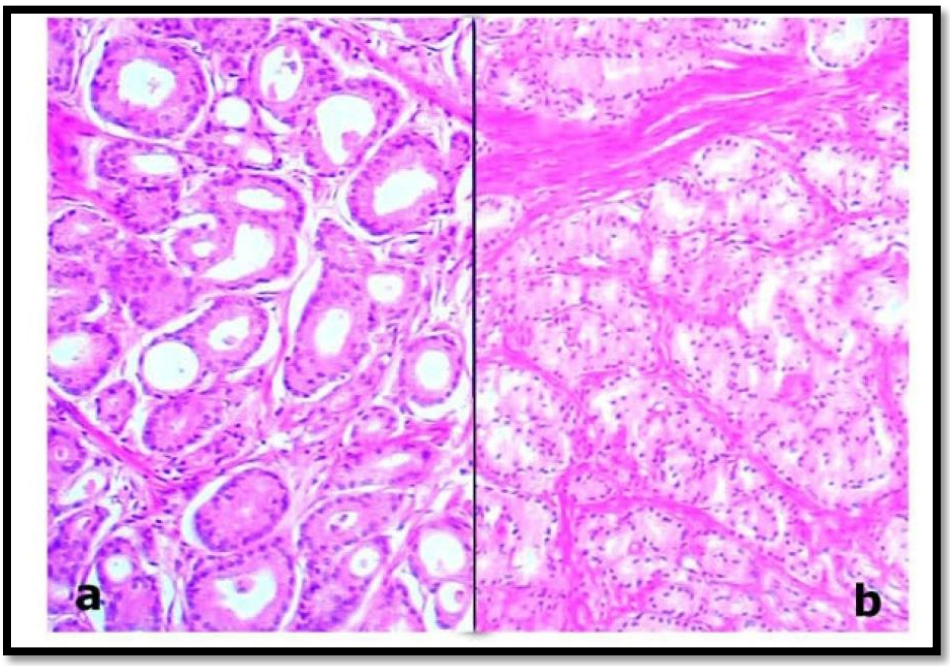


Figure 14: Prostatic adenocarcinoma, Gleason's score 3+4=7/10

a) pattern 3 showing closely packed single glands

b) pattern showing fused glandular pattern (H&E, 100x)

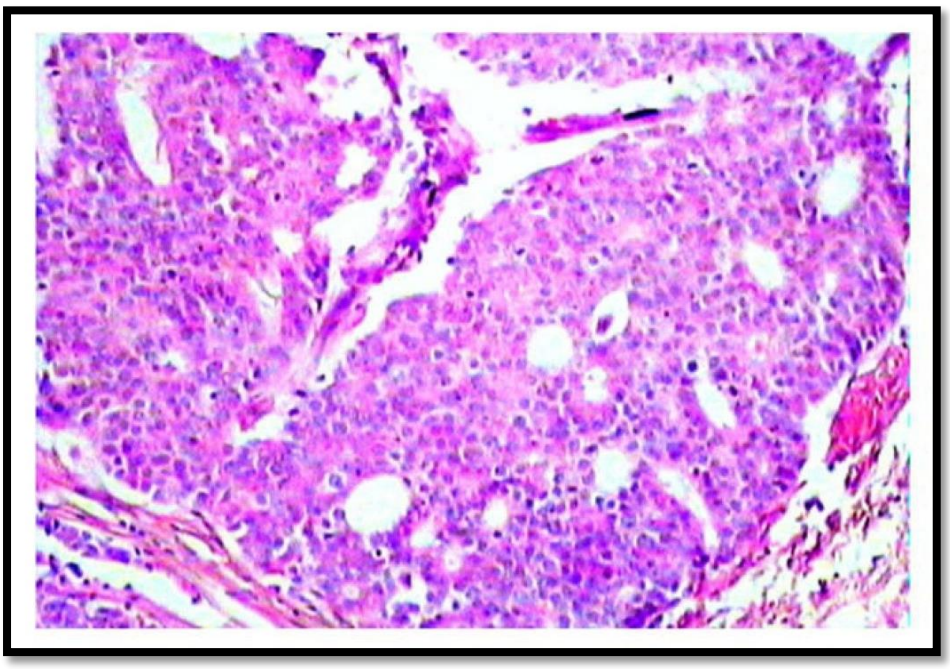


Figure 15: Prostatic adenocarcinoma, Gleason's score 4+4=8/10, Showing cribriform gland with irregular border (H&E, 100x) (H&E, 100x)

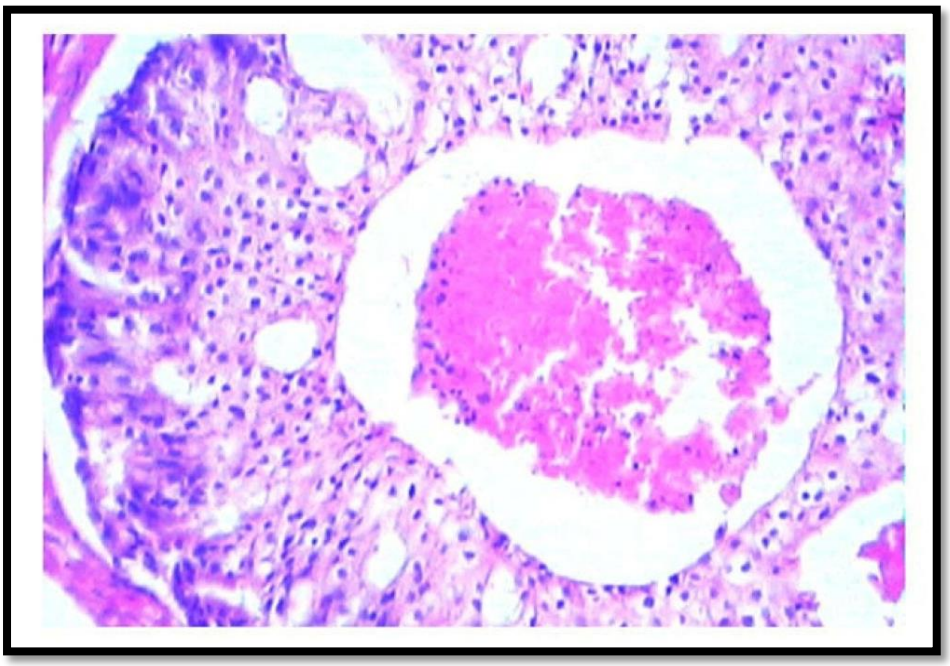


Figure 16: Gleason's pattern 5 with central comedo necrosis (H&E, 100x)

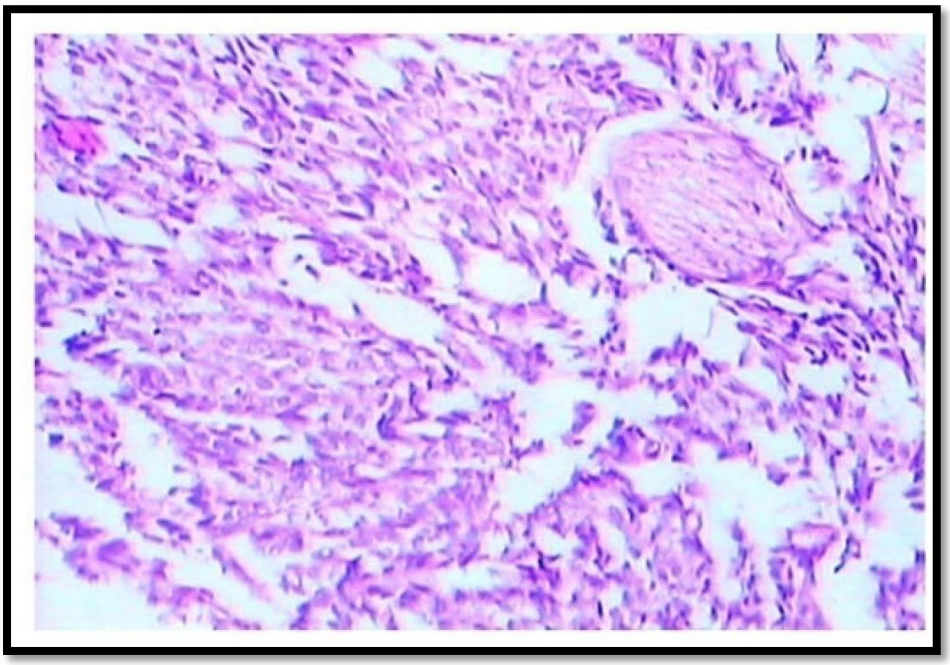


Figure 17: Perineural invasion showing tumor cells invading the perimeurium (H&E, 100x)

