

## HISTOPATHOLOGICAL ANALYSIS OF PROSTATE CANCER IN JAMMU AND KASHMIR

**Zaffar Iqbal Waloo**

Research Scholar

Rayat Bahra University Mohali Punjab India

**Mr.K S Rana**

Associate professor

MLS Pathology

**Dr Afiya Shafi**

HOD Pathology

SKIMS Medical College and Hospital Bemina Srinagar Kashmir India

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### ABSTRACT

*Prostate cancer is a major cause of morbidity and mortality due to cancer in the world and is ranked one of the most common malignancies among the elderly men. The gold standard of diagnosis, grading, and prognostication remains to be performed with the help of histopathological examination, but this method is suggested to be not exhaustive given the regional heterogeneity of disease trends. This cross-sectional randomized study is descriptive because it was carried out on 52 men aged 57-73 years of age with a clinical suspicion of having prostate disease. The biopsy samples which were collected through transrectal ultrasound-guided biopsy or transurethral resection of the prostate (TURP) were processed and examined histologically and the lesions were categorized into benign prostatic hyperplasia (BPH), prostatitis, or adenocarcinoma. The Gleason/ISUP system was also used in further classification of adenocarcinoma cases. The average age of the patients was 64.9 years old. The most frequent lesion (51.9%), was BPH, then prostatitis (40.4%) and adenocarcinoma (7.7%). Serum PSA was between 8.2122.4 ng/mL (mean 13.9 +/-4.2 ng/mL), and was mostly more elevated in cancerous lesions. Out of all cases of adenocarcinoma, 75 percent of the cases exhibited intermediate-to-high tumor grades that depict aggressive disease morphology. In general, the results indicate that prostate pathology is mostly common in elderly men with benign lesions as the predominant feature of diagnosis although a significant percentage of the cancers also occurs at advanced grade levels, which is an indication that they have been detected late. Histopathological analysis cannot be replaced by PSA as it is an essential diagnostic and prognostic tool whereas PSA is now a helpful, yet not diagnostic, auxiliary method.*

**Keywords:** Prostate cancer, Histopathology, Gleason Grade, PSA, Adenocarcinoma, Benign Prostatic Hyperplasia



## 1. INTRODUCTION

Prostate cancer is one of the most commonly diagnosed cancer types in men all over the world, and one of the major causes of cancer morbidity and mortality. The incidence of it increases significantly after the sixth decade of life as combination of aging, hormonal imbalance, genetic vulnerability, lifestyle alterations, and environmental exposures. With the trend in life expectancy gaining momentum in the global population, the pressure of prostate cancer is bound to grow even more and more especially in the developing world whereby screening coverage and awareness is likely to be low. Besides malignancy, benign diseases of the prostate, including benign prostatic hyperplasia and prostatitis, are also likely to be associated with similar clinical manifestations, such as urinary obstructions, weak stream, hesitancy, or high levels of prostate-specific antigen (PSA). This clinical overlap often makes diagnosis complicated and it explains the relevance of effective pathological verification.

Although there has been a progress in diagnostic radiology, endoscopic procedures, and the use of tumor markers to screen prostate cancer, histopathology is the gold standard form of identifying prostate lesions. Microscopic analysis permits intense evaluation of glandular structure, cellular dysplasia, nuclear patterns, stromal response, and invasion. Adenocarcinoma represents over 95 percent of all malignant prostate tumors and is traditionally graded according to either the Gleason/International Society of Urological Pathology (ISUP) system. In addition to the reflection of tumor differentiation, this grading system shows a strong correlation with the clinical outcome, biological aggressiveness, risk of recurrence and probability of survival. Therefore, histopathological examination is important in the diagnosis of prostate cancer as well as in treatment, counselling of patients, and prognosis prediction.

