Jimma University

Faculty of medical sciences

Department of Pathology

Histopathological Patterns of Prostate Biopsy in Jimma University Medical Center, Jimma, Southwest Ethiopia: A Five-year retrospective study

By: Lijalem Birhane (MD)

A Research Thesis Submitted to Jimma University Department of Pathology for Partial Fulfillment of Post Graduate Diploma in Human Anatomic Pathology

August 2020

Jimma, Ethiopia

Histopathological Patterns of prostate Biopsy to Jimma University Medical Center, Jimma, Southwest Ethiopia

A five-year retrospective cross-sectional study

By: Lijalem Birhane (MD)

Advisers:

Gebi Nemo (MD, Assistant professor of pathology)

Kifle Woldemichael (MD, MPH, professor of Epidemiology)

August 2020

Jimma, Ethiopia

Summary

Introduction: the frequency of prostate disorders, such as prostatitis, benign hyperplasia, and carcinomas that are sent to pathology for diagnosis, is increasing. Histological examination is important because different disorders can be diagnosed with the best accuracy. Benign prostate hypertrophy is a common disorder of the prostate. The prevalence of BPH increases from 20% at 40 years of age to 90% by the eighth decade of life. Prostate cancer is one of the most common malignancies in men. Compared with European Americans, African American men are 1.7 times more likely to develop prostate cancer, are generally younger at diagnosis and are approximately 2.5 times more likely of dying from the disease

Objective: To identify histopathologic patterns of prostate biopsy, seen at the pathology department of Jimma university medical center, from Sept. 2014 to Aug 2019.

Method: a hospital-based retrospective cross-sectional study design was applied to records of patients seen at JUMC pathology department with a prostate specimen conducted from September 2014 to August 2019. Data was collected using structured checklists manually by histopathology technicians working in the department. Data were entered into Epi data v.3.1., cleared and exported to SPSS V.23 for analysis

Result: There were 235 cases of patients with prostate mass. All were broadly classified into benign in 181 (77.02%) cases, intraepithelial neoplasm in 4(1.7%), and malignant in 50 (21.28%) cases. The age of the patients ranged from 42 to 87 years, with the mean age of 65.40±9.24 years. The age group 60-69 (7^{th} decade) was in which most cases 102 (43.4%) were seen. Benign Prostatic Hyperplasia (BPH) was the most common histological lesion in 181 cases (77.02%) and of these BPH 47 (26.11%) were associated with prostatitis. Out of 50 cases of prostatic cancer, adenocarcinoma was the most common histological type encountered in 49 (98%) cases and a single rhabdomyosarcoma.

Conclusion: The pattern of prostatic diseases in JUMC was found to be similar to other reports in Africa and the world. BHP was the most encountered lesion seen in the prostate and was associated with prostatitis. seventh decade was the age group both BPH and malignancy most found.

Keywords: histopathology, prostate, hyperplasia, cancer.

Acknowledgment

I am very grateful to my advisors, Dr. Gebi Nemo, and prof. Kifle Woldemichael for their scholarly guidance, provision of materials, commenting, and correcting this work and continuous encouragement throughout the work.

I am also grateful to Jimma University and Pathology Department for their support.

Table of Contents

Abbreviations/Acronyms

AAH ……..atypical adenomatous hyperplasia

BBJ ……. ...BioBank Japan

BCH ……..……..basal cell hyperplasia

BPH……. ……benign prostatic hyperplasia

COID19…….corona virus disease 2019

DRE …….digital rectal examination

EAU …….Europian Urological association

GS ……Gleason score and Gleason sum

HGPIN …….……High grade prostatic intraepithelial neoplasia

HPP …….……histopathologic patterns

IEN …….. Intraepithelial Neoplasms

IDCP …… ..……Intraductal carcinoma of the prostate

JUMC…….Jimma University medical center

LUTS ……Lower urinary tract symptoms

PIEN …… …..…..prostatic intraepithelial neoplasia

PPE ……...Personal protective equipment

PSA …….……..prostate-specific antigen

PSAP ……prostate-specific acid phosphatase

SAPCS ……Southern Africa Prostate Adenocarcinoma Study

SEER ……Surveillance, Epidemiology, and End Results

SPSA …….…….……..serum prostatic specific antigen

TUR …….……. ……..transurethral resection

TURP ……..……..transurethral resection of the prostate

Lists of tables

Lists of figures

Chapter one: INTRODUCTION

1.1 Background

The prostate is a round-shaped glandular organ that weighs up to 20g within the normal man and depends on its differentiation and subsequent growth on androgenic hormones [1,2]. It is most commonly divided into the anterior fibro-muscular stroma and three distinct glandular zones: peripheral zone, transition zone, central zone [1].

The prostate can be divided into the outer larger zone and the inner smaller zone and the outer zone is composed of large branched glands and is a site for cancer whereas the inner zone is composed of submucosal glands and is a site for Benign Prostatic Hyperplasia [2].

The glandular component of the organ is commonly divided into acini and ducts, little morphologic difference between the two. Both contain luminal secretory cells, a surrounding outer layer of basal cells, and scattered neuroendocrine cells. Histologically, secretary cells form an undulating luminal surface and are characterized by relatively pale cytoplasm that contains minute closely packed vacuoles [1].

Histological examination is important for prostatic disorders because different disorders can be diagnosed with the best possible accuracy. It surpasses all other methods by having the highest diagnostic accuracy, differentiating acute from chronic conditions. Furthermore, it is important for evaluating grades of tumors, response to therapy, the staging of diseases, metastasis and most importantly differentiating benign lesions from malignant lesions [2, 3].

Benign prostatic hypertrophy is a common benign disorder of the prostate which represents a nodular enlargement of the gland caused by hyperplasia of both glandular and stromal components [1].

Prostate cancer is one of the most common malignancies in men whose prevalence increases with age. Due to its importance and prevalence, screening tests are performed annually after the age of 50 and even at lower ages in people with a positive family history [4].

The known risk factors for prostate malignancies include increasing age, family history, and African ancestry. Compared with European Americans, African American men are 1.7 times more likely to develop prostate cancer, are generally younger at diagnosis,

present with a more aggressive disease phenotype, and are approximately 2.5 times more likely of dying from the disease [5, 6].

The Gleason grading system is unusual in that it is based entirely on architectural features of the tumor, rather than the cytological appearances, and is not based on the worst pattern. The Gleason score (GS) takes into account the two most common patterns that are present [7].

Grading of conventional prostatic adenocarcinoma using the (modified) Gleason system is the strongest prognostic factor for clinical behavior and treatment response. The Gleason score is incorporated in nomograms that predict disease-specific survival after prostatectomy [6]. For a grading system to be successful, three criteria must be met: (i) prognostic ability exceeding clinical parameters, (ii) reproducibility among pathologists, and (iii) grading results on random biopsies sufficiently representative for entire cancer [8].

Gleason scores were assigned to grade groups, from 1 to 5, to better reflect the prognostic implications Although Gleason scores theoretically range from 2 to 10, the lowest score assigned in contemporary practice is 6 [7, 9].
Intraductal carcinoma of the prostate (IDC-P) is an intraluminal growth of carcinoma cells within acini and/or ducts with histological features exceeding and more alarming than those for high-grade prostatic intraepithelial neoplasia (PIEN) [9].

The 2014 ISUP consensus recommended not grading IDC-P. The presence of IDC-P should be subtracted when grading the concurrent admixed invasive carcinoma, IDC-P is isolated no grade should be reported [9].
Secretary cells produce prostate-specific acid phosphatase (PSAP) and prostate-specific antigen (PSA), which have been proved of great diagnostic utility because of their organ-related specificity [1]. PSA is another means for prostate cancer diagnosis. The normal level of PSA which varies with age is as follows up to 49 years (2.5 ng/dl), Up to 59 years:(3.5 ng/dl), Up to 69 years (4.5 ng/dl) and Up to 79 years (6.5 ng/dl.) are expected [11]. EAU guidelines classifies PSA score to low-risk (<10ng/ml), intermediate-risk (10-20 ng/ml) and high- risk (>20ng/ml) [6, 10].

1.2 statement of the problem

Diseases of the prostate gland are an important source of morbidity and mortality in male patients. The spectrum of diseases consists of inflammatory conditions, nodular hyperplasia, malignancy, etc. The risk of diseases increases with age. Prostate biopsy is essentially a test that detects cancer and other benign conditions of the prostate in patients who have specific indications for it. Biopsy with the histopathological examination is the gold standard for the final diagnosis [1, 11].

Benign prostatic hyperplasia is a frequent urological condition in men. The prevalence of BPH increases from 20% at 40 years of age to 90% by the eighth decade of life [12].

It has been established that prostatic nodular hyperplasia occurs only in individuals with intact testes and that it is an androgen-dependent disorder and the treatment for nodular hyperplasia includes medical or surgical management. The involved area may be excised by various techniques, such as transurethral resection (TUR), suprapubic prostatectomy, and laser enucleation [1].

The other pathologic conditions are an inflammatory condition of the prostate, prostatitis; -which is categorized into two based on duration. Acute prostatitis is rarely seen in surgical specimens. Chronic prostatitis is more common and diagnosed along with other patterns. Pathologists do not report the presence of chronic inflammation on biopsy unless it is quite marked and only with the descriptive term "marked chronic inflammation." Prostatitis is often accompanied by elevation of serum **PSA**, particularly following a digital rectal examination [1, 13].