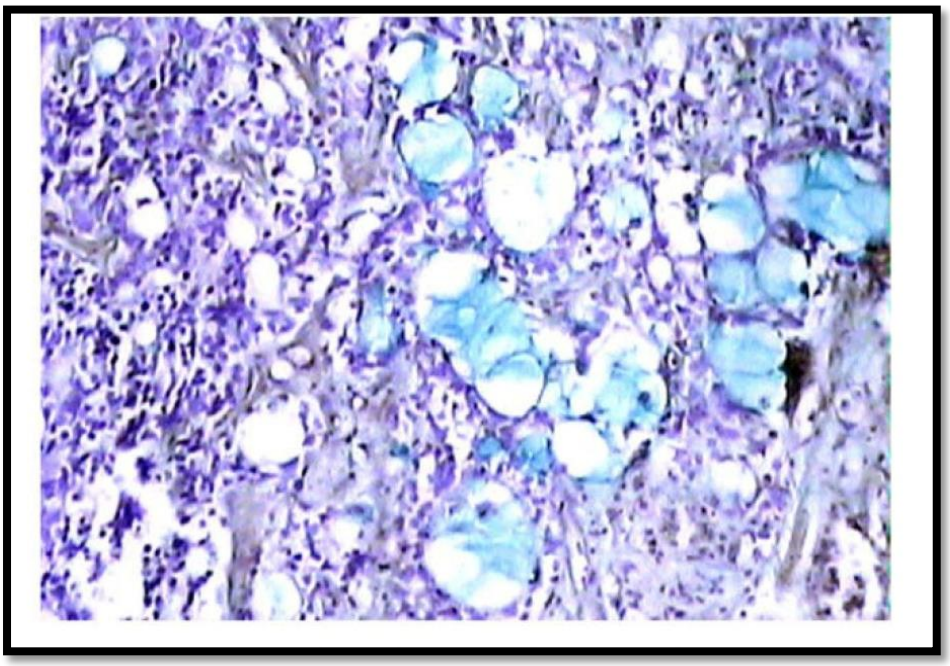


Figure 18: Intraluminal acidic mucin in lumens of neoplastic glands in a case of prostatic adenocarcinoma (Alcian blue pH 1, 100x)

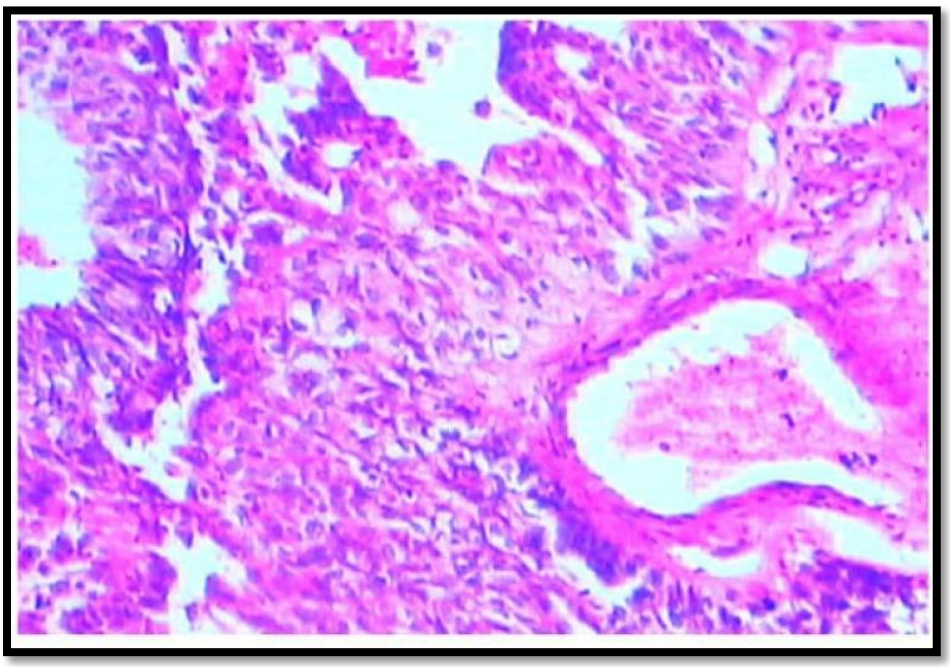


Fig-19 Transitional cell carcinoma of bladder metastatic to prostate (H&E,100x)

DISCUSSION

The present study was a prospective and non-interventional type of study. Total 100 numbers of patients each from January 2016 till January 2017 were recruited.

Enlargement of prostate is an age related process and incidence increases with increasing age beginning in the forties. The incidence of BPH increases from an average of 23 to 88% by the ninth decade. [51]

Hyperplasias

Gross:

1. TURP specimens consisted of multiple gray white soft tissue bits. The weight ranged from 2-30 grams.
2. Needle biopsy consisted of 3-4 linear soft tissue bits measuring 1-1.5 cm in length having thickness of 2-4 μm.
3. Prostatectomy specimens showed hyperplastic lateral lobes. The cut section was nodular with solid and cystic areas.

Most patients over the age of 50yrs will have histological evidence of BPH and many will suffer symptoms from urethral compression. Data indicate that on microscopic examination both epithelium and stroma are involved in varying degrees and predominant pattern is fibroadenomatous hyperplasia.

In the present study adenofibromyomatous hyperplasia was seen in 85 cases where hyperplasia of both epithelial and stromal components was seen. According to study by Bostwick et al. BPH is composed of varying proportion of epithelium and stroma.

The most common nodules reported in their study was adenofibromyomatous nodules which contained all elements. [25] (Fig. 5)

PROSTATITIS

In the present study out of 100 cases, 12 cases had prostatitis. These include:

Table 11: Showing the incidence of prostatitis

Chronic non specific prostatitis	10 (84%)
Granulomatous prostatitis	2 (16%)

In the study by Granados et al, 25 cases of prostatic abscess were studied which showed sheets of neutrophils in and around the acini[52] (Fig. 9).

In cases of chronic non-specific prostatitis lymphocytes, plasma cells, macrophages were seen. Bostwick in his study has reported more cases of chronic are bacterial as compared to bacterial prostatitis. [25] (Fig 10).

In the present study 2 cases of non-specific granulomatous prostatitis were noted, out of which one of the case showed well formed epitheloid granulomas with giant cell.

There was no evidence of caseation and special stain for AFB was negative.

Out of 12 cases of prostatitis urine culture was done in 6 cases of which E. Coli was seen in 2 cases, 2 cases showed growth of Klebsiella and one case each of Enterococci and pseudomonas.

In a study by Still well 200 cases of granulomatous prostatitis were reported amongst which 138 were of non specific granulomatous prostatitis (69%) and 49 cases were of post biopsy granulomas (3.5%) and 6 cases were of systemic granulomatous disease (3%). [53]

IHC was done for Leucocyte Common Antigen (LCA) in a case to distinguish distorted lymphocytes in the stroma, (artifactual) which were appearing as signet ring cells. The cells showed positive membrane reaction[54] (Fig. 13). [73]

PIN

In the present study out of 100 specimens examined 7 cases showed PIN, 7 cases showed LGPIN.