The local-level researches are very helpful in understanding the patterns of disease that are population specific, differences in presentation and health seeking behavior. Nevertheless, even though the clinical value of prostate disease is significant, there has been scanty reported research in Jammu and Kashmir region on the histopathological features of prostate lesions. Local data are important in order to know the disease burden, help clinicians diagnose, and aid in health policy planning. It is against this background that this paper was conducted in order to examine the histopathological spectrum of prostate lesions in prostate disease patients who are presented with suspected prostate disease in Jammu and Kashmir with particular reference



to adenocarcinoma of the prostate. Another goal of the study was to draw the correlation between microscopic results and age, PSA levels, thus, providing the region-specific evidence to the scientific community and contributing to the better field practice in the area.

### **1.1 Background of the Study**

Prostate cancer is a high incidence malignancy in the male population of the world and one of the major causes of cancer morbidity and mortality, especially in old men. Its prevalence rises progressively with age and most of the cases arise after the sixth decade of age. Even though diagnostic imaging and serum biomarkers like prostate-specific antigen (PSA) have become more widespread in identifying the disease, histopathological studies remain the expected standard of diagnosis, evaluation of the tumor grade, and prognosis. Malignancy is not the only prostate pathology, however. Such benign conditions like benign prostatic hyperplasia (BPH) and prostate inflammation are very common and can have similar clinical manifestations with lower urinary tract obstruction and increased levels of PSA. This overlap usually complicates clinical identification and the importance of tissue examination.

Differences in clinical presentation, disease burden, and tumor biology by regions give rise to the necessity of local research. Published data on histopathological spectrum of prostate lesions are scarce in Jammu and Kashmir and there is still a necessity of improved understanding of the trends of benign and malignant prostate disease in the local population. The value of generating such evidence is not merely to enhance clinical diagnosis and management but it is also relevant in informing strategies to promote effective population health in regions with high rates of late presentation and where screening coverage is minimal to result in poor outcomes.

Thus, the current research was carried out to analyze the histopathological features of the prostate lesions, and in particular the prostate adenocarcinoma and to compare these results with the age of patients and the level of PSA. This study will help to enhance the early detection, risk stratification, and patient care within the region by setting up locally relevant data.

## 2. LITERATURE REVIEW

**Angurana (2014)** carried out histopathological research of prostate diseases in Jammu and found that benign prostatic hyperplasia (BPH) was the leading lesion that was observed, followed by prostatitis and adenocarcinoma. The research pointed out that most of the affected patients were of older age, and this confirms that increasing age is closely linked to prostate pathology. The author also reported that the adenocarcinoma was more common among elderly males, and this implies that malignancy was more likely to occur at a later stage in life where cumulative hormonal and genetic factors could be a big factor. The results also highlighted the diagnostic importance of the histopathology in distinguishing between the benign enlargement and malignant transformation which is frequently unachievable when alone using clinical or biochemical evaluation.

**Farooq et al. (2019)** tested prostate specimens in a tertiary care hospital in Kashmir and outlined broad range of histopathology patterns that include benign lesions and malignant tumors. They found out that BPH was the most common diagnosis; chronic prostatitis and adenocarcinoma were also very common. The authors found that clinical and radiologic manifestations of inflammatory alterations were frequent in patients who presented with urinary complaints, and the conditions frequently simulated malignancy. The research stressed that histopathology was a vital part of outlining the benign and malignant lesions in the case of patients who exhibited the similarity in clinical manifestations and patients with borderline increases in PSA. This article advocated the necessity of regular biopsy assessment in cases of suspicion to facilitate the correct diagnosis and early cancer diagnosis.

**Humphrey (2017)** described the morphological features that were used to diagnose and grade adenocarcinoma. The author was able to describe the following key microscopic characteristics glandular architecture, cellular atypia, the enlargement of the nucleus, prominent nucleoli, and infiltrative patterns of growth. Special attention was given to the Gleason grading system according to which the tumors were classified according to the glandular differentiation and the structure. The review has revealed the prognostic importance of such a grading system in that, an increase in Gleason scores corresponded with worse prognosis, increased recurrence and metastatic potential. The author also showed the use of histopathological analysis in the

management of the treatment decisions e.g. planning surgical operations, radiotherapy, and hormones in treatment.