Cancer is one of the leading causes of morbidity and mortality worldwide with an estimated 14.1 million new cancer cases occurring in 2012. It is now the third leading cause of death worldwide with 8.2 million deaths in 2012 [14].

Another spectrum of the disease is carcinoma of the prostate, the most common internal malignancy among men in the US, and is responsible for 10% of cancer deaths in this population and an estimated 180,890 new cases of prostate cancer were diagnosed in 2016. Rates among black males are one and a half times that of white males. Its incidence is low in patients with hyper-estrogenism resulting from liver cirrhosis [1].

Prostate cancer represents the second and fourth leading cause of cancer incidence and mortality among men worldwide. In 2012, 1.1 million cases were recorded, resulting in

307,000 deaths) [1]. Prostate cancer represents the third and sixth leading cause of cancer incidence and mortality in Japan with 73,145 men diagnosed in 2012 and 11,507 prostate-cancer related deaths recorded in 2014 [15].

In Europe, prostate cancer is the most common solid neoplasm, with an incidence rate of 214 cases per 1000 men, outnumbering lung, and colorectal cancer [6, 16].

In Africa cancer is emerging as a critical public health problem. In 2008, an estimate of 715,000 new cancer cases and 542,000 cancer deaths occurred in Africa [17]. In sub-Saharan African countries cancers of prostate (20.3%), liver (9.7%), and Kaposi – sarcoma (9.2%) are the three commonest cancers in males [18].

In Ethiopia, the entire number of latest cancer cases among males altogether ages in 2018, is 21200. The prostate is 1701 (8%) and the fourth leading cancer causes after; leukemia, Colo-rectal CA, and non- Hodgkin lymphoma [14].

In Ethiopia, similar to other low-income countries, non-communicable diseases including cancer are emerging. Prostate cancer is the third most incident cancer next to breast and cervical. In 2015, there were 2269 estimated new patients of prostate cancer in Ethiopia. The 2017 Global Burden of Disease estimation for Ethiopia indicates prostate cancer caused 1851 deaths and 33,056 disability-adjusted life years [19].

According to the latest WHO data published in 2017, Prostate Cancer Deaths in Ethiopia reached 1,335(0.21%) of total deaths. The age-adjusted Death Rate of 6.62 per 100,000 population ranks Ethiopia #154 in the world [13, 20].

Almost 75% of the men diagnosed with prostate cancer are age 65 or older, but the tumors can be seen in younger patients. Their frequency increases with age, a fact well substantiated by careful observations at autopsy [1].

Age at diagnosis has dramatically reduced over time as a direct consequence of PSA screening, leading to earlier stage at diagnosis. Lack of PSA screening contributes to increased overall age at prostate carcinoma diagnosis within the SAPCS compared with the SEER study (mean 71.0 years, range 49–101 years) with significant age differences (P=0.0046) when comparing urban (mean 69.2 years) and rural localities (mean 71.8 years) [5].

Prostatic carcinomas can be divided into two major histologic categories which are acinar and ductal. The large majority of the tumors are acinar, and most studies dealing with grading, staging, prognosis, and therapy of prostatic carcinoma refer exclusively to them [1,7].

Specimen types received from the prostate include the following: prostate biopsies (transrectal- transperineally), transurethral resections, enucleations, radical prostatectomies, and lymphadenectomies [3].

1.3 significance of the study

Researches show that there is a significant variation in prostatic disease distribution in different geographic areas of the world. In addition to this, the research done in Ethiopia is scarce; so, this research will be a good supplementary material for different clinical practices and baseline for other researches.

The current study aims to present the overall histological perspective of benign and malignant prostate disease as seen in our practice. Different researches done on prostate show prostate diseases are common health problems among old age and black Africans and so, this research is also important in assessing the relations of PSA to prostatic cancer for early detection and also screening.

In light of this and the need to improve patient outcomes in our environment, this study aims to describe the pattern of presentation of prostate lesions in Jimma University medical center, Jimma, Ethiopia. It is hoped that the information obtained will help guide the formation and establishment of protocols which are geared towards improving the morbidity and mortality associated with this disorder in our environment.

Chapter two: Literature review

2.1 General overview

Each prostatic sample is generally grouped into non-neoplastic and neoplastic. Each category was then sub-classified into specific types according to the standard classification systems [12]. Benign prostatic hyperplasia and adenocarcinoma are the two most common conditions affecting the prostate gland [1, 11, 21].

Worldwide, the incidence of prostate cancer is growing, in particular in low- and middle-income countries. It is the most common cancer among men worldwide, with higher mortality in low and middle-income countries [19].

In Ethiopia, it is the second most common cause of cancer morbidity and mortality among men. Despite a few studies done regarding the disease burden, the evidence is scarce about the survival and prognostic determinants of prostate cancer patients in Ethiopia [19].

2.2 Distribution of prostate lesions by histopathologic diagnosis

A three years retrospective research was done at Raja Muthiah Medical College, India resulted in Benign Prostate Hyperplasia (BPH), the most common histological lesion encountered in 79 cases (74.52%) with a maximum incidence in the seventh decade; and chronic Prostatitis was the most common associated lesion in cases of BPH presenting in 20 (25.31%) patients [22]. A similar result was reported from other research done in Kashmir on 433 prostate specimens with 324 (74.83) cases of BPH and age ranges of 42 to 89 years old; and the most common co-existing finding with benign nodular hyperplasia was found to be chronic prostatitis (8.31%) [23].

A retrospective study done in Nepal showed that nodular hyperplasia of the prostate was the most frequent histopathological diagnosis seen in 86 (89.58%) patients. Twenty-four (25%) cases of nodular hyperplasia of prostate had associated prostatitis, out of which 22 cases were of chronic non-specific prostatitis and two cases were of acute prostatitis. Microscopic findings associated with nodular hyperplasia of prostate comprised hyperplasia of both epithelial and stromal cells with cystically dilated glands and corpora amylacea [24].

In another study done in India; BPH was the most frequent finding and was observed in 285 of the 364 cases (78.3%). BPH alone was seen in 126 (34.6%) cases, whereas BPH

was associated with acute and chronic prostatitis in 119 (32.7%) cases, granulomatous prostatitis in 13 (3.6%) cases, basal cell hyperplasia (BCH) in 14 (3.9%) cases, infarct in 2 (0.6%) cases, squamous metaplasia in 3 (0.8%) cases, and low-grade prostatic intraepithelial lesions in 2 (0.6%) cases. Six cases of atypical adenomatous hyperplasia (AAH) and 2 of atrophy constituted 1.7% and 0.6% of the total cases, respectively [12].

In the study done in Ahmedabad of 100 specimens, 93 showed benign lesions and a glandular-stromal pattern of hyperplasia (72%), the most frequent histological pattern which occurred. The stromal pattern of hyperplasia (4%) was less common. In those 45(45%) cases were benign prostatic hyperplasia (BPH) only. BPH with co-existing chronic prostatitis was 10(10%), acute on chronic prostatitis 6(6%), acute prostatitis 3(3%), and granulomatous prostatitis 1(1%). The less frequent finding was BPH with clear cell cribriform hyperplasia 3(3%), BPH with basal cell hyperplasia 1(1%) and BPH with squamous metaplasia 2(2%). BPH was seen in the 61- 70 years age group [11].

Study in Lagos, Nigeria, showed of 767 prostatic samples BPH was the commonest prostatic lesion and accounted for 544 (70.9%) cases and an age range of 40 to 94 years with a mean of 67(± SD = 8.8) years. BPH was most prevalent (45%) in the 60-69 years age group [25]. Two hundred and twenty-two malignant tumors were recorded constituting 28.9% of all prostatic biopsies [25]. And inflammatory lesions (n=54) were associated with BPH, the most commonly associated inflammatory lesion was chronic non-specific prostatitis which accounted for 42(76.4%) of all inflammatory lesions [25].

Retrospective research done in Eritrea showed that most of the biopsies were benign in 106(69.28%) and malignant in 47(30.72%) of cases and also showed that the largest proportion of the cases were in the 70–74 age band and the lowest proportion was in the < 50 years age [26].

In Ethiopia, a prospective cross-sectional study, out of 154 patients operated upon, 148 (96%) had confirmed BPH, 5 (3%) had bladder neck stenosis, and 1 had a posterior urethral stricture. Biopsy results were returned for 83 (54%) patients four (5%) of these 83 patients had prostate cancer [27].

2.3 Distribution of prostatic lesions by age, PSA value, and type of specimens

A retrospective study done in Pakistan, out of the 574 cases of BPH detected on TUR (transurethral prostatectomy) or enucleation specimens, 28 (4.9%) had serum PSA in the borderline range (4-10) and a suspicion of malignancy was raised by the clinician [28].

A case-control study done in Pakistan showed the value of PSA increasing as the age of patients increases and found that PSA value is approximately twice higher in BPH and 8 times higher in prostatic cancer than the control group [29].