LGPIN was characterized by epithelial crowding and stratification with anisonucleosis but no prominent nucleoli was observed (Fig. 12).

In our study PIN was seen most commonly in the age group of 61 –70 yrs. In the study by McNeal and Bostwick frequency of PIN was highest in the age group 60 – 69yrs. [53] In the study by Lee et al, the mean age of PIN was 65 yrs.

Prostatic Carcinoma

In the present study peak incidence of both PIN and prostatic carcinoma was seen in age group of 61-70 yrs. It has been observed that PIN occur at least a decade earlier compared to prostatic carcinoma. But in present study no such age difference was noted.

Many recent studies show a higher incidence of prostatic carcinoma in the age group of 61-70 yrs. However in studies of Moore and Baron the peak incidence was seen in age group of 51-60 yrs. This may indicate change in trend of prostatic carcinoma.

Table 12- Age incidence of prostatic carcinoma in different studies

Sl. No.	Authors	21-30	31-40	41-50	51-60	61-70	71-80	81-90	Total
1	Rich(1934)[55]	-	-	-	7	8	12	0	27
2	Moore(1935)[55]	-	-	9	18	13	7	-	47
3	BaronandAngrist(1941)[55]	-	-	20	26	25	6	-	77
4	Andrews(1949)[55]	-	-	2	7	7	-	-	16
5	Edward et al (1953)[55]	-	-	3	10	12	3	-	28
6	Franks(1954)[55]	-	-	38	53	70	17	-	178
7	Scottetal(1961)[55]	-	-	-	-	36	26	-	62
8	Holund(1980)[55]	-	-	2	7	24	13	-	46
9	Presentstudy	**-**	**-**	**1**	**3**	**7**	**3**	**1**	**15**

Commonest of prostatic carcinoma is adenocarcinoma. Among 15 cases of prostatic carcinomas encountered 7 (46.6%) are adenocarcinoma (Fig. 14. 15. 16) and and one case was metastasis from transitional cell carcinoma of bladder (Fig. 19).

There is wide variation in the incidence rate of prostate cancer in different parts of the world. The age adjusted incidence rates in Bangalore is 5.2 per 100000.[56] The prevalence rate of 9.3% observed in present study is comparable with study by Muruli et al[57], which showed a prevalence rate of 8.5%. The increased incidence of prostatic carcinoma in industrialized world is partly due to increased number of cases diagnosed by screening and case finding by serum PSA testing.[58]

Table 13-Prevalence of prostatic carcinoma in different studies

Sl. No.	Authors	No. of prostatic specimens	No. of prostatic carcinoma	Prevalence
1	Newman et al (1982)[55]	500	71	14.20
2	Muruli et al (1985)[55]	222	19	8.56
3	Moore et al (1986)[55]	143	31	21.68
4	Murphy et al (1986)[55]	386	66	17.10
5	Yamabe et al (1986) (Japan)[55]	191	24	12.57
6	Yamabe et al (1996) Netherlands)[55]	452	57	12.61
7	Eble and Tejada (1986) [55]	700	132	18.56
8	Rohr (1987)[55]	457	65	14.22
9	Present study	100	15	15

Histochemical stains for mucin in the present study demonstrated neutral mucin in all LGPIN cases and in these cases acidic mucin was absent. All cases of carcinoma showed positivity for acidic mucin.[59] (Fig.18) Present study showed 85% BPH/Prostatitis, 7% LGPIN and 8% prostatic carcinoma. W. Horinger et al in his study reported 73.1% BPH/Prostatitis, 4.7% HGPIN and 22.2% prostatic carcinoma.[60]. Anna Pacelli and David G. Bostwick reported incidence of 81.7% of BPH and18.3% adenocarcinoma[61]. In the present study all cases of adenocarcinoma were showing basement membrane disruption, with 3 cases showing perineural invasion (Fig. 17). These pathological changes have been well documented in literature,[62] Carter HB and Partin AW reported the distribution of Gleason score in 703 men with clinically localized prostatic carcinoma.[63]

Table 14-Comparative incidence of carcinoma with reference to Gleason's score

Studies	Gleason score	No. of patients(%)
Carter HB and Partin AW	2-4	64(9)
	5	168(24)
	6	303(43)
	7	130(19)
	8-10	38(5)
	Total	703(100)
Present study	2	0
	3	0
	4	0
	5	0
	6	0
	7	4(58)
	8	2(28)
	9	1(14)
	Total	7(100)

In the present study low grade adenocarcinoma was not detected probably because these lesions are usually asymptomatic

Bob Djavan et al reported 22% incidence of carcinoma. Mean age of patients was 67 yrs and mean Gleasons score was 7.[64]

Table 15-Incidence of prostatic carcinoma mean age and mean Gleason's score

Studies	Incidence of prostate cancer	Mean age	Mean score
Bob Djavan	22%	67	6
Present study	15%	68	7

Richard Babajan et al studied 151 men between September 1998 and September 1999 at university of Texas M.D Anderson cancer center. Cancer was detected in 24.5% of men biopsied. Mean age of all 151 men was 62yrs (range 43-74). Gleason score was 6 in 12 patients 7 in 1 and 8 in 1.[65]

Table 16-Incidence of prostatic carcinoma, median age and Gleason's score

Studies	Incidence of prostatic carcinoma	Median age	Gleason score
Richard J Babian et al	24.5%	62	6-12 patients 7-1 patient 8-1 patient
Present study	12%	68	7-4 patients 8-2 patients 9-1 patients

Table No 17:- Benign and malignant Prostatic lesion: Comparison between PSA level with other study.

PSA range	Benign Prostatic hyperplasia				Malignant prostatic lesion				
(ng/ml)	Kshitij et al[66]	Ishtiaq Ali Khan et al[67]	Jasani et al[68]	Present study	Kshitij et al[66]	H.A Mwalyoma et al[69]	Sladana Zivkovic et al[70]	Jasani et al[68]	Present study
0 -4.0	71.6%		63.7%	57.6%	10.5%		2.50%	1.7%	20%
4 - 10.0	22.6%	85%	27.4%	25.9%	26.3%	5.3%	27.50%	12%	13.3%
>10	3%	15%	8.8%	16.5%	63.15%	94.7%	70.0%	86.2%	66.7%

Table no 17 shows cases of BPH most commonly present between PSA level 0 -4.0 ng/ml (57.6%), which is compared with study of Khitij *et al.* and cases of Adenocarcinoma is more commonly present at PSA level >10.0 ng/ml (66.7%) and it is compared with other study.

Serum PSA Levels

BPH is a common cause of serum PSA elevation and accounts for 60-70% of cases. Studies of patients with histologically confirmed BPH have shown that 21-86% have elevated serum PSA levels. The degree of elevation is modest (2.1-10ng/ml),[71] in 57 cases and in 6 cases the degree of elevation was severe(10-20ng/ml). 10 cases had levels more than 20.1 ng/ml. This is because these cases of BPH were associated with prostatitis, abscesses and granulomatous prostatitis. According to a study in chronic prostatitis serum PSA was high in 99% of the cases. Also prostatic manipulations including cystoscopy, needle biopsy and TURP are known to elevate serum PSA levels. In a small percentage of men digital rectal examination (9%), prostatic massage (6%) and trans rectal ultrasound scanning

(11%) result in elevation of serum PSA levels.[72]Acute urinary retention also elevates the PSA values.[73]

Serum levels of PSA were frequently elevated in patients with PIN ranging from 0.3 to 22.3 mg/ml (mean 4.0).[74] In the present study, they showed normal levels (< 4 ng/ml)

In the present study, 9 cases of prostatic carcinoma had high levels of PSA (>12ng/ml), however 3 cases had PSA levels below 4ng/ml this can be attributed to study in which it was reported that prostate cancers detected at lower PSA levels are more likely to have a small volume (less than 0.5ml) and are of low grade.[75]

LIMITATIONS OF STUDY

1. In the cases of needle biopsy the tissue obtained was from the transition zone and not from the peripheral zone, hence diagnosis of malignancy may be missed inspite of strong clinical suspicion of malignancy.