Kuten et al. (2020) relative to the use of histopathology and immunohistochemistry as reference standards, the staging of prostate cancer with PET/CT imaging with either of the following techniques:  $^{68}\text{Ga}$ -PSMA-11 and the  $^{18}\text{F}$ -PSMA-1007. They said that the two tracers were high in diagnostic accuracy in primary and metastatic lesions but some variations in localization of lesions and background uptake were observed. It was shown that newer modalities of molecular imaging were of great significance as complements to histopathological diagnosis as it enhanced the accuracy of pre-treatment staging and also provided the opportunity to have more accurate determination of disease burden. These results supported the combination of imaging and pathology in the management of prostate cancer in present times.

**Le et al. (2015)** studied the correlation between multiparametric MRI outcomes and whole-mount histopathology in the diagnosis of multifocal prostate cancer. They claimed that MRI had been effective in detecting much of the clinically significant lesions, especially the higher-grade tumours but some small or multifocal lesions were not detected. The authors made the conclusion that MRI improved the accuracy of the diagnosis and localization of lesions, but histopathology was still necessary to confirm the diagnosis, multifocality of the tumor, and the assessment of the tumor margins. Their results emphasised the complementary nature of imaging and tissue examination particularly in directing targeted biopsy and surgical planning.

**Lee et al. (2014)** created and tested a multi-view canonical correlation analysis (sMVCCA) method under supervision which combined histological and proteomic attributes to forecast recurrent prostate cancer after treatment. They have shown that using the combination approach of histopathological data and molecular profiling enhanced prognostic predictions compared to the traditional histological method. The model was able to determine high-risk patients, who were susceptible to disease recurrence. The results endorsed the emerging position of computational pathology, artificial intelligence, and biomarker-based analytics in complementing standard microscopic diagnosis and augmenting individualized treatment plans.

### **3. RESEARCH METHODOLOGY**

The study was set to assess the histopathological spectrum of prostate lesions in people who appear to have prostate disease. The descriptive cross-sectional study design has been chosen because it would allow a systematic analysis of samples of prostate tissue that are submitted to the histopathological examination and compare the observed results with the corresponding clinical parameters. Tissue processing, staining, and microscopic evaluation were done in a standardized way to provide accuracy and reproducibility of the results. This chapter explains in great detail the study setting, study population, sample size, inclusion and exclusion criteria, specimen processing procedures and diagnostic assessment procedures used in the study.

#### **3.1 Research Design**

The study was a descriptive cross-sectional study that involved the Departments of Pathology and Urology in Sher-i-Kashmir Institute of Medical Sciences (SKIMS) Medical College and Hospital, Bemina, Srinagar. The paper dealt with the histopathological spectrum of the lesions of the prostate, particularly the diagnosis and the grading of prostate adenocarcinoma.

#### **3.2 Sample Size**

The sample size of the study included 52 male patients who were aged between 57 and 73 years and presented themselves to the study with clinical suspicion of having prostate disease within the study period. All registered patients had a transrectal ultrasound-guided prostate biopsy carried out or transurethral resection of the prostate (TURP) and tissue specimens obtained were forwarded to the histopathology lab (sample size  $n = 52$ ).

The patients were eligible when they were male in the age bracket, had histopathology samples by way of either biopsy or TURP and supplied proper and well preserved tissues in 10 percent neutral buffered formalin. Poorly preserved or autolyzed specimens, non-prostatic tissues and cases having incomplete clinical information were not part of the study. General procedures all specimens were standard procedures: Stained with paraffin wax and sectioned to thickness of 35 microns using a rotary microtome. Staining of the sections was done with hematoxylin and eosin (H&E) under microscopic observation and in special cases, special stains and immunohistochemical markers were used to differentiate between benign and malignant lesions.

### 3.3 Microscopic Evaluation

The tissue sections were studied through a light microscope, and histopathological evaluation in detail was done to analyze the glandular structure, cellular abnormality, cellular nucleus, stromal reaction, and signs of the local tissue invasion. The lesions, as per their microscopic features were categorized into three broad diagnostic effects, which are benign prostatic hyperplasia (BPH), prostatitis, and adenocarcinoma of the prostate.