Research done by Bio-Bank Japan (BBJ) project comprises a large cohort including 12 medical institutes consisting of 67 hospitals in Japan. Participants in this study were diagnosed with prostate cancer (4793; 2.4%). The age-specific distribution of prostate cancer patients, the mean age of the patients was 72.5 (range, 42-97) years [15].

A retrospective study done in Pakistan showed that BPH was most commonly seen in the seventh decade. The age range of BPH was 41 to 92 years. Carcinoma was most commonly seen in the seventh decade. The age range for adenocarcinoma was 45 to 86 years. The mean and median age was 56 and 59 years respectively. Overall 130 out of 190 patients (68.4%) were 65 years in age or older [28]. A study done in Kashmir on 433 prostatic specimens reported the age of the patients varied from 42 years to 89 years. The most common age of presentation was sixth to the seventh decade of life. Almost all neoplasms of the prostate were prostatic adenocarcinomas with most of the cases seen in the sixth to seventh decade of life with another peak in the seventh to eighth decade of life [23]. This study included 344 TURP chips, 82 TRUS guided biopsies, and 7 prostatectomy specimens [23].

A study done in Nepal; reported 85 (88.54%) TURP and 11(11.46%) prostatectomy specimens. Most of the prostatic lesions were benign 86 (89.58%) cases. Malignant lesions comprised 8 (8.34%) cases of all prostatic lesions. HGPIN was observed in 2(2.08%) cases [24].

Pakistan reported, out a total of 785 prostate specimens received during the study period 621 (79.1%) were TUR, 80 (10.2%) enucleation and 84 (10.7%) needle biopsies. Five hundred ninety-five (75.8%) and 190 (24.2%) of the cases were benign and malignant

(carcinoma) respectively [12]. One hundred twenty-seven (66.8%) out of 190 cases of adenocarcinoma were detected on TUR and enucleation specimens, 53 (41.7%) clinically benign, while 74 (58.3%) were clinically malignant [28].

A study done in India showed, among the BPH patients, S.PSA levels were available in 29 cases; eight cases of BPH, had serum PSA values in the range of 0-4ng/ml and 16 cases had S.PSA levels in the range of 4-20 ng/ml. The highest value of serum PSA among the BPH patients was 32.33 ng/ml. Among the 25 carcinoma patients, S.PSA levels were available in 16 cases of Adenocarcinoma and 4 cases of small cell carcinoma. Six cases of Carcinoma prostate had serum PSA values in the range of >80 ng/ml [22]. Another study conducted in India; on Serum PSA levels showed 132 benign and 53 malignant cases. PSA levels >20 ng/ml were seen in 17(12.9%) benign cases and 45 (84.9%) malignant cases. On comparison of PSA levels of >20, ng/ml in nonneoplastic versus neoplastic lesions, a *P*-value of 0.005 was obtained, and that they concluded that a PSA value of >20 ng/ml is highly suggestive of carcinoma of the prostate [12]. In a Kashmir study serum prostate-specific antigen was available in 23 cases of prostatic adenocarcinoma cases out of which twenty-one (91.3%) cases had serum prostate-specific antigen levels greater than 10 ng/ml [23].

In Belgium, the likelihood ratio test indicated that the difference in histopathologic stages between PSA subgroups (<=10, >10–20 and >20 ng/ml) is highly significant ($p < 0.001$). However, there was no significant difference ($p = 0.132$) in final histopathology between biopsy GS subgroups (7 [3+4] and 7 [4+3]). Nevertheless, the combination of PSA and biopsy GS subgroups contributed significantly to the prediction of the pathologic stage in the multinomial log-linear regression ($p < 0.001$). The model with PSA and biopsy GS main effects was selected as the final model. This model is better (borderline against PSA) than the models with PSA or GS as a single predictor variable ($p = 0.061$ and $p < 0.001$) [30].

A study in Lagos, Nigeria of 767 prostatic samples, comprised 3.6 % of all biopsies, showed 545(71%), and 222(29%) were trucut and open prostatectomy specimens respectively. And only 137(17.9%) had their PSA values recorded in their case files. One malignant lesion and 12 BPH lesions were seen with PSA values of less than 4ng/ml. Malignant and benign lesions were accountable for PSA levels of 4.1ng/ml to

49.9ng/ml while values of 50ng/ml and above were seen exclusively in malignant lesions [25].

A study done in Ghana, on HPP of prostate cancer, mean age at presentation was 71.7 ± 8.72 years and age ranged from 53 to 96 years with a peak in the seventh decade of life (n = 41, 52.6%) [31].

In Ethiopia, a research was done on Survival and prognostic determinants of prostate cancer patients in Tikur-Anbessa Specialized Hospital; out of 116 (85%) patients with a tumor marker (pre-treatment serum PSA level) test result, 105 (90%) have a PSA level above 4 ng/ml [19]. In this study, the age ranges from 43 to 91 years with a median age of 68 years. More than one-third (36.5%) of patients were in the age group between 61 and 70 years and 81 (59.1%) of patients were residents of Addis Ababa city, followed by Oromia region 33 (24.1%) [19].

A study undertaken in Ethiopia on 154 trans-vesical prostatectomies found fourteen patients (9%) were between 40 and 49 years of age, 41 (27%) 50 to 59 years old and 67 patients (44%) between 60 and 69 years of age. Addis Ababa was the residence of 81%; the remaining 19% came from 3 different regions of Ethiopia [27].

A prospective study done in Ethiopia, among 79 patients whose histology findings were negative for cancer, 26 had a PSA below 4 ng/ml, and 12 had a PSA between 8 and 12 ng/ml. Twenty-two patients had PSA values between 4 and 8 ng/mL, 1 of whom had histologically confirmed prostate cancer. Eleven patients had PSA values between 12 and 30 ng/ml, among whom 1 biopsy sample was positive for cancer and four patients had PSA values greater than 30 ng/ml, and 2 of these had histologically confirmed prostate cancer [27].

2.4 Distribution of prostatic carcinoma by grade, histologic type, and Gleason score

A study done in Kashmir on 433 prostatic specimens showed 53 cases as prostatic adenocarcinoma was graded with modified Gleason's criteria. The most common predominant tumor pattern (primary pattern score) was found to be 4 and the most common secondary pattern score was also found to be 4. The commonest overall Gleason's score or sum obtained by combining the primary and secondary scores was found to be 7 (4+3) in 12 cases and 7(3+4) in 08 cases [23].

A study done in Ahmedabad showed out of 100 specimens, seven cases of adenocarcinoma prostate had modified Gleason score. Histopathology of the biopsy showed single, separate, much more variable glands (Gleason's grade 3). The second most predominating pattern is fused glandular, cribriform pattern, and hyper-nephroid (Gleason's grade 4). The most common predominant grades observed in this study were grade 3 and grade 4. The most common score obtained was 6 in 4 [11].

Retrospective research was done in India, of 25 Carcinoma, 20 (80%) and 5 (20%) were adenocarcinomas of the prostate and Small cell carcinoma of prostate respectively [22]. A similar study was done in India in 364 cases; prostatic adenocarcinoma accounted for 73 (92.4%) of 79 neoplastic lesions. The most common pattern seen was angulated glands in 45 (61.6%) cases, a fused glandular pattern in 24 (32.8%) cases and a cribriform pattern in 22 (30.1%). A sheeting pattern was observed in 17 (23.3%), a hyper-nephroid pattern in 15 (20.6%), comedo-necrosis in 9 (12.3%), and a single separate uniform glandular pattern in 4 (5.5%) cases [12]. Perineural invasion was seen in 31(42.5%) of the 73 cases of prostatic adenocarcinoma. Gleason grading was done in 68 cases of which 35(51.5%) cases were an intermediate grade, followed by 19(27.9%) low grade and 14(20.6%) high grade [12].

A study in Pakistan reported 74 cases of carcinoma out of 190 had Gleason score 7. Of these, 42 had Gleason grade 2(3+4=7), and 32 had Gleason grade 3 (4+3=7). Gleason score 7 was the commonest in the study followed by Gleason score 9. Almost 86% of all TUR/enucleation specimens showed a Gleason score of 7 or above [28].

Over 1,000 participants with or without prostate carcinoma enrolled within the Southern African Prostate adenocarcinoma Study (SAPCS) by using genome-wide profiling found Gleason score and tumor grades available for 346 (60.1%) and 304 (52.8%) cases, respectively. While 35.5% (123/346) presented with a Gleason score greater or equal to 8, an increase to 151(43.6%) when considering Gleason score 7 (4+3) was observed. A total of 79(26%) of men were presented with a poorly differentiated tumor [5]. A similar study conducted in Ghana on 78 prostate cancer cases showed 43(55.1%) poorly differentiated, followed by 20(25.6%) moderately differentiated and 15(19.2%) well-differentiated samples [31].

A study was done in Lagos; Nigeria reported adenocarcinoma in 220 (99.1%) of 222 malignant tumors and the remaining two cases were a squamous cell carcinoma and

neuroendocrine tumor respectively. Adenocarcinoma showed an age range of 40 to 98 years with a mean age of 66 years [25]. Gleason score of nine was the most frequent in 37 (16.8%) while score two was the least in 2(1.8%). Most adenocarcinomas were poorly differentiated in 40%, while moderately differentiated and well-differentiated adenocarcinomas constituted 22.7% and 28.2% cases respectively [25].