2. Immuno histochemistry was done in one case. Due to lack of facilities and financial constraints it was not done in all the suspected cases.

SCOPE FOR IMPROVEMENT

The correct diagnosis of adenocarcinoma should be made in order to prevent radical prostatectomy; which has high rate of morbidity in elderly males. Since serum PSA was increased in few benign and most of the malignant cases, newer modalities of measuring PSA like PSA density, PSA velocity, age specific reference rates should be adopted to distinguish between benign and malignant lesions.

Diagnosis of HGPIN should be included since it is a precursor of adenocarcinoma. Most of the cases of prostatic adenocarcinoma encountered were of high grade. Since low-grade lesions are usually asymptomatic, awareness of serum PSA level estimation, digital rectal examination should be brought among elderly males who are prone for malignancy. Male individuals with a positive family history for prostatic carcinoma must undergo relevant screening test.

CONCLUSION

The present study was a prospective and non-interventional type of study.

1. Out of 100 prostatic specimens studied benign lesions were common, which accounted for 85% and malignant lesions accounted for 15%.
2. Benign lesions were common in the age group of 61-70yrs, with common symptoms of frequency, difficulty in voiding and acute retention.
3. Prostatitis was commonly encountered in the age group of 61-70yrs.
4. Among 85 cases of benign lesions, 73 cases (85.78%) were diagnosed as Benign prostatic hyperplasia without prostatitis and 12 cases (14.13%) were diagnosed as Benign prostatic hyperplasia with prostatitis.
5. LGPIN accounted for 7 cases. LGPIN were reported in view of complete description of histologic variants. Incidence of isolated HGPIN was low because most of the specimens studied included TURP, which is from transition zone, and HGPIN is common in peripheral zone.
6. Malignant lesions showed a peak incidence in the age group of 61-70 years with a common symptoms of frequency, incomplete voiding and dysuria.
7. In benign lesions serum PSA was normal in 49 cases (57.9%). Modest elevation [4.1-10 ng/ml] was seen in 23 cases (26.81%) and marked elevation [>10 ng/ml] in 13 cases (15.29%) due to associated conditions like chronic prostatitis, granulomatous prostatitis . In malignant prostatic lesion 8 cases (53.3%) showed marked elevation in serum PSA levels (>20 ng/ml).
8. Among the malignant lesions, commonest lesion was prostatic adenocarcinoma (47%).

9. Gleason's microscopic grading was adopted for grading prostatic adenocarcinoma in which the commonest Gleason score was score 7 (57.14%), followed by score 8 (28.57%) and score 9 (14.29%). Low-grade lesions were not encountered probably because these lesions are usually asymptomatic.
10. Acidic mucin was demonstrated in the lumens, in all cases of prostatic adeno carcinoma demonstrated by Alcian Blue pH1 .
11. In this study we did not encounter any case of infarct, calculi, malakoplakia, low- grade adenocarcinoma and other rare variants of malignant neoplasms.

Most of the cases of prostatic adenocarcinoma encountered were of high grade. Since low-grade lesions are usually asymptomatic, awareness of serum PSA level estimation, digital rectal examination should be brought among elderly males who are prone for malignancy. Male individuals with a positive family history for prostatic carcinoma must undergo relevant screening test.

SUMMARY

1) Total of 100 prostatic specimens were included in this study, received in the the pathology laboratory at Dhiraj hospital, piparia- vadodara from January 2016 to January 2017.

2) Most of the specimens received were TURP 90 (90%), followed by needle biopsy 8 (8%) and total prostatectomy 2 (2%).

3) The cases were studied in relation to age, common presenting symptoms and were correlated with serum PSA levels.

4) Benign lesions were seen after the age of 41 years. Benign lesions included benign prostatic hyperplasia without prostatitis (73%) and benign prostatic hyperplasia with prostatitis (12%).

5) 7 cases (7%) of cases showed PIN, of these 7% (7 cases) were LGPIN, which was reported in view of complete description of histologic variants.

6) Out of 12 cases of prostatitis (12%), 10 cases (83.3%) had chronic non-specific prostatitis and 2 cases (16.6%) of granulomatous prostatitis.

7) Clinical diagnosis of prostatic carcinoma was done in 15 cases, out of which 7 cases correlated histologically and one case sent as metastatic transitional cell carcinoma was confirmed to be the same.

8) In benign cases serum PSA was normal in 49 cases (57.9%). Modest elevation [4.1-10 ng/ml] was seen in 23 cases (26.81%) and marked elevation [>10 ng/ml] seen in 13 cases (15.29%).

9) Digital rectal examination finding showed nodularity in 93 cases and hard nodule in 7 cases.

10) Both PIN and malignancy showed peak in the age group of 61-70 years.

11) In the malignant lesion, prostatic adenocarcinoma was the commonest (47%), one case of metastatic transitional cell carcinoma (6.6%) was seen.

12) The commonest pattern encountered in prostatic adenocarcinoma is acinar pattern followed by cribriform, sheets, trabeculae, cords, strands and clear cells.

13) Gleason's microscopic grading was adopted to grade prostatic adenocarcinoma cases and score 7 (57.14%) was the commonest.

14) All cases of adenocarcinoma showed acidic mucin in the lumens as demonstrated by Alcian blue pH1 and all the cases of LGPIN showed negativity for Alcian Blue and positive PASd.

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ANNEXURE – I

INFORMED CONSENT FORM (ICF) FOR PARTICIPANTS IN RESEARCH PROGRAMMES INVOLVING STUDIES ON HUMAN BEINGS

Title of the study: Diagnostic utility of PSA for detection of prostatic lesions

Study No. : SVU / SBKS / _____/2015-2018 _____
Participant's Name:_____
Date of Birth:_____ Age: _____ years

1. I confirm that I have read and understood the information sheet dated _____ for the above study and had the opportunity to ask questions
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without, my medical care or legal right being affected
3. I understand that the investigator to this study, others working on investigator's behalf, the ethics committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study, I agree to this access. However I understand that my identity will not be revealed in any information related to third party or published.
4. I agree not to restrict the use of any data or results that arise from this study, provided such a use is only for scientific purpose(s).
5. I agree to take part in the above study.

Signature/thumb impression of the participant

Date: _____

Legally acceptable representative Signatory's Name _____
Signature of the investigator _____ Date:_____

Study investigator's name _____ _____

Signature of impartial witness _____ Date: _____

Name of the witness_____

ANNEXURE II

હ્યુમન બેઇજિંગ પરના અભ્યાસક્રમોમાં સામેલ અભ્યાસક્રમો માટે સહભાગી સંમતિ (આઈસીએફ)