## 4. RESULTS

The current research, the histopathology spectrum of prostate lesions in 52 male patients who came with suspected prostate disease was examined. The results are described in the format of descriptive statistics which are frequencies, percentages, and distribution patterns in various clinical and pathological categories. Findings involve patient age distribution, histopathological diagnosis of the lesions in prostate, serum PSA levels, as well as tumor grading of the cases of adenocarcinomas. These observations are used to give an idea about the relative load of benign and malignant prostate pathology among the study population.

### 4.1 Age Distribution

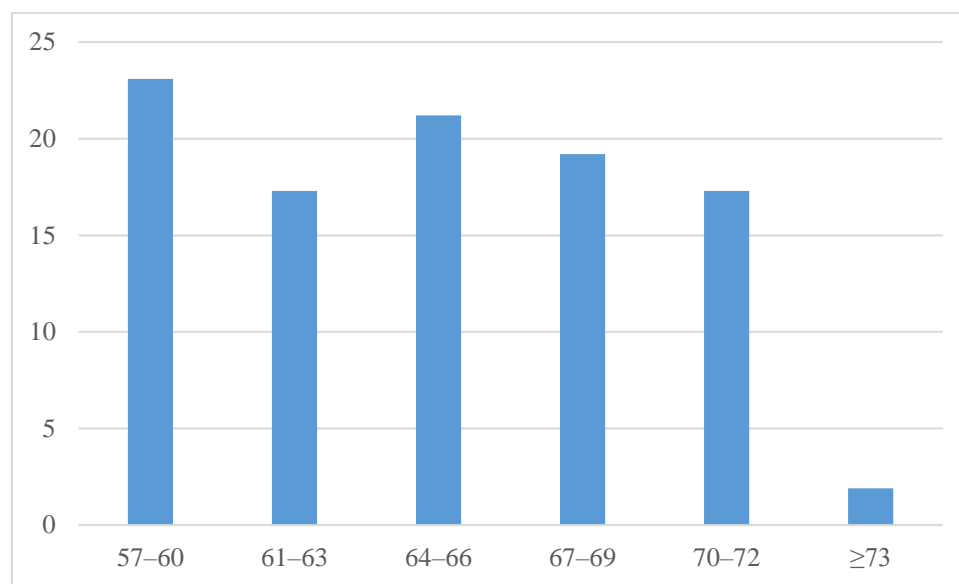
In this table, the distribution of the study participants according to the age groups is shown and the frequency and percentage of the number of patients in each group are provided (n = 52) is stated.

**Table 3.1:** Age-wise Distribution of Study Participants

Age Group (Years)	Frequency (n)	Percentage (%)
57–60	12	23.1
61–63	9	17.3
64–66	11	21.2
67–69	10	19.2
70–72	9	17.3
≥73	1	1.9

<b>Total</b>	<b>52</b>	<b>100.0</b>
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The age groups with the largest percentage represented the 57-60 years (23.1), 64-66 years (21.2) and 67-69 years (19.2). The age of the one patient (1.9%) was 73 years or above. In general, most of the cases of prostate diseases were seen in men aged between the sixth and the seventh decades of life and this shows that prostate pathology is an old age disease.



**Figure 1:** Graphical Representation of the Percentage of Age-wise Distribution of Study Participants

The percentage of the study participants by age groups is presented in figure 1. As demonstrated in the graph, most of the patients were clustered around the sixth and the seventh decades of life and more specifically in the age brackets of 57-60 years old, 64-66 years old, and finally 67-69 years old. The proportion of patients aged 73 years and above was very small. This trend shows that elderly men were the most prevalent users of the prostate disorders, which corroborates the already established relationship between increasing age and prostate disease.