Retrospective prostate cancer study in Kampala, Uganda showed the age range of 43 to 99 years. The majority of the patients, (n = 77, 36.5%) were between 61 and 70 years. Patients with age between41 and 50 years, were only 7.6% (n = 16) [32]. The majority of the patients had high tumor grade (poorly differentiated) 94(44.6%) and 66(31.3%) of the cases had low tumor grade (well-differentiated) [32].

Retrospective research done in Eritrea showed that of the malignant cases adenocarcinoma in 46(97.9%) and only one squamous cell carcinoma case was seen. And the most frequent grade was grade 3 (Gleason score 4 + 3 = 7) in 12(25.5%) and the least grade is grade 1 (Gleason score ≤ 6) in 6(12.8%) of cancer cases [26].

A retrospective cohort study done in Ethiopia showed that histopathology test results available for 92 patients with a histopathology test report of 89 (96.7%) cases have adenocarcinoma, 50(54.3%) of them were poorly or undifferentiated prostate cancer cells [19]. The study reported that 58 (63.0%) of patients with a Gleason score report, 19 (32.8%) with a score of 6 or less, 11 (19.0%) had 7, and 28 (48.3%) had 8 and above [19].

Chapter three: Objectives

3.1 General objective

- To characterize histopathologic patterns of prostate disease in JUMC, Jimma, Southwest Ethiopia from September 2014 to August 2019

3.2 Specific objectives

- To describe the distributions of prostate disease by specific histologic types
- To determine the relationship of prostate cancer with Gleason grading
- To characterize the distributions of histopathologic diagnosis by residence and age
- To compare the relationship of clinical diagnosis with histopathologic diagnosis

Chapter four: Methods and materials

4.1 Study area and study period

The study was conducted in Jimma university medical center [JUMC] which is found in Jimma town, Oromia regional state. Jimma town is located in the Southwest part of Ethiopia which is 356km away from Addis Ababa, the capital city of Ethiopia [33]. JUMC is teaching university hospital serving as a specialized referral hospital for most of southwestern Ethiopia including Jimma town [34].

The estimated catchment area of the hospital 17,500 sq. km with 15 million people is believed to get the service over 800 beds [34]. The pathology department is among the most actively functioning departments with a staff profile of 4 pathologists, 14 practicing pathology residents, one general practitioner, 2 histopathologists, and 10 technical assistants. The department activities are subdivided into Histopathology, hematopathology, and cytopathology units. The histopathologic service is the area where this research focused on. It uses the routine Hematoxylin and Eosin stain, having an average annual patient flow of more than 1800. The study period for conducting this research was from June to July 2020 G.C.

4.2 Study Design

A facility-based descriptive retrospective cross-sectional study design was applied.

4.3 Populations

4.3.1 Source population

All male patients for whom biopsy was summated to JUMC department of pathology for histopathologic diagnosis from September 2014 to August 2019.

4.3.2 Study population

All male patients with the diagnosis of prostate lesions for whom biopsy was summated to JUMC department of pathology for histopathologic diagnosis from September 2014 to August 2019, fulfilling inclusion and exclusion criteria.

4.4 Inclusion and exclusion criteria

4.4.1 inclusion criteria:

All biopsy reports of male Patients with the diagnosis of the prostate lesion from September 2014 to August 2019

4.4.2 exclusion criteria:

Biopsy reports with a histopathologic diagnosis that does not have at least two of those variables: patient Age, Residence, and clinical diagnosis value.

4.5 Sample size and sampling techniques

All prostate biopsy report with histopathologic diagnosis in the time frame of the study period that fulfilled the inclusion criteria were included in the study. Two hundred thirty-five biopsies during the study period were included. All biopsy received are formalin-fixed and hematoxylin and eosin-stained before microscopic diagnosis.

4.6 Data collection procedures

All biopsy reports containing histopathologic diagnosis, age, residence, clinical diagnosis and PSA value were retrieved and recorded from the patients' request form and pathology department data archive. Structured checklists developed by the principal investigator containing the study variables was used. For any missed variables, the surgical department registry book was retrieved by the medical registration number in the central card room. The data was collected by selected and trained technical assistant staff. The completeness of the data was checked by the principal investigator.

During selecting and training data collectors and while data collection all measures were undertaken to protect from COID-19 by wearing PPE (mask, gloves, and gown), social distancing, and using sanitizers according to the national infection prevention protocol guideline [35].

Patients' names were not used to respect their confidentiality.

4.7 Variables

- Histopathologic diagnosis
- Clinical diagnosis
- Age
- Residence
- PSA value
- Clinical features

4.8 Data processing and analysis

Immediately after the data collection was completed, data were coded and entered into computer software of EPIData version 3.1. cleared and exported to SPSS V.23 for

analysis and data was cleaned, edited, compiled, and described. Descriptive analysis was employed to describe the variables. Tabulation was done to measure the degree of association between variables. The results were presented using text narrations, different tables, and graphs.

4.9 Data quality control

All the data collectors were given training for three days on how to locate, retrieve, categorize, and record the data. The principal investigator followed and supervised while the data collectors were retrieving, the results from the pathology department by using checklists. The collected data were checked for completeness and accuracy by the principal investigator according to their specific accession number and study identification.

4.10 Ethical considerations

Before data collection ethical clearance was obtained from the Institutional Review Board (IRB) of JUMC and permission was obtained for data collection from the pathology department, surgical and central card room. The name of the patient was excluded from all information obtained from patients and confidentiality was ensured.

4.11 Dissemination plan

The result will be presented and printed copy will be submitted to Jimma university, department of pathology and surgical department, and finally to the main Jimma university library. Efforts will be made to publish the finding in a peer-reviewed scientific journal.

4.12 Operational definition

Urban: is defined as those who came from Jimma town.

Rural: in the catchment outside Jimma town.

Chapter Five: Result

A total of 7925 biopsy specimen were seen in five years period in Jimma university medical center, department of pathology, histopathology unit. Two hundred thirty-seven prostatic specimens were received during the study period. All but two cases had no histopathologic diagnosis. Two hundred thirty-five cases of prostate lesions were studied from the hospital records of the histopathology section.

The highest number of biopsies seen was 54 (23.0%) in the 2015/16 followed by 50(21.3%) in the 2017/18-year and the lowest number of prostate biopsies seen was 38 (16.2%) in the 2014/15. The total number of biopsies done each year was increasing throughout the study years, but the number of prostate specimens was fluctuating (Table 1 and figure 1). Two hundred ten patients had their residency chronicled and when categorized to rural and urban in 143 and 67, respectively (Table 1).

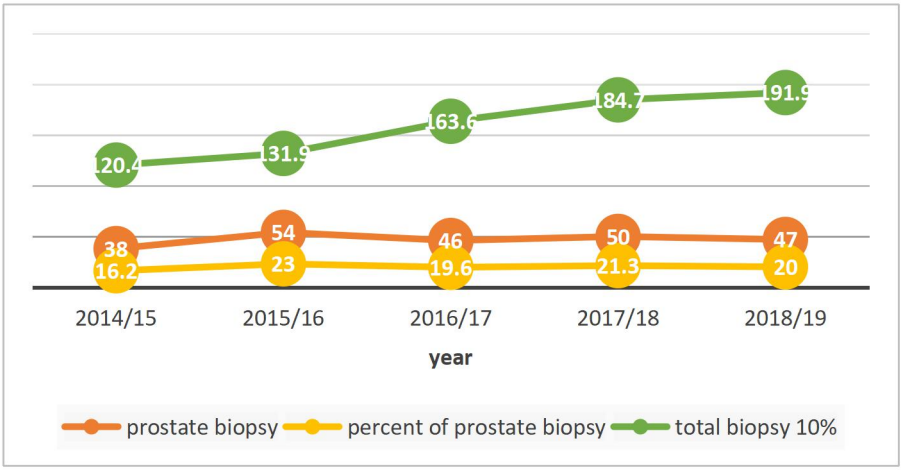

Figure 1. The five years pattern of prostate specimens diagnosed in JUMC, Sep. 2014 to Aug. 2019.

Age range from 42year to 87 years (45) with the mean age of patients with prostatic disorders was 65.40 y (-/+SD=9.24), the median age noted was 65 years and the most frequent age was 60 year in 39 cases (16.6%). Among 235 cases age group 60-69 (7^{th} decade) was the most cases seen in 102 cases (43.4%) and only 5(2.1%) of cases were seen in the age group less than 50 years (Table 1).

Table 1. Pathological characteristics of prostate specimen of patients at JUMC, Jimma, September 2014– august 2019.

Variables		Frequency	Percent
Residency	Urban	67	28.5
	Rural	143	60.9
Biopsy year	2014/15	38	16.2
	2015/16	**54**	**23.0**
	2016/17	46	19.6
	2017/18	**50**	**21.3**
	2018/19	47	20.0
Age group	<50	5	2.1
	50-59	44	18.7
	60-69	102	43.4
	70-79	57	24.3
	>=80	27	11.5
Pathologic diagnosis	Benign	181	77.0
	IEN	4	1.7
	Malignant	50	21.3

All prostate specimens were broadly classified into benign in 181 (77.02%) cases, intraepithelial neoplasm and malignant in 4(1.7%) and 50 (21.28%) cases respectively, were seen [Table 1] and fig. 2.