અભ્યાસનું શીર્ષક: પ્રોસ્ટેટિક જખમની તપાસ માટે પીએસએની ડાયગ્નોસ્ટિક ઉપયોગિતા

અભ્યાસ નંબર: એસવીયુ / એસબીકેએસ / _____ / 2015-2018 _____

સહભાગીનું નામ: _____

જન્મ તારીખ: _____ ઉંમર: _____ વર્ષ

1. હું પુષ્ટિ કરું છું કે મેં ઉપરોક્ત અભ્યાસ માટે _____ ના માહિતી શીટ વાંચી અને સમજી લીધી છે અને પ્રશ્નો પૂછવાની તક મળી છે
2. હું સમજું છું કે અભ્યાસમાં મારી સહભાગિતા સ્વૈચ્છિક છે અને તે કોઈપણ કારણ વગર, કોઈપણ સમયે, મારી તબીબી સંભાળ અથવા કાયદેસરના અધિકારોને પ્રભાવિત કર્યા વગર કોઈપણ સમયે પાછી ખેંચી લેવા માટે મુક્ત છું
3. હું સમજી શકું છું કે આ અભ્યાસમાં તપાસ કરનાર, તપાસકર્તાની વતી કામ કરતા અન્ય લોકો, નૈતિક સમિતિ અને નિયમનકારી સત્તાવાળાઓને વર્તમાન અભ્યાસના સંદર્ભમાં અને આગળ કોઈ સંશોધન માટે, મારા સ્વાસ્થ્યના વિકમોને જોવાની મારી પરવાનગીની જરૂર નથી. તે સંબંધમાં હાથ ધરવામાં આવે છે, જો હું અભ્યાસમાંથી પાછો ખેંચી લો, તો હું આ ઍક્સેસથી સંમત છું જો કે હું સમજી શકું છું કે મારી ઓળખ તૃતીય પક્ષ સાથે સંબંધિત કોઈપણ માહિતીમાં અથવા પ્રકાશિત કરવામાં આવશે નહીં.
4. હું આ અભ્યાસમાંથી જન્મેલા કોઈપણ ડેટા અથવા પરિણામોના ઉપયોગને મર્યાદિત ન કરવા માટે સંમત છું, જો કે આવા ઉપયોગ વૈજ્ઞાનિક હેતુ (ઓ) માટે જ છે.
5. હું ઉપરના અભ્યાસમાં ભાગ લેવા માટે સંમત છું.

સહભાગીની હસ્તાક્ષર / અંગૂઠાની છાપ

તારીખ: _____

કાયદેસરના સ્વીકૃત પ્રતિનિધિ સહી કરનારનું નામ _____

તપાસકર્તાની હસ્તાક્ષર _____ તારીખ: _____

અભ્યાસ તપાસનીસનું નામ _____ _____

નિષ્પક્ષ સાક્ષીના હસ્તાક્ષર _____તારીખ: _____

સાક્ષીનું નામ_____

ANNEXURE III

<u>मानव जाति पर अध्ययन कार्यक्रमों में भागीदारी के लिए भागीदारों के लिए सूचित सहमति पत्र (आईसीएफ)</u>

अध्ययन का शीर्षक: प्रोस्टेटिक घावों का पता लगाने के लिए पीएसए की नैदानिक उपयोगिता

अध्ययन संख्या: एसवीयू / एसबीकेएस / _____ / 2015-2018 _____
प्रतिभागी का नाम: _____
जन्म तिथि: _____ आयु: _____ वर्ष

1. मैं पुष्टि करता हूं कि मैंने उपरोक्त अध्ययन के लिए _____ के सूचना पत्र को पढ़ और समझ लिया है और सवाल पूछने का अवसर मिला है
2. मैं समझता हूं कि अध्ययन में मेरी भागीदारी स्वैच्छिक है और मैं बिना किसी कारण के बिना किसी भी समय वापस लेने के लिए स्वतंत्र हूं, मेरी चिकित्सा देखभाल या कानूनी अधिकार प्रभावित हो सकता है
3. मैं समझता हूं कि इस अध्ययन के अन्वेषक, अन्वेषक की ओर से काम करने वाले अन्य, नैतिकता समिति और नियामक प्राधिकरणों को मेरे मौजूदा स्वास्थ्य अध्ययन के संबंध में मेरे स्वास्थ्य अभिलेखों की जांच करने की मेरी अनुमति की आवश्यकता नहीं होगी, दोनों इसके संबंध में आयोजित, यहां तक कि अगर मैं अध्ययन से वापस लेता हूं, तो मैं इस पहुंच से सहमत हूं। हालांकि मैं समझता हूं कि मेरी पहचान तीसरी पार्टी से संबंधित किसी भी जानकारी या प्रकाशित में प्रकाशित नहीं होगी।
4. मैं इस अध्ययन से उत्पन्न होने वाले किसी भी डेटा या परिणामों के उपयोग को प्रतिबंधित करने के लिए सहमत हूं, बशर्ते इस तरह का उपयोग केवल वैज्ञानिक उद्देश्य (ओं) के लिए है।
5. मैं उपरोक्त अध्ययन में भाग लेने के लिए सहमत हूं।
प्रतिभागी के हस्ताक्षर / अंगूठे का निशान

तारीख: _____

कानूनी रूप से स्वीकार्य प्रतिनिधि हस्ताक्षरकर्ता का नाम _____
जांचकर्ता के हस्ताक्षर _____ दिनांक: _____

अध्ययन अन्वेषक का नाम _____ _____

निष्पक्ष गवाह के हस्ताक्षर _____ दिनांक: _____

साक्षी का नाम_____

ANNEXURE IV

PROFORMA

PARTICIPATION INFORMATION

Name of the patient:

Age:

Sex:

Address:

Occupation:

Education:

Marital status:

Income:

Date of admission:

Date of examination:

IPD/OPD number

ANNEXURE- V

PARTICIPANT INFORMATION SHEET

Study Title:

1. **Introduction**

   Carcinoma of prostate is one of the common tumors of old age in men. With digital rectal examination (DRE), prostate specific antigen (PSA) is a major screening tool for prostate cancer.

2. **What is the purpose of this study?**

   To evaluate the utility of PSA as a method of investigation in diagnosis of prostatic lesion.

3. **Why have I been chosen?**

   Your clinical and laboratory findings coincide with the study which can help us in better evaluation.

4. **Do I have to take part?**

   Participation is of voluntary nature.

5. **How long will the study last?**

   Study will last for one year.

6. **What will happen to me if I take part?**

   After the clinical examination and laboratory investigations no further active participation is required. If need arises, you will be informed.

7. **What do I have to do?**

   You have to give complete medical history along with chief complaints to the clinician. Also blood sample to be given for laboratory investigation.

8. **What is the drug being tested?**

   No drug will be tested in this study.

9. **What are the benefits of the study?**

   This study has both individual and community benefits by early detection of prostatic carcinomas.

10. **What are the alternatives for treatment?**

    Medical drugs and surgical procedures. No active intervention will be performed fro my side.

11. What are the side effects of the treatment received during the study?

There is no side effect of any treatment during study with patient's full co-operation.

12. What if new information becomes available?

It will have a benefit in patient's outcome. But the study will target the issue concern with the topic only.

13. What happens when the study stops?

Error from any parts will be analyzed. Mistakes will be corrected and try to proceed the study. If at all the study stops inspite of these than data will be collected with whatever the study has been done. It will be analyzed using appropriate statistical test like mean, mode, standard deviation or chi- square test.

14. What if something goes wrong?

If any problem develops you can contact:

Dr. Nikita Bansal

Department of Pathology, S.B.K.S MI & RC, Pipariya. Tal. Waghodia. District Vadodara.

Ph. No.- 9824444672

15. Will my taking part be kept confidential?

Information regarding patient's health and other personal facts if any, will be kept confidential.

16. What else should I know?

If need arises, the patient may be contacted to inquire about past, personal and family history. Also religious background, social customs, beliefs etc can be inquired into.

17. Additional Precautions

As such in this study no experiment will be done on patient so there is no issue of adverse effect or risk and so no need of any additional precautions.

18. Who to call with questions?

Dr. Nikita Bansal

Department of Pathology, S.B.K.S MI & RC, Pipariya. Tal. Waghodia. District Vadodara.

Ph. No.- 9824444672

ANNEXURE- VI

પક્ષકાર માહિતી શીટ

અભ્યાસ શીર્ષક:

1. પરિચય

   પરૂષોમાં વૃદ્ધાવસ્થાના સામાન્ય ગાંઠોમાં પ્રોસ્ટેટનો કાર્સિનોમા એક છે. ડિજિટલ રેક્ટલ પરીક્ષા (ડીએઆરઇ) સાથે, પ્રોસ્ટેટ વિશિષ્ટ એન્ટિજેન (પીએસએ) પ્રોસ્ટેટ કેન્સર માટે એક મુખ્ય સ્ક્રિનિંગ ટૂલ છે.

2. આ અભ્યાસનો હેતુ શું છે?