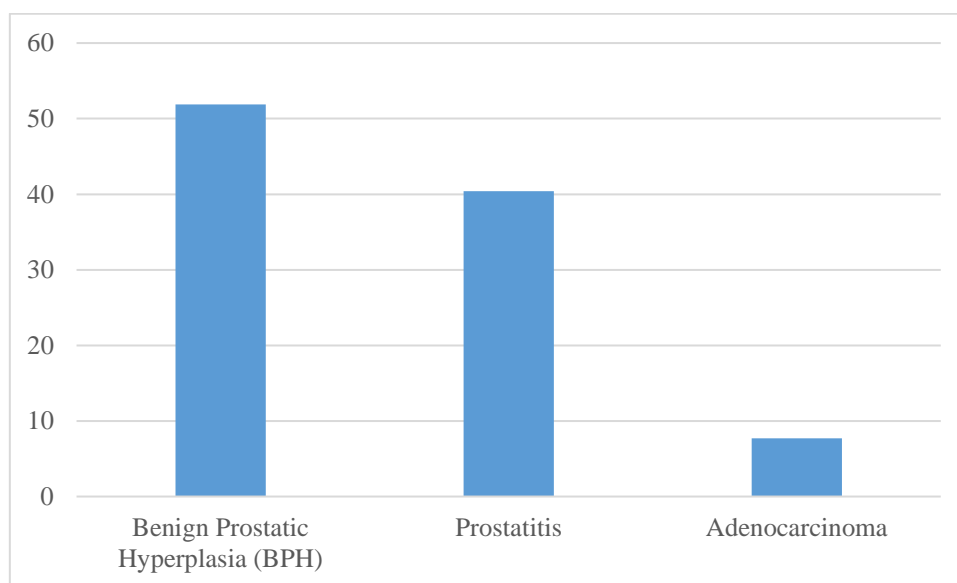
#### 4.2 Diagnostic Spectrum

The table shows frequency and percentages distributions of different prostatic lesions that were diagnosed on histopathological examination of the 52 participants in the study.

**Table 3.2:** Distribution of Prostatic Lesions Based on Histopathological Diagnosis

Diagnosis	Frequency (n)	Percentage (%)
Benign Prostatic Hyperplasia (BPH)	27	51.9
Prostatitis	21	40.4
Adenocarcinoma	4	7.7
<b>Total</b>	<b>52</b>	<b>100.0</b>

Among the four cases of adenocarcinoma, one (25%) of the cases was low grade, 2 cases (50%) were intermediate grade, and 1 case (25%) was high grade. In this way, 75 % of the tumors exhibited at least an intermediate-grade nature, which implies a shift towards more aggressive tumor biology and that the majority of patients might present themselves at a rather advanced pathological stage.



**Figure 2:** Graphical Representation of the Percentage of Distribution of Prostatic Lesions Based on Histopathological Diagnosis

As shown in the graphical representation, BPH constitutes a little more than half of all lesions that are being diagnosed, and then there is prostatitis that constitutes a little bit more than one-third of the cases. Adenocarcinoma carries the least percentage. The visual representation of

the figure supports the fact that the indolent conditions are predominantly high in frequency than malignant pathology in patients who show complaints that are related to prostate.