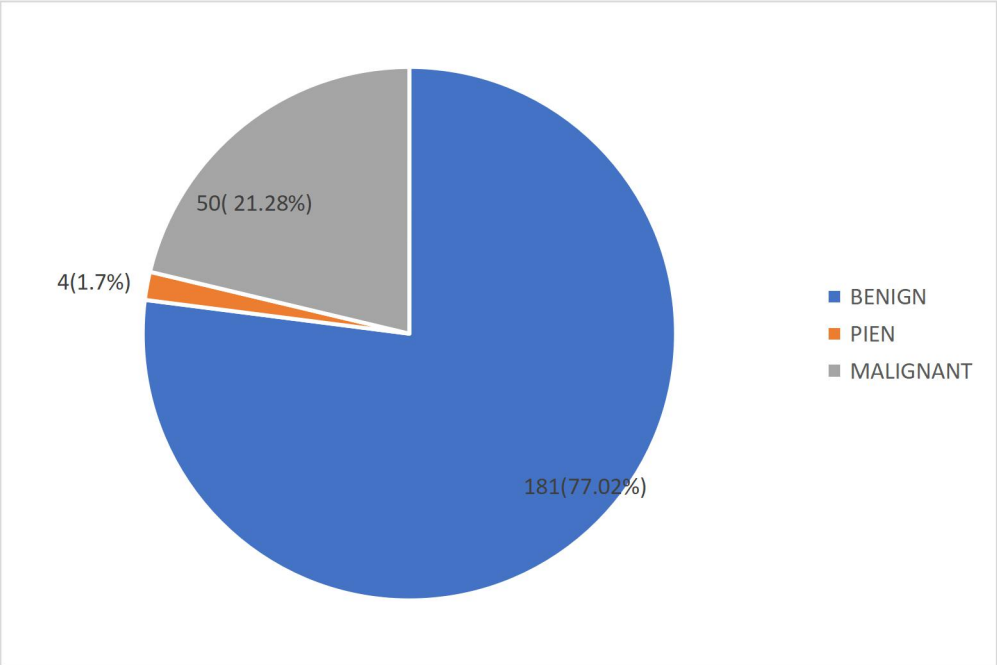

Figure 2. The five years distribution of prostate specimens by diagnosed in JUMC, Sept. 2014 to Aug. 2019.

Benign Prostatic Hyperplasia (BPH) was the most common histological lesion encountered in 181 cases (77.0%) and of these in 129 (54.89%) were BPH alone, in 48 (20.45%) were associated with prostatitis along with single case of prostatic abscess with BPH and in 4(1.7%) cases with metaplasia [Fig-3 and 4]. In four (1.7%) cases prostatic intraepithelial neoplasia (PIEN) was found and of this PIEN two cases were along with BPH.

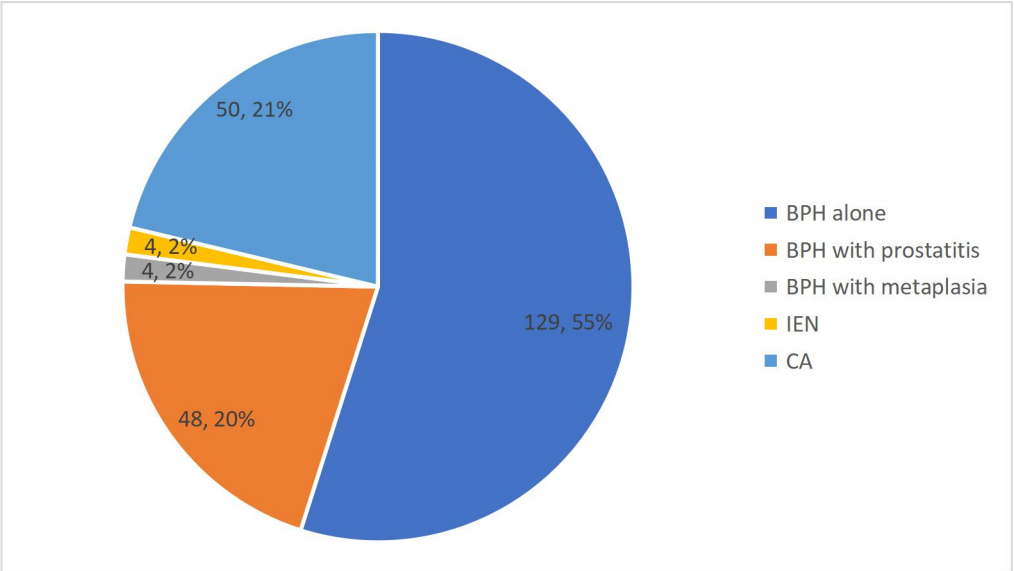

Figure 3. Distribution of prostate specimens' histopathologic diagnosis in JUMC, Sep. 2014 to Aug. 2019.

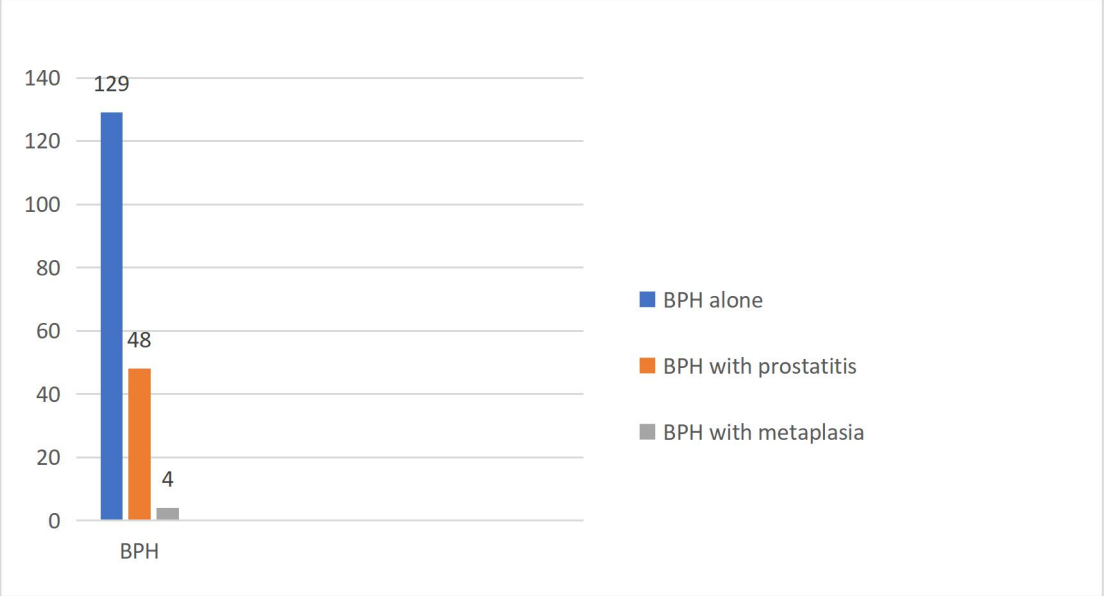

Figure 4. Distribution of histopathologic BPH diagnosis by associated change in JUMC, Sept. 2014 to Aug. 2019.

BPH was most prevalent in 79(43.65%) cases in the 60-69 years age group and similarly, 21 (42%) malignant cases and two intraepithelial neoplasms were noticed in this age group, respectively. The lowest cases of BPH was seen in age group below 50 year in 4(1.7%) of total biopsies and only a single malignant case seen in this age group (table -2 and fig. 5).

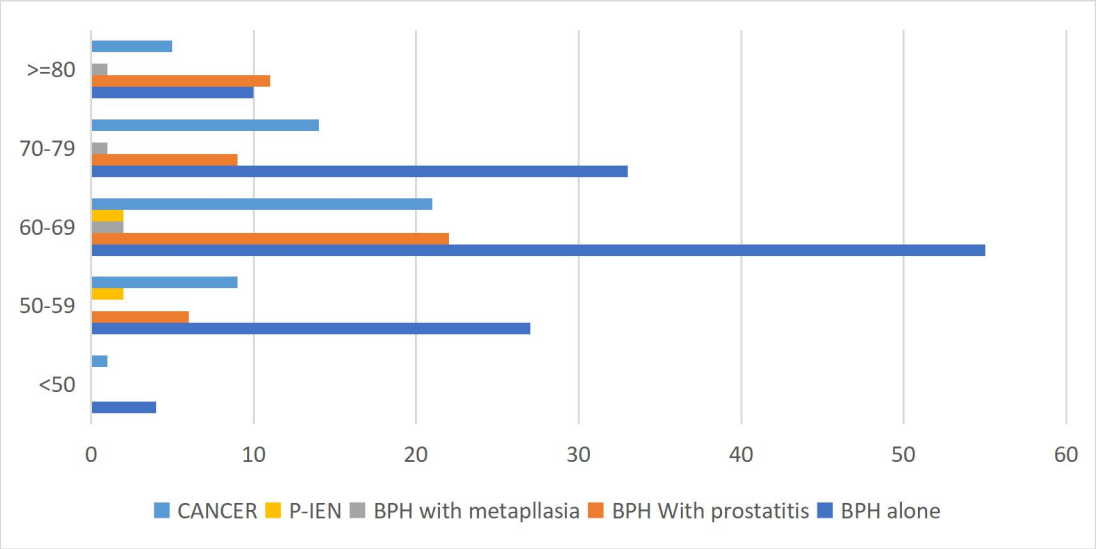

Figure 5. Distribution of histopathologic diagnosis by age group of prostate specimens diagnosed in JUMC, Sep. 2014 to Aug. 2019.