   પ્રોસ્ટેટિક જખમના નિદાનમાં તપાસની એક પદ્ધતિ તરીકે પીએસએની ઉપયોગિતાનું મૂલ્યાંકન કરવું.

3. શા માટે મને પસંદ કરવામાં આવ્યા છે?

   તમારી ક્લિનિકલ અને પ્રયોગશાળાના તારણો અભ્યાસ સાથે સંબંધ ધરાવે છે જે અમને વધુ મૂલ્યાંકન કરવામાં મદદ કરી શકે છે.

4. શું મને ભાગ લેવાની જરૂર છે?

   સહભાગી સ્વૈચ્છિક સ્વભાવનું છે.

5. અભ્યાસ કેટલા સમય સુધી ચાલશે?

   અભ્યાસ એક વર્ષ માટે ચાલશે.

6. જો હું ભાગ લેતો હોઉં તો શું થશે?

   ક્લિનિકલ પરીક્ષા અને પ્રયોગશાળા તપાસ પછી કોઈ વધુ સક્રિય ભાગીદારી જરૂરી નથી. જો જરૂર ઊભી થાય તો તમને જાણ કરવામાં આવશે.

7. મારે શું કરવું છે?

   તમારે મુખ્ય ફરિયાદો સાથે તબીબી ઇતિહાસમાં સંપૂર્ણ તબીબી ઇતિહાસ આપવો પડશે. લેબોરેટરી તપાસ માટે પણ રક્ત નમૂના આપવામાં આવશે.

8. ડ્રગ કેવી રીતે પરીક્ષણ કરવામાં આવે છે?

   આ અભ્યાસમાં કોઈ ડ્રગની ચકાસણી કરવામાં આવશે નહીં.

9. અભ્યાસના લાભો શું છે?

   પ્રોસ્ટેટિક કાર્સિનોમાના પ્રારંભિક શોધ દ્વારા આ અભ્યાસમાં બંને વ્યક્તિગત અને સમુદાય લાભો છે.

10. સારવાર માટેના વિકલ્પો શું છે?
    તબીબી દવાઓ અને શસ્ત્રક્રિયાની પ્રક્રિયાઓ મારી બાજુથી કોઈ સક્રિય હસ્તક્ષેપ કરવામાં આવશે નહીં.
11. અભ્યાસ દરમ્યાન મળેલ સારવારની આડઅસરો શું છે?
    દર્દીના સંપૂર્ણ સહકાર સાથે અભ્યાસ દરમિયાન કોઈપણ સારવારની કોઈ આડઅસર નથી.
12. જો નવી માહિતી ઉપલબ્ધ થાય તો શું?
    તે દર્દીના પરિણામ માં લાભ મેળવશે. પરંતુ આ મુદ્દો માત્ર વિષય સાથેની સમસ્યાને લક્ષમાં રાખશે.
13. જ્યારે અભ્યાસ બંધ થાય છે ત્યારે શું થાય છે?
    કોઈપણ ભાગમાંથી ભૂલનું વિશ્લેષણ કરવામાં આવશે. ભૂલો સુધારવામાં આવશે અને અભ્યાસ આગળ વધવાનો પ્રયાસ કરશે. જો તમામ અભ્યાસમાં અટકાયેલો હોય તો ડેટા કરતાં આનો તફાવત હોવા છતાં અભ્યાસ ગમે તે કરવામાં આવે છે. તેનો અર્થ સરેરાશ, સ્થિતિ, પ્રમાણભૂત વિચલન અથવા ચી-ચોરસ ટેસ્ટ જેવા યોગ્ય આંકડાકીય પરીક્ષણનો ઉપયોગ કરીને કરવામાં આવશે.
14. જો કંઈક ખોટું થાય તો શું?
    જો કોઇ સમસ્યા વિકસે તો તમે સંપર્ક કરી શકો છો:
    ડો નિકિતા બંસલ
    ડિપાર્ટમેન્ટ ઓફ પેથોલોજી, એસ.બી.કે.એસ.એમ.આઈ. એન્ડ આરસી, પિપરિયા. તાલ વાઘોડિયા જીલ્લા વડોદરા
    ફોન નંબર- 9824444672
15. શું મારો ભાગ ગુપ્ત રાખવામાં આવશે?
    દર્દીના સ્વાસ્થ્ય અને અન્ય અંગત હકીકતો જો કોઈ હોય તો તેની માહિતી, ખાનગી રાખવામાં આવશે.
16. વાટ્સ બીજું હું જાણું છું?
    જો જરૂર ઊભી થાય તો દર્દીને ભૂતકાળ, વ્યક્તિગત અને પારિવારિક ઇતિહાસ વિશે પૂછપરછ કરવા માટે સંપર્ક કરી શકાય છે. પણ ધાર્મિક પૃષ્ઠભૂમિ, સામાજિક રિવાજો, માન્યતાઓ વગેરે માં તપાસ કરી શકાય છે.

17. વધારાની સાવચેતીઓ

    જેમ કે આ અભ્યાસમાં દર્દી પર કોઈ પ્રયોગ કરવામાં આવશે નહીં, તેથી પ્રતિકૂળ અસર અથવા જોખમનો કોઈ મુદ્દો નથી અને તેથી કોઈ વધારાની સાવચેતીની જરૂર નથી.

18. પ્રશ્નો સાથે કોને કૉલ કરવો?

    ડો નિકિતા બંસલ

    ડિપાર્ટમેન્ટ ઓફ પેથોલોજી, એસ.બી.કે.એસ.એમ.આઈ. એન્ડ આરસી, પિપરિયા. તાલ વાઘોડિયા જીલ્લા વડોદરા

    ફોન નંબર- 9824444672

ANNEXURE-VII

भाग लेने वाली सूचना पत्र

अध्ययन शीर्षक:

1. परिचय

   प्रोस्टेट का कार्सिनोमा पुरुषों में बुढ़ापे के आम ट्यूमर में से एक है। डिजिटल रेक्टल परीक्षा (डीआरई) के साथ, प्रोस्टेट विशिष्ट एंटीजन (पीएसए) प्रोस्टेट कैंसर के लिए एक प्रमुख स्क्रीनिंग टूल है।

2. इस अध्ययन का उद्देश्य क्या है?

   प्रोस्टेटिक घाव के निदान में पीएसए की जांच की एक विधि के रूप में उपयोगिता का मूल्यांकन करने के लिए।

3. मुझे चुना गया है क्यों?

   आपकी नैदानिक और प्रयोगशाला के निष्कर्ष अध्ययन के साथ मेल खाते हैं जो हमें बेहतर मूल्यांकन करने में सहायता कर सकते हैं।

4. क्या मुझे भाग लेना है?

   सहभागिता स्वैच्छिक प्रकृति का है।

5. अध्ययन पिछले कितने समय तक होगा?

   अध्ययन एक वर्ष तक चलेगा।

6. अगर मैं भाग लेता हूं तो मेरे साथ क्या होगा?

   नैदानिक परीक्षा और प्रयोगशाला जांच के बाद और सक्रिय भागीदारी की आवश्यकता नहीं है। यदि जरूरत पड़ी तो आपको सूचित किया जाएगा।

6. मुझे क्या करना है?

   आपको मुख्य शिकायतों के साथ चिकित्सकीय को पूरा चिकित्सा का इतिहास देना होगा इसके अलावा प्रयोगशाला जांच के लिए रक्त का नमूना दिया जाना चाहिए।

8. क्या दवा का परीक्षण किया जा रहा है?

   इस अध्ययन में कोई दवा का परीक्षण नहीं किया जाएगा।

9. अध्ययन के क्या लाभ हैं?

इस अध्ययन में प्रोस्टेटिक कार्सिनोमा का पता लगाने के लिए व्यक्तिगत और सामुदायिक लाभ दोनों हैं।

10. उपचार के विकल्प क्या हैं?

चिकित्सा दवाओं और शल्यचिकित्सा प्रक्रियाएं मेरी तरफ से कोई सक्रिय हस्तक्षेप नहीं किया जाएगा।

11. अध्ययन के दौरान प्राप्त उपचार के दुष्प्रभाव क्या हैं?