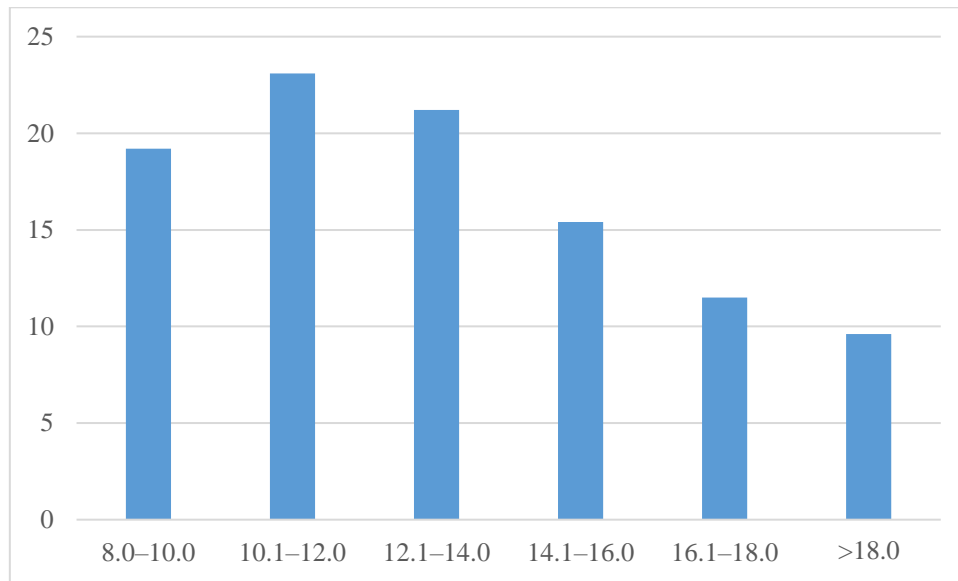
### 4.3 PSA Levels

The table below summarizes the distribution of serum PSA levels of the study population with the ranges of PSA classified as clinically significant.

**Table 3.3:** Distribution of Serum PSA Levels Among Study Participants

PSA Level (ng/mL)	Frequency (n)	Percentage (%)
8.0–10.0	10	19.2
10.1–12.0	12	23.1
12.1–14.0	11	21.2
14.1–16.0	8	15.4
16.1–18.0	6	11.5
>18.0	5	9.6
<b>Total</b>	<b>52</b>	<b>100.0</b>

The largest percentage of participants fell within the range of 10.1-12 ng/mL (23.1%), then there was 12.1-14 ng/mL (21.2%). Only 9.6 percent of the patients exhibited PSA levels of more than 18.0 ng/mL. In general, PSA levels were moderately high in the majority of cases, and a higher level of concentration was usually connected with the malignant lesions. This confirms the diagnostic utility of PSA as a screening test, but it is still a nonspecific test that should be used in conjunction with histopathological results.



**Figure 3:** Graphical Representation of the Percentage of Distribution of Serum PSA Levels Among Study Participants

The bar graph shows that most patients are in the mid-range categories of PSA (1014 ng/mL) with gradually decreasing number of patients having very high PSA levels. The reason why this pattern is exhibited is that, whereas PSA elevation is prevalent among men with prostatic disorders, significantly high levels are relatively uncommon and can be regarded as an indication of increased risk of malignancy.

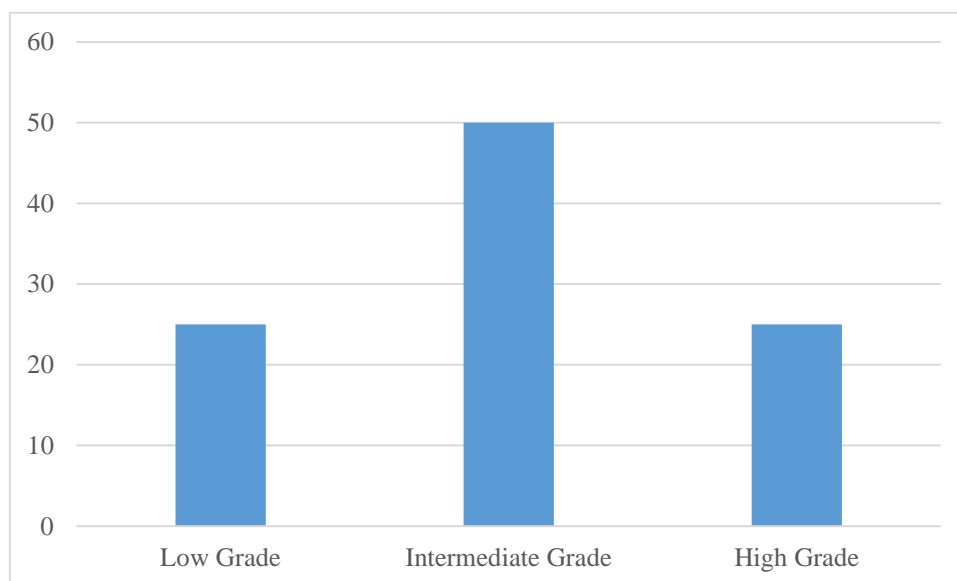
#### 4.4 Tumor Grading (Adenocarcinoma Only, n = 4)

The following table shows the percentage and frequency of tumor grade of four histologically confirmed incidences of adenocarcinoma.