Table 2. Cross-tabulation age group with histopathologic diagnosis of prostate specimen patients at JUMC, Jimma, September 2014– august 2019.

Histopathologic diagnosis		Age group					Total
		<50	50-59	60-69	70-79	>=80	
	BPH alone	4	27	**55**	33	10	129
	BPH With Prostatitis	0	6	22	9	11	48
	BPH With Metaplasia	0	0	2	1	1	4
	IEN	0	1	1	0	0	2
	IEN AND BPH	0	1	1	0	0	2
	CA	1	9	**21**	14	5	50
Total		5	44	102	57	27	235

Among sixty-seven urban dweller 56 (83.58%) cases were BPH histologically and 11(16.42%) cases carcinoma diagnosed histologically. Whereas among 143 rural patients BPH were diagnosed in 112 (78.32%), cancer diagnosed in 28 (19.58%) and prostate IEN in 3 (2.10%) cases.

Difficulty of urination along with LUTS was the most common presentation in 159 patients (67.7%) followed by acute urinary retention in 30 patients (12.8%) in which half was associated with prior history of difficulty of urination. Frequency and urgency were presenting symptoms in 13 (5.5%) cases.

One hundred ninety-five patients' specimens were reported with clinical diagnosis. Benign in 136 (69.7%), malignant in 9 (4.6%) and BPH to rule-out cancer in 50(25.7%) cases. The most common benign clinical diagnosis was BPH alone in 133 patients (68.2%), two BPH with prostatitis and single prostatitis (Table-3). Clinically diagnosed BPH alone of 133 patients, histologically diagnosed as BPH alone in 73 (54.9%), in 36 (27.1%) as BPH with prostatitis, in 2 (1.5%) as BPH with metaplasia and in 18 (13.5%) cases as cancer (Table-3).

Table 3. Cross tabulation of clinical diagnosis with histopathologic diagnosis of prostate specimen patients at JUMC, Jimma, September 2014– august 2019.

		Histopathologic diagnosis					**Total**
		BPH ONLY	BPH With Prostatitis	BPH With Metaplasia	PIEN	CA	
clinical diagnosis	Prostatitis	0	0	0	0	1	1
	BPH alone	73	36	2	4	18	133
	BPH with prostatitis	0	1	0	0	1	2
	CA	3	1	1	0	3	8
	CA And prostatitis	0	0	0	0	1	1
	BPH R/O CA	30	4	1	0	15	50
	Not Recorded	23	6	0	0	11	40
Total		129	48	4	4	50	235

Of fifty malignant (21.28%) cases seen, adenocarcinoma of the prostate was the most common histological type of carcinoma encountered in 49 cases (98%) and rhabdomyosarcoma (1 case –2%). Among the adenocarcinoma cases seven of them

reported as; occult in four cases, incidental in two, and one as a focus of adenocarcinoma (Table-4).

In the present study, there were 37 (75.51%) cases of adenocarcinoma of the prostate with a Gleason score. Gleason score 6 or less was the commonest score found in 19 (51.35%) cases, followed by 9 (24.32%) cases each with Gleason score 8 and Gleason score 7 was reported in 6 (16.22%) cases, Gleason score 9 in 3 (8.10%) cases and no case with Gleason score 10 noticed. Grading of differentiation was done in 43 cases of adenocarcinoma in which 27(62.79%) cases were low grade, followed by 15(34.88%) and intermediate grade and one case (2.33%) high grade, respectively (Table-4).

S.PSA levels were available in 20 cases in the range of 0.4 ng/ml to 101.0 ng/ml. The highest value of S.PSA noted among the BPH patients was 85.8ng/ml and the lowest value 0.4ng/ml. Among the carcinoma patients, S.PSA levels were available in two cases of Adenocarcinoma (5.4 and 101ng/ml). In 13 (65%) cases they were in the range of 10 ng/ml or less and PSA values above 20 ng/ml were seen in 5 (25%) cases (Table-4).

Table 4. Pathological characteristics of malignant lesions with histologic type, GS, and PSA value of patients at JUMC, Jimma, September 2014– August 2019.

Variables		Frequency	Percent
Malignant	adenocarcinoma	49	98
	Sarcoma (RMS)	1	2
Gleason sum	GS ≤6	19	51.35
	GS 7	6	16.22
	GS 8	9	24.32
	GS 9	3	8.11
	GS 10	0	0
Adenocarcinoma differentiation	Low	27	62.79
	Intermediate	15	34.88
	High grade	1	2.33
PSA	0-10.0 ng/ml	13	65
	10.1-20 ng/ml	2	10
	>20.0 ng/ml	5	25

Chapter Six: Discussion

This study retrospectively investigated the histopathological profile of 235 patients with prostate biopsies. Prostatic specimens constitute a good fraction of the surgical pathology workload. This study was undertaken to evaluate the several histological lesions which histologically confirmed cases discussed and comparison with other studies were undertaken of cases over a period of five years.

6.1 Distribution of prostate biopsy in sociodemographic status

Prostatic specimens were broadly classified into benign in 181 (77.02%) cases, intraepithelial neoplasm in 4(1.7%) and malignant in 50 (21.28%) cases in this study. Almost similar result was found from a study in India by Yadav et al [11] here 93(93%) cases were benign and 7(7%) cases malignant. Retrospective research in Eritrea showed benign in 106 (69.28%) and malignant in 47(30.72%) cases [26].

Lesions of prostate are enormously common over the age of 50 years. The age of the patients in this research ranged from 42 to 87 years (45), with the mean age of 65.40±9.24 years, the median age noted was 65 years. In line with this study, the mean age of 68.6 years was observed in Indian by Garg et al [12]. A similar age range by Yadav et al was 45-85 years [11]. Nigerian study by Anunobi et al reported age range of 40 to 94 years [25]. In Ethiopia study age range from 43 to 91 years with a median age of 68 years was reported [19].

This research reported that age group 60-69 (7^{th} decade) was the group in which most cases 102 (43.4%) were seen and this is similar to report by Yadav et al [11]. The results of the present study agree with the studies in Ethiopia, in which 67 patients (44%) between 60 and 69 years of age were noted by Seife et al [27]. Another Ethiopian study reported that more than one third (36.5%) of patients were in the age group 61 and 70 years [19]. In Eritrea, the lowest proportion was in the < 50 years age [26], in line with 5(2.1%) cases in this age group in the present study . The age beyond >80 year had 27 (11.5%) of the total specimens. The decline in the number of cases past the age 80 years reflects the average life span of people in our country. Most cases of prostate cancer are diagnosed after 50 years of age, but prostate cancer can be seen in younger adults, in our study single case was observed in this age group.

The present study reported 210 patents' resident. Among sixty-seven urban dweller 56 (83.58%) cases were BPH and 11(16.42%) cases carcinoma histologically. Whereas among 143 rural patients BPH was diagnosed in 112 (78.32%), cancer diagnosed in 28 (19.58%) and prostate IEN in 3 (2.10%) cases. This showed similar prevalence of BPH and carcinoma between urban and rural with ratio of 1 to 1.07 and 1 to 0.87 respectively; but, three PIEN was seen in rural resident only.

6.2 Distribution by histopathologic and clinical diagnosis

Benign prostatic hyperplasia (BPH) and adenocarcinoma are the two most common conditions affecting prostate gland [1, 21]. In this study, Benign Prostatic Hyperplasia (BPH) was the most common histological lesion encountered in 181 cases (77.02%) and of this BPH 47 (26.11%) cases were associated with nonspecific prostatitis. Similarly, Garg et al reported BPH in 285 (78.3%), BPH alone in 126 (34.6%) cases, and associated with prostatitis in 119 cases (32.7%) [12]. The results of the present study agree with the studies by Deshmukh et al that noticed BPH in 207 (92.04%) cases and Yadav et al who reported peak incidence in the seventh decade [17,11]. Anunobi et al [25] reported BPH in 70.9% cases. But Deshmukh et al found one (0.44%) case with high grade prostatic intraepithelial neoplasia which is lower than that observed in the present study, four (1.7%) cases [17]. Table-5 compares three different researches on the histopathological diagnosis.

Table 5. A comparison of the findings of the current study with other studies

Histopathological diagnosis	**Anunobi *et al* et al. [25] (Nigeria)**	**Medhin et al. [26] (Eritrea)**	**Garg et al. [12] (India)**	**Present study**
Total no. of cases	767	156	364	235
NH	70.9	69.28	67.31	76.6
With prostatitis	10.1	-	32.69	26.11
With metaplasia	-	-	0.82	2.22
PIEN	-	-	0.55	1.7
Adenocarcinoma	28.7	30.06	20.05	20.85
Sarcoma	-	-	0.55	0.43

Benign prostatic hyperplasia (BPH) and carcinoma of the prostate are increasingly frequent with advancing age [1,21]. The current study showed BPH as most prevalent 79(43.65%) in the 60-69 years age group and malignant consisting of 21(42%) cases and two cases of intraepithelial neoplasms were noticed in this age group, respectively. The findings in our study are comparable with (45%) in the 60-69 years age group in Nigerian study by Anunobi et al [25] and 38% and 51.21% cases of BPH by Yadav et al and Deshmukh et al, respectively, were seen in the 7th decade [11,17].