रोगी के पूर्ण सहयोग के अध्ययन के दौरान किसी भी उपचार का कोई दुष्प्रभाव नहीं है।

12. यदि नई जानकारी उपलब्ध हो तो क्या होगा?

रोगी के नतीजे में इसका लाभ होगा। लेकिन अध्ययन केवल विषय के साथ ही इस मुद्दे की चिंता को लक्षित करेगा।

13. जब अध्ययन बंद हो जाता है तो क्या होता है?

किसी भी हिस्से से त्रुटि का विश्लेषण किया जाएगा। गलतियां ठीक हो जाएंगी और अध्ययन आगे बढ़ने का प्रयास करें। यदि सभी अध्ययनों में स्टैप्स बंद हो जाता है तो डेटा के मुकाबले इनके बावजूद अध्ययन किया जाएगा। यह उचित सांख्यिकीय परीक्षण जैसे कि माध्य, मोड, मानक विचलन या ची स्क्वायर टेस्ट का उपयोग करके विश्लेषण किया जाएगा।

14. अगर कुछ गलत हो जाए तो क्या होगा?

अगर कोई समस्या विकसित होती है तो आप संपर्क कर सकते हैं:

डॉ। निकिता बंसल

पैथोलॉजी विभाग, एसबीकेएस एमआई एंड आर सी, पिपरिया ताल। जिला वडोदरा, फोन नंबर- 9824444672

15. क्या मेरी हिस्सेदारी गोपनीय रखी जाएगी?

रोगी के स्वास्थ्य और अन्य व्यक्तिगत तथ्यों, यदि कोई हो, के बारे में जानकारी गोपनीय रखी जाएगी।

16. मुझे और क्या पता होना चाहिए?

अगर जरूरत पड़ी तो, मरीज को पिछले, व्यक्तिगत और पारिवारिक इतिहास के बारे में पूछताछ करने के लिए संपर्क किया जा सकता है इसके

अलावा धार्मिक पृष्ठभूमि, सामाजिक रीति-रिवाज, विश्वास आदि की जांच कर सकते हैं।

17. अतिरिक्त सावधानी

जैसे कि इस अध्ययन में रोगी पर कोई प्रयोग नहीं किया जाएगा, इसलिए प्रतिकूल प्रभाव या जोखिम का कोई मुद्दा नहीं है और इसलिए किसी भी अतिरिक्त सावधानी की आवश्यकता नहीं है।

18. प्रश्न पूछने वाले कौन?

डॉ। निकिता बंसल

पैथोलॉजी विभाग, एसबीकेएस एमआई एंड आर सी, पिपरिया ताल। जिला वडोदरा

फोन नंबर- 9824444672

ANNEXURE-VIII

LIST OF ABBREVATIONS

BPH	Benign Prostatic Hyperplasia
PSA	Prostate Specific Antigen
DRE	Digital Rectal Examination
H&E	Haematoxylin And Eosin
HGPIN	High Grade Prostatic Intraepithelial Neoplasm
LGPIN	Low Grade Prostatic Intraepithelial Neoplasm
IHC	Immunohistochemistry
PAS	Periodic acid Schiff
PASd	Periodic Acid Schiff Diastase
PAP	Prostatic Acid Phosphatase
TURP	Transurethral Resection Of Prostate
TRUS	Transrectal ultrasound
PIN	Prostatic Intraepithelial Neoplasia
BCH	Basal Cell Hyperplasia
SCC	Squamous Cell Carcinoma
PDGF	Platelet derived growth factor
UTI	Urinary tract infection
BCG	Bacille Calmette Guerin
PSMA	Prostate specific membrane antigen
SPP	Suprapubic prostatectomy
AFB	Acid fast bacilli
LCA	Leucocyte Common Antigen
WHO	World Health Organization

ANNEXURE-IX

KEY TO MASTER CHART

Clinical investigations

DRE	Digital rectal examination
PSA	Prostate specific antigen
TURP	Transurethral resection prostate

Microscopy

G. Hyp	Glandular hyperplasia
FMH	Fibromuscular hyperplasia
TR MT	Transitional Metaplasia
CC METP	Clear cell cribriform hyperplasia
SQ METP	Squamous metaplasia
MONO	Mononuclear cells
BCH	Basal cell hyperplasia
PIN	Prostatic intraepithelial neoplasia
C/S	Urine culture and sensitivity
CA	Carcinoma
GL SCR	Gleason score
Final	Final histopathological diagnosis
BPH	Benign Prostatic hyperplasia
LGPIN	Low-grade prostatic intraepithelial neoplasia
TCC	Transitional cell carcinoma

MASTER CHART

Sl. No.	Age (Yrs)	clinical investigations		clinical diagnosis	GROSS		Microscopy									GL SCR	Final
		DRE	PSA (ng/ml)			G.Hyp	FMH	TR MT	CC METP	SQ METP	MO NO	BCH	PIN	Others	CA		
1	75	nodularity	3.2	BPH	TURP,10cc	+	+										BPH
2	55	hard nodule	38	?Ca	TURP, 10cc	+	+								nests,comedo,cords,cribr iform, perinural invasion	9	Adenocarcinoma - High-grade
3	70	nodularity	2.1	BPH	TURP, 5cc	+	+				+			prostatitis			BPH with prostatitis
4	55	nodularity	3	BPH	TURP, 4cc	+	+	+									BPH
5	70	nodularity	2.3	BPH	TURP, 5cc	+	+	+									BPH
6	75	nodularity	2.72	BPH	TURP 10cc	+	+					+					BPH
7	67	nodularity	32	?Ca	TURP, 8cc	+	+								cribriform,trabeculae, sheets,inflam, HGPIN	8	Adenocarcinoma - High-grade
8	65	nodularity	98	?Ca	TURP, 10cc	+	+								small acinar,sheets,trabeculae, inflam, HGPIN	7	Adenocarcinoma - High-grade
9	75	nodularity	1.46	BPH	TURP, 5cc	+	+										BPH
10	77	nodularity	4.2	BPH	TURP, 10cc	+	+										BPH
11	65	nodularity	4.32	BPH	TURP, 10cc	+	+					+					BPH
12	65	nodularity	7.6	BPH	TURP, 5cc	+	+										BPH
13	53	nodularity	3.2	BPH	TURP, 5cc	+	+										BPH
14	65	nodularity	5.8	BPH	TURP, 10cc	+	+	+									BPH
15	69	nodularity	3.23	BPH	TURP, 7cc	+	+										BPH
16	54	nodularity	16.45	BPH	TURP, 10cc	+	+				+			Prostatitis, C/S- E. coli			BPH with prostatitis
17	73	nodularity	3.2	BPH	TURP 5cc	+	+			+							BPH
18	62	nodularity	3.2	BPH	TURP, 5cc	+	+										BPH
19	70	nodularity	0.49	BPH	TURP, 6cc	+	+								Perineural invasion smal acinar,sheets,cords,trabeculae	8	Adenocarcinoma - High-grade
20	71	nodularity	5.24	BPH	TURP, 10cc	+	+			+							BPH
21	75	nodularity	2.1	BPH	TURP, 30cc	+	+					+					BPH
22	76	nodularity	8.26	BPH	TURP, 7cc	+	+	+									BPH
23	62	nodularity	3.2	BPH	TURP, 5cc	+	+	+									BPH
24	57	nodularity	0.21	BPH	TURP, 4cc	+	+		+								BPH
25	45	nodularity	2.1	BPH	TURP, 3cc	+	+										BPH
26	82	nodularity	2.1	BPH	TURP, 5cc	+	+										BPH
27	85	nodularity	9.86	BPH	Needlebiopsy	+	+				+			prostatitis, C/S- Pseudomonas			BPH with prostatitis
28	85	nodularity	9.86	BPH	TURP, 6cc	+	+										BPH