**Table 3.4:** Histopathological Tumor Grade Distribution Among Adenocarcinoma Cases

Tumor Grade	Frequency (n)	Percentage (%)
Low Grade	1	25.0
Intermediate Grade	2	50.0
High Grade	1	25.0
<b>Total</b>	<b>4</b>	<b>100.0</b>

The distribution of the four cases of adenocarcinoma was one (25%) which was low grade, two (50%) which were intermediate grade, and one (25%) which was high grade. In such a way, 75% of the tumors exhibited at least intermediate-grade characteristics which is an indicator of a tendency towards increased aggression in the tumor biology and suggests that a large number of patients will be diagnosed at a relatively advanced stage of pathological progression.



**Figure 4:** Graphical Representation of the Percentage of Histopathological Tumor Grade Distribution Among Adenocarcinoma Cases

The figure 4, it can be observed that the highest percentage of cases of prostate cancer in this study is comprised of intermediate grade tumors with the same percentage of low and high grade tumors. This visual pattern is also supportive of the fact that most diagnosed malignancies have more biologically aggressive lesions.

## 5. DISCUSSION

The current research determined the histopathology profile of prostate lesions in old men in Jammu and Kashmir and confirmed that prostate pathology is essentially an age-related disease. The average age of 64.9 years of the present research is similar to the tendencies in the world and country; the most frequent reporting of prostate disorders occurs during the 6<sup>th</sup> and 7<sup>th</sup> decades of life. This may be caused by age-associated hormonal disparities, lifelong genetic modifications, and enduring inflammatory provocation.

Benign Prostatic Hyperplasia (BPH) became the most common histological diagnosis then there was prostatitis. The fact that benign lesions are more predominant indicates that as much as obstruction to urinary symptoms is widespread among the elderly males, malignancy has a smaller yet significant proportion. Prostatitis was found to be more than one-third of the cases and this goes to confirm the idea that chronic inflammation is a common comorbidity in the aging prostate and would be one of the reasons why PSA would increase and cause diagnostic confusion in clinical practice.

A total of 7.7% were adenocarcinoma of the prostate consistent with the results of biopsy based studies in the same areas. It is important to note that 75 percent of cancers were intermediate-to-high grade indicating the aggressive biological potential and late clinical detection. This strengthens the need to screen and refer to biopsy in time among high-risks patients.

The levels of PSA were moderate to significantly high in the study group, and higher levels mostly were found in malignant lesions. Although, PSA is a biomarker of prostatic pathology, it increases even in the presence of benign lesions as well as inflammatory lesions which once again confirms the idea that PSA cannot in any way differentiate the type of lesion and should, therefore, be used with histopathological results.

## **6. CONCLUSION**

This paper has shown that prostate lesions occur in old men with benign prostate lesions including benign prostatic hyperplasia and prostatitis accounting majority of the histopathological diagnosis. Despite the lower percentage of adenocarcinoma, majority ascribed morphological characteristics of the cancers were of intermediate-to-high grade, indicating aggressive potential of the tumor and late-clinical manifestation. High levels of serum PSA were observed in several patients and demonstrated a overall correlation with malignant lesions; nevertheless, PSA is not a diagnostic specific test and it is rather applied as the supplementary tool to the histopathological examination. Histopathology is hence the ultimate technique of accurate diagnosis, tumor grading, and prognostication on prostate disease. The results reveal that more awareness should be created, and early detection methods, as well as timely biopsy assessment, must be employed to uplift clinical outcomes in managing prostate cancer in the region.

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