Carcinoma of prostate is the second most common malignancy in men, second only to lung cancer in the world [21]. In our study 50 (21.3%) cases were prostatic carcinoma, of which adenocarcinoma was the most common histological type of carcinoma encountered in 49 (98%) cases, and a single rhabdomyosarcoma. This is pretty similar to 79 (20.1%) prostatic neoplasms of the total cases, 73 (92.4%) adenocarcinoma and 2 cases of rhabdomyosarcoma reported by Garg et al [12]. Nigerian study reported adenocarcinoma in 99.1% of cases and malignancy in 28.9% [25]. Research done in Eritrea showed that of the malignant cases adenocarcinoma was in 46(97.9%) [26]. In Ethiopia a study by Beksisa et al, reported 89 (96.7%) cases of adenocarcinoma and 2 (2.2%) cases of sarcoma [19]. Another Ethiopian study by Seife et al, reported 5% prostatic carcinoma [27] and this is lower than 21.3% observed in our study. Numerous factors can contribute to this discrepancy. For example, in recent times, the incidence rates of prostate carcinoma have been inclined by the diagnosis of cancer in early stages. Moreover, this study was carried out in a tertiary health institution of speciality hospital, which puts a high selective index on the data.

It is known that the room for clinical features to alert men to seek medical services is little. However, if such features are not just overlooked, they can aid in making men get alarmed and hence start seeking screening services for possible detection of prostate cancer at early stage. The current study showed clinical presentation with the difficulty of urination along with LUTS was most common in 67.7% cases followed by acute urinary retention in 12.8% cases in which half was associated with prior history of difficulty of urination, and frequency and urgency were presenting symptom in 5.5% cases. Josephine A, reported difficulty in micturition was the most common presentation in 60.28% cases followed by frequency of micturition in 19.15% cases [22]. Ugandan study found majority presented by incomplete voiding with LUTS in 43.6%

Yahaya [32]. Seife et al [27] reported relatively higher presentation, Sixty-one patients (39%) with acute urinary retention.

One hundred ninety-five patients' specimens were reported with clinical diagnosis in present study: benign in 136 (69.7%), malignant in 9 (4.6%) and BPH to rule-out cancer in 50(25.7%) cases. Clinically diagnosed BPH alone of 133 patients were histologically diagnosed as BPH alone in 73 (54.9%), BPH with prostatitis in 36 (27.1%), BPH with metaplasia in 2 (1.5%) and cancer in 18 (13.5%) cases. With this benign clinical diagnosis had positive predictive value of 82.35% (112 of 136 benign) and negative predictive value 44.45% (only 4 in 9 malignant diagnoses) only. This showed clinicians their benign diagnosis is lower in relation to histologic diagnosis.

6.3 Discussion of malignancy with Gleason grading, differentiation and PSA

Histological grade has been recognized as a powerful prognostic predictor of prostate cancer in staging and progression. In the present study, there were 37 (75.51%) cases of adenocarcinoma of the prostate with a Gleason score. Gleason score 6 or less was the commonest in 19 (51.35%) cases, followed by Gleason score 8 in 9 (24.32%) cases, Gleason score 7 in 6 (16.22%) cases, Gleason score 9 in 3 (8.10%) cases no Gleason score 10 case. Similar results were noticed by Yadav et al, with a Gleason score of 6 in 57.1% and a Gleason score of 7 and above reported in 42.9% and in Belgium study by Joniau et al, with Gleason score ≤7 (3+4) in 119 (59.5%) and Gleason score >7 (4+3) in 81 (40.5%) [11, 30]. Our study exhibited difference to that reported by Deshmukh et al**,** Gleason score 9 in 33.34% followed by 27.77% cases each with Gleason score 7 and 8 [27]. A study done in Ethiopia [19] reported 19 (32.8%) cases have a score of 6 or less, 11 (19.0%) have 7, and 28 (48.3%) have 8 and above.

The current study reported differentiation of adenocarcinoma in 43 cases in which 27(62.79%) cases were well-differentiated, 15(34.88%) intermediate and 1(2.33%) poorly differentiated. In contrast to the present study Garg et al [12] reported intermediate grade in (51.5%), low grade (27.9%) and high grade (20.6%). Beksisa et al showed 50(54.3%) poorly or undifferentiated, 23 (25%) intermediate, and 12 (20.3%) well-differentiated prostate cancer cells [19]. Aboagye et al reported (55.1%) poorly, (25.6%) moderate, 15 (19.2%) well-differentiated [31]. Ugandan study by Yahaya et al reported high tumour grade (poorly differentiated) in 94 (44.6%) and in 66 (31.3%) low

tumour grade (well differentiated) [32]. A possible explanation is that in our case the report didn't follow the current modified Gleason grading system [6, 21].

PSA when used alone cannot be used as an effective screening tool for carcinoma of prostate due to its' low sensitivity and specificity, especially in the low and intermediate range [6]. PSA levels with ultrasound result can be used as risk stratification of prostate cancer [1, 6, 21]. The correlation of PSA levels with nonneoplastic and neoplastic lesions was analysed. PSA levels were available in 20 cases (18 nonneoplastic and 2 neoplastic) which make only 8.5% in current study. Reported cases of the 767 patients only 137(17.9%) had their PSA values recorded in their case files by Anunobi et al [25]. The present study found range of PSA levels from 0.4ng/ml to 101.0ng/ml. The highest value of S.PSA noted among the BPH patients was 85.8 ng/ml and the lowest value 0.4ng/ml. Among the carcinoma patients, S.PSA levels were available in two cases of Adenocarcinoma (5.4 and 101ng/ml). In our study in 13(65%) cases were in the range of ≤10 ng/ml, in 2 (10%) cases between 10 ng/ml and 20 ng/ml and in 5 (25%) had PSA >20ng/ml. The result agrees with Joniau et al [30] 49% reported PSA <10 ng/ml, and 22% cases had > 20 ng/ml and by Seife et al [27] of 79 cases, 58(73.4%) cases had PSA level < 12 ng/ml. The low PSA testing rate is because prostate biopsy in our institution is performed in symptomatic patients as an outpatient procedure in a significant number of patients and PSA testing is not requested in these cases.

Chapter seven: Conclusion and Recommendations

7.1 Conclusion

This study has found the pattern of prostatic diseases in JMC, which is similar to other researches in Africa and the world. A variety of benign and malignant lesions were seen in prostatic specimens. These need to be differentiated and classified. Benign nodular hyperplasia was the most common benign lesion seen in the prostate and was on many occasions associated with prostatitis. Prostatic adenocarcinoma is the most common malignant lesion of Prostate. Prostatic adenocarcinoma in the majority of cases was of low-grade adenocarcinoma and of Gleason score 6. This was different to most researches and standard textbooks. Serum PSA is a useful adjunct in cases where the values are higher but, testing request significantly low.

7.2 recommendations

1. Clinician should have high index of suspicion for prostate cancer as early treatment and follow up will change the outcome of the disease. Patients' PSA levels should be requested prior to surgery and should in our opinion be used as a component of a strategy integrating multiple diagnostic approaches for prostate cancer screening and not to be used alone in our environment.
2. Efforts should be made to apply modified Gleason's system in case of adenocarcinoma of prostate to advance management. The report of the pathology department should follow the standard guidelines in interpreting the finding with relation to Gleason grading system. The GS should be stated in sum and separate Gleason patterns. Prostate IEN should be categorized to low grade and high grade as the two have different malignant potential.
3. Detailed studies with different methodology and wider sample size in collaboration with surgery department to determine risk factors, management outcome and follow-up of the patients should be done to further characterize the disease.
4. The study recommends the use of immunohistochemistry markers in order to comfortably diagnose the disease.