MASTER CHART

Sl. No.	Age (Yrs)	clinical investigations		clinical diagnosis	GROSS		Microscopy									GL SCR	Final
		DRE	PSA (ng/ml)			G.Hyp	FMH	TR MT	CC METP	SQ METP	MO NO	BCH	PIN	Others	CA		
29	60	nodularity	5.46	BPH	TURP, 2cc	+	+										BPH
30	41	nodularity	2.1	BPH	TURP, 4 cc	+	+				+			prostatitis			BPH with prostatitis
31	70	nodularity	5.2	BPH	TURP, 6cc	+	+						LG PIN				LGPIN
32	60	nodularity	86	?Ca	Needle biopsy		plus	plus							small acinar,cords,sheets	7	Adenocarcinoma - High-grade
33	85	nodularity	1	BPH	TURP, 40 cc	+	+						LG PIN				LGPIN
34	65	nodularity	15.22	BPH	TURP, 20 cc	+	+	+									BPH
35	60	nodularity	12	BPH	TURP, 3 cc	+	+										BPH
36	60	nodularity	1.13	BPH	TURP, 10 cc	+	+										BPH
37	82	nodularity	3.8	BPH	TURP, 5 cc	+	+										BPH
38	65	nodularity	3	BPH	TURP, 5 cc	+	+			+							BPH
39	65	nodularity	1.2	BPH	TURP, 5 cc	+	+										BPH
40	70	nodularity	4.17	BPH	TURP, 20 cc	+	+										BPH
41	70	nodularity	0.9	BPH	TURP, 8 cc	+	+	+									BPH
42	58	nodularity	2.4	BPH	TURP, 8 cc	+	+				+			prostatitis, C/S-enterococcus			BPH with prostatitis
43	70	nodularity	7.26	BPH	TURP, 20 cc	+	+										BPH
44	70	nodularity	3	BPH	TURP, 20 cc	+	+										BPH
45	65	nodularity	4.2	BPH	TURP, 10 cc	+	+										BPH
46	70	hard nodule	20.9	?Ca	Needle biopsy		+							C/S-Klebsiella	small acinar, cords, sheets,	7	Adenocarcinoma: High grade
47	75	hard nodule	24.8	?Ca	Needle biopsy	+	+										BPH
48	75	hard nodule	24.8	?Ca		+	+				+			prostatitis			BPH with prostatitis
49	76	nodularity	5.2	BPH	TURP, 10 cc	+	+										BPH
50	61	nodularity	1.2	BPH	TURP, 10 cc	+	+										BPH
51	60	nodularity	1.2	BPH	TURP, 10 cc	+	+										BPH
52	75	hard nodule	21	?Ca	Needle biopsy	+	+										BPH
53	50	nodularity	6	BPH	TURP, 5 cc	+	+										BPH
54	80	nodularity	16	BPH	TURP, 25 cc	+	+						LG PIN				LGPIN
55	60	nodularity	32	BPH	Needle biopsy	+	+										BPH
56	72	nodularity	0.3	BPH	TURP, 20 cc	+	+										BPH
57	60	nodularity	32	BPH	TURP, 10 cc	+	+										BPH
58	70	nodularity	25.12	BPH	TURP, 12 cc	+	+										BPH

MASTER CHART

Sl. No.	Age (Yrs)	clinical investigations		clinical diagnosis	GROSS		Microscopy									GL SCR	Final
		DRE	PSA (ng/ml)			G.Hyp	FMH	TR MT	CC METP	SQ METP	MO NO	BCH	PIN	Others	CA		
59	60	nodularity	1.65	BPH	TURP, 5cc	+	+										BPH
60	69	nodularity	1.14	BPH	TURP, 5 cc	+	+										BPH
61	54	nodularity	21.20	BPH	TURP, 10 cc	+	+						LG PIN				LGPIN
62	69	nodularity	9.47	BPH	TURP, 20cc	+	+							granulomatous AFB-ve			BPH with granulomatous prostatitis
63	52	nodularity	6.32	BPH	TURP, 10 cc	+	+										BPH
64	50	nodularity	0.8	BPH	TURP, 10 cc	+	+										BPH
65	45	nodularity	4	BPH	TURP, 5 cc	+	+										BPH
66	48	nodularity	3	BPH	TURP, 8 cc	+	+						LGPIN				LGPIN
67	70	nodularity	2.6	BPH	TURP, 20 cc	+	+										BPH
68	52	nodularity	0.4	BPH	TURP, 10 cc	+	+										BPH
69	50	nodularity	0.6	BPH	TURP, 6 cc	+	+										BPH
70	55	nodularity	5	BPH	TURP, 4 cc	+	+										BPH
71	68	nodularity	21.72	BPH	TURP, 8 cc	+	+				+			Prostatitis, C/S-Klebsiella			BPH with prostatitis
72	72	nodularity	2.8	BPH	TURP, 20 cc	+	+										BPH
73	60	nodularity	4.8	BPH	TURP, 15 cc	+	+										BPH
74	78	nodularity	3	BPH	TURP, 1 cc	+	+										BPH
75	71	nodularity	28.0	BPH	TURP, 15 cc	+	+						LG PIN				LGPIN
76	65	nodularity	4	BPH	TURP, 2 cc	+	+										BPH
77	63	nodularity	3.2	BPH	TURP, 2 cc	+	+										BPH
78	65	nodularity	2.2	BPH	TURP, 5 cc	+	+										BPH
79	53	nodularity	11	BPH	TURP, 5 cc	+	+							granulomatous, AFB - Ve			BPH with granulomatous prostatitis
80	71	nodularity	1	BPH	TURP, 5 cc	+	+										BPH
81	61	nodularity	6.35	BPH	TURP, 10 cc	+	+										BPH
82	75	nodularity	8.4	BPH	TURP, 5 cc	+	+						LG PIN				LGPIN
83	65	nodularity	0.8	BPH	Prostatectomy	+	+										BPH
84	66	nodularity	29.3	?Ca	Needle biopsy	+	+				+			Prostatitis, C/S-Klebsiella			BPH with prostatitis
85	70	hard nodule	23.3	?Ca	TURP, 4 cc	+	+								small acinar,cribriform, HGPIN	7	Adenocarcinma High- Grade

MASTER CHART

Sl. No.	Age (Yrs)	clinical investigations		clinical diagnosis	GROSS		Microscopy								GL SCR	Final
		DRE	PSA (ng/ml)			G.Hyp	FMH	TR MT	CC METP	SQ METP	MO NO	BCH	PIN	Others	CA		
86	70	nodularity	6.6	BPH	TURP, 6 cc	+	+										BPH
87	65	nodularity	0.6	BPH	TURP, 10 cc	+	+										BPH
88	65	nodularity	4.75	BPH	TURP, 10 cc	+	+										BPH
89	85	nodularity	2.2	BPH	TURP, 10 cc	+	+				+			Prostatitis			BPH with prostatitis
90	65	nodularity	2.86	BPH	TURP, 10 cc	+	+										BPH
91	70	nodularity	1.8	BPH	TURP, 10 cc	+	+										BPH
92	60	nodularity	3.2	BPH	TURP, 15 cc	+	+				+			prostatitis, C/S-E-coli			BPH with prostatitis
93	65	hard nodule	12	?Ca	TURP, 15 cc	+	+								TCC bladder		TCC bladder
94	78	nodularity	20.2	BPH	Needle biopsy	+	+										BPH
95	69	nodularity	4	BPH	TURP, 15 cc	+	+	+									BPH
96	65	nodularity	2.8	BPH	TURP, 20 cc	+	+										BPH
97	60	nodularity	8.83	BPH	TURP, 20 cc	+	+	+									BPH
98	70	nodularity	16.8	BPH	Prostatectomy	+	+										BPH
99	80	nodularity	1.07	BPH	TURP, 10 cc	+	+										BPH
100	70	nodularity	2.7	BPH	TURP, 20 cc	+	+										BPH