References

1. McKenney JK. Prostate and Seminal Vesicles. In: Goldblum JR, Lamps LW, McKenney JK, editors. Rosai and Ackerman's Surgical Pathology. Eleventh Ed. Philadelphia: Elsevier; 2018. p1097-1134.
2. Hassan AU, Hassan G, Rasool Z, Zubeida. Aims and Objectives of Histological Studies of Prostate. Uni J of Cli Medicine 1(2): 13-21, 2013 http://www.hrpub.org DOI:10.13189/ujcm.2013.010201
3. Oxley J, Varma M, Berney D. Standards and datasets for reporting cancers Dataset for histopathology reports for prostatic carcinoma. The Royal College of Pathologists: London; 2016.
4. Tadayon F, Arezegar H, Khorrami M, Juzdani HR, Shahdoost A, Mellat M. Evaluation of prostatic cancer prevalence in patients with prostatic-specific antigen between 4 and 10 and normal digital rectal examination. Adv Biomed Res 2016; 5:112.
5. Tindal EA, Monare LR, Petersen DC, et al. Clinical Presentation of Prostate Cancer in Black South Africans. The Prostate; 2014:7(4):880-891.
6. Heidenreich A, Bastian PJ, Bellmunt J, et al. The European Association of Urology (EAU) Guidelines Group for Prostate Cancer: march 2013.
7. Short E, Warren AY, Varma M. Gleason grading of prostate cancer: a pragmatic approach. Diagnostic histopathology.2019;25(10)P371-378. https://doi.org/10.1016/j.mpdhp.2019.07.001
8. Kweldam CF, Leenders GJ, Kwast TV. Grading of prostate cancer: a work in progress (2019) Histopathology 74, 146–160. https://doi.org/10.1111/his.13767
9. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma. Am J Surg Pathol 2016; 40: 244e52
10. Ballentine H. Diagnosis and staging of prostate cancer. In: Allaf ME, Carter HB, editors. Textbook of urology. Wein-Campbell-Walsh Urology. Philadelphia: Saunders Company; 2007. p. 291-231.
11. Yadav M, Desai H, Goswami H. Study of Various Histopathological Patterns in Prostate Biopsy. Int J Cur Res Rev 2017;9(21):58-63. **DOI:** 10.7324/IJCRR.2017.9219

12. Garg M, Kaur G, Malhotra1 V, Garg R. Histopathological spectrum of 364 prostatic specimens including immunohistochemistry with special reference to grey zone lesions; Prostate Int 2013;1(4):146-151 • http://dx.doi.org/10.12954/PI.13026
13. National cancer control plan of Ethiopian-(2016-2020): Ethiopian ministry of health; 2015.
14. Memirie ST, Habtemariam MK, Asefa M, et al. Estimates of cancer incidence in Ethiopia in 2015 using population-based registry data. J Glob Oncol 2018;(4):1-11. https://doi.org/10.1200/JGO.17.00175. PMID: 30241262.
15. Ukawa S, Nakamura K, Okada E, et al. Clinical and histopathological characteristics of patients with prostate cancer in the BioBank Japan project. J Epi; 27 (2017): S65-S70.
16. Boyle P, Ferlay J. Cancer incidence and mortality in Europe 2004. Ann Oncol 2005 Mar;16(3):481-8. http://www.ncbi.nlm.nih.gov/pubmed/15718248
17. Deshmukh BD, Ramteerthakar NA, Sulhyan KR. Histopathological study of lesions of prostate: A five-year study. Int J Health Sci Res. 2014;4(1):1-9.
18. Tefera B, Assefa M, Abebe B, Rauch D. Patterns of Cancer at the University of Gondar Hospital: North-West Ethiopia. J Oncol Med & Pract:2016;1(2):106.
19. Beksisa J, Getinet T, Tanie S, Diribi J, Hassen HY**.** Survival and prognostic determinants of prostate cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A retrospective cohort study: https://doi.org/10.1371/journal.pone.0229854
20. Adeloye D, David RA, Aderemi AV, et al. An Estimate of the Incidence of Prostate Cancer in Africa: A Systematic Review and Meta-Analysis. PLoS ONE 2016;11(4): DOI: 10.1371/journal.pone.0153496
21. Epstein JI, Oxley J, Ro JY, Kwast VD, Zhou M. Intraductal carcinoma. In: Moch H, Humphrey PA, Ulbright TM, Reuter VE, 4th eds. WHO classification of tumors of the urinary system and male genital organs. IARC, 2016; 164-5
22. JOSEPHINE A. Clinicopathological Study of Prostatic Biopsies. J Clin Dia. Research. 2014;8(9): FC04-FC06. DOI: 10.7860/JCDR/2014/8591.4843.
23. Farooq S, Bilal S, Khaliq BI, Sidieq F, Aslam H, Shah I. The spectrum of histopathological patterns observed in prostate specimens in a tertiary care hospital in Kashmir. International Journal of Contemporary Medical Research 2019;6(4): D1-D3. **DOI:** http://dx.doi.org/10.21276/ijcmr.2019.6.4.11

24. Bhatta S, Hirachan S. PROSTATIC LESIONS: HISTOPATHOLOGICAL STUDY IN A TERTIARY CARE HOSPITAL. JMMIHS. 2018;4(1):12-19
25. Anunobi CC, Akinde OR, Elesha SO, Daramola AO, Tijani KH, Ojewola RW. Prostate diseases in Lagos, Nigeria: A histologic study with tPSA correlation.
26. Medhin LB, Achila OO, Syum BE, et al. Incidence of prostate cancer in Eritrea: Data from the National Health Laboratory, Orotta Referral Hospital, and Sembel Hospital 2011-2018. (2020) PLoS ONE 15(4): e0232091. https://doi.org/10.1371/journal.pone.0232091
27. Seife H, Deneke A. A descriptive study of transvesical prostatectomy outcomes at a general hospital in Addis Ababa, Ethiopia. East Cent Afr J Surg:2018;23(1):22–6 https://dx.doi.org/10.4314/ecajs.v23i1.5
28. Arshad H, Ahmad Z. Overview of Benign and Malignant Prostatic Disease in Pakistani Patients: A Clinical and Histopathological Perspective. Asian Pacific J Cancer Prevention; 14(2013):3005-3010.
29. Naz S, Ahmed S, Gamfoor F, Butt NS, Akhtar MW. Free and total PSA in BPH and prostate cancer. JCPSP. 2004;14(2):69-71.
30. Joniau S, Hsu C, Lerut E, et al. A Pretreatment Table for the Prediction of Final Histopathology after Radical Prostatectomy in Clinical Unilateral T3a Prostate Cancer; European urology. 2007; 51:388–396.
31. Aboagye E, Asante E, Owusu- Afriyie F, Titiloye N, Duduyemi B. Histopathological Pattern of Prostate Cancer in a Tertiary Hospital in Ghana *Am J Clin Pathol* 2019;152: S37-S75 DOI: 10.1093/ajcp/aqz113.
32. Yahaya JJ. Clinical and Histopathological Profile of Patients with Prostate Cancer in Kampala, Uganda. *Medical Journal of Zambia; 2019; 46 (1): 19 – 27.*
33. Seifu J. A HISTORICAL SURVEY OF JIMMA TOWN (1936-1974) [master's thesis]. Addis Ababa: Addis Ababa University; June 2002.
34. Jimma university website. file:///I:/jumc-erasmus-mc-establish-collaboration-cancer-care.html. Accessed on June 18, 2020.
35. Federal Ministry of health. National comprehensive COVID19 management handbook. Ethiopia, April 2020.

Annex:

Checklist

Data collection checklist to study histopathologic patterns of prostate lesions

No.	Variables	Options	Choice
1	Biopsy No. _____ MRN No. _____		
2	Year of biopsy	A. Sep.2014-agu.2015 B. Sep.2015- agu.2016 C. Sep.2016- agu.2017 D. Sep.2017- agu.2018 E. Sep.2018-agu.2019	
3	Age at diagnosis (years)	In years	
4	Residence	A. Urban B. Rural	
5	PSA (ng/ml)	A. 0-4 B. 4.1-10 C. 10.1-20 D. >20.1 specify_____	
6	Type of specimens	A. TURP B. R. Prostatectomy C. TVRP D. Other. Specify_____	
7	Clinical Diagnosis		
8	Histopathologic diagnosis	A. Prostatitis B. BPH only C. BPH With prostatitis D. BPH With metaplasia E. Type of metaplasia e.1._____ F. Intraepithelial neoplasms G. CARCINOMA	
9	If cancer, Gleason score	1*____And 2*____=_____	
10	If cancer, grade	A. Well-differentiated B. Moderately differentiated C. Poorly/undifferentiated	
11	The histological type of cancer	A. Adenocarcinoma B. Sarcoma C. Others_specify_____	

Institutional consent form
To: Jimma university MC pathology department

Hello! My name is Dr. Lijalem Birhane final year pathology resident in the Jimma University, pathology department. I am studying "Histopathologic Patterns of Prostate Biopsy Sent to Jimma University Medical Center, Jimma, Southwest Ethiopia: A Five-year retrospective study."

The objective of the study is to describe a histologically diagnosed prostate biopsy, seen at the pathology department of Jimma university medical center, from September 2014 to August 2019. Method impalement will be a hospital-based cross-sectional study that will be conducted. Records (secondary data) of all patients diagnosed with pathological diagnosis of prostate disease in the pathology department from September 2014 to August 2019 will be included in the study.

During selecting and training data collectors and while data collection all measures will be undertaken to protect from COID-19 such as wearing PPE, social distancing, and using sanitize-rs according to the national infection prevention protocol guideline. I will not use the patients' names to respect their confidentiality. So, I would like to kindly request the department to permit me to use the data for my research.

With regards,

ASSURANCE OF PRINCIPAL INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Faculty of Public Health in effect at the time of grant is forwarded as the result of this application.

Name of the student:

Dr. Lijalem Birhane Date._____ Signature _____

APPROVAL OF THE FIRST ADVISOR

Name of the first adviser:

Dr. Gebi Nemo Date._____ Signature _____

Name of the second advisor:

Prof. Kifle Woldemichael Date._____ Signature _____