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Original Research Article

Correlation between Pretreatment Serum Prostate-Specific Antigen (PSA) Level and Gleason Grade Group in Prostatic Adenocarcinoma

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Abstract

Introduction: Adenocarcinoma of the prostate may be clinically suspected based on elevated serum PSA (Prostate Specific Antigen) and/or abnormal digital rectal examination. Patients with high S/PSA are at increased risk of advanced carcinoma prostate and screening at an earlier stage would help to manage it accordingly. The aim of this study is to determine association between pretreatment serum prostatic specific antigen (PSA) levels and Gleason grade group in prostatic adenocarcinoma patients.

Material and Method: A total 50 prostatic carcinoma cases were studied in this hospital based cross sectional study carried out in the department of pathology, Gauhati Medical College and hospital.

Trans rectal ultrasound (TRUS) guided biopsy specimen sent from urology and renal transplant department were processed for H&E stain and studied histomorphologically. Adenocarcinoma cases were assigned Gleason score and Gleason grade group. Pretreatment serum PSA level is correlated with Gleason grade group using chi square test, a P value of <0.05 was considered statistically significant.

Result: all 50 cases were adenocarcinoma. The mean PSA level 77.38±49.14 ng/ml. Grade group 1 was seen in 5(10%) cases, Grade Group 2 was seen in 11(22%) cases grade group 3 was seen in 22(44%) cases, Grade group 4 was seen in 5(10%) cases and grade group 5was seen in 7(14%) cases. A statistically significant correlation was found between pretreatment serum PSA level and Gleason Grade Group (P<0.028).

Conclusion: Carcinoma of prostate associated with an elevated serum PSA level is more likelyto be of higher grade than carcinoma with normal PSA levels.

Keywords: Serum PSA, Adenocarcinoma Prostate, Gleason Grade Group.

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Introduction

Worldwide prostate cancer is the third most common malignancy in men with an estimate of about 1.2 million new cases in 2018. [1] Several factors, including age, race, family history, hormone levels, and environmental influences are suspected to play a role in pathogenesis. [2] Most of the prostatic carcinomas are adenocarcinomas (85-90%) and mainly located in the posterior/ posterolateral peripheral zone [3].

Incidence of carcinoma of prostate has gradually increased worldwide since the last fifty years due to the availability of better diagnostic techniques, widespread use of serum prostate specific antigen (PSA) testing, increased life expectancy and awareness of the population in general. [4] Serum PSA, a glycoprotein identified by Wang et al (1979), is produced exclusively by the benign and malignant prostatic tissue with normal levels of 0-4ng/ml. [5] increased serum PSA levels are seen in all prostatic diseases but markedly elevated levels are indicative of carcinoma prostate. [6] Whenever carcinoma of prostate is suspected clinically, a digital rectal examination (DRE), serum PSA testing, and biopsy of the prostate are performed. [7] Currently TRUS (Tran's rectal ultrasonography) is the first modality of choice to image and biopsy in case of suspected prostatic pathology [8]. Various histopathological grading systems have been developed to correlate with the prognosis of adenocarcinoma of prostate. Gleason grading is one of the best predictors of biological behaviour and influential factors used to determine prostate carcinoma treatment [9].

The aim of the present study is to evaluate the histopathology of carcinoma of prostate and its grade (Gleason grade) in TRUS guided prostatic biopsy specimens and correlate it with serum PSA levels.

Material and Methods

After obtaining approval from institutional ethical committee (no. MC/190/2007/PT-II/JULY-2021/TH-8) the hospital based cross sectional study was conducted in the department of pathology, Gauhati Medical College and Hospital for a period of one year from July 2021 to June 2022. Tran's rectal ultrasound (TRUS) guided prostatic core biopsy were received from the department of urology, Gauhati Medical college and Hospital in separate vials to the department of Pathology for processing and histopathological examination. Clinical data, imaging findings and pretreatment serum PSA level were collected from hospital records. All carcinoma cases of prostate were included in the study. Non neoplastic conditions, inadequate sample and medical data and cases under treatment were excluded from the study. Total 50 cases of carcinoma prostate were studied who presented with mostly lower urinary tract symptoms (LUTS). All the biopsy specimens were fixed in 10% neutral buffered formalin and were subjected to routine processing for paraffin embedding. Minimum two sections were cut from each block and stained with Hematoxylin and Eosin (H&E) and seen under light microscope for histopathological diagnosis and Gleason scores/grades were evaluated. Under light microscopy using Gleason grade grouping system of 2014 and 2019 ISUP grade grouping system modification carcinoma of the prostate were classified into five grade groups, Group 1(score of 3+3=6), Group 2 (score of 3+4=7), Group 3 (score of 4+3=7), Group 4 (score of 4+4=8), Group 5 (score of 9-10). Serum PSA level > 4ng/ml was taken as cut-off point for abnormal serum PSA.

Statistical Analysis: The results were analysed using IBM SSPS software v21. Descriptive statistics was done for Pretreatment PSA level and Gleason grading along with age distribution and other clinical parameters, digital rectal examination findings, bony metastasis, perineural invasion, lympho-vascular invasion, and ultrasonographic findings

Chi square test was used to evaluate association between Gleason grade group and pretreatment serum PSA level. P <0.05 was considered statistically significant.

Result

Total 50 cases were analysed histopathologically and studied for association of Gleason grade group with pretreatment serum PSA level.

The age of the patient ranged from 37 to 87 years. Maximum no of cases were seen in the age group 70 -79 years followed by 60-69 years. Least number of cases seen in the age group 30-39 years.

All cases were clinically presented with lower urinary tract symptoms. The most prevalent presenting complaint among the patient was increased frequency of urine (34%) followed by acute retention of urine (28%). Difficulty in passing urine was seen 20% of cases, dysuria was seen in 8% cases, haematuria was seen in 4% cases, and hesitancy was seen as least presenting complaints (2%). Reduced stream was seen in 4% cases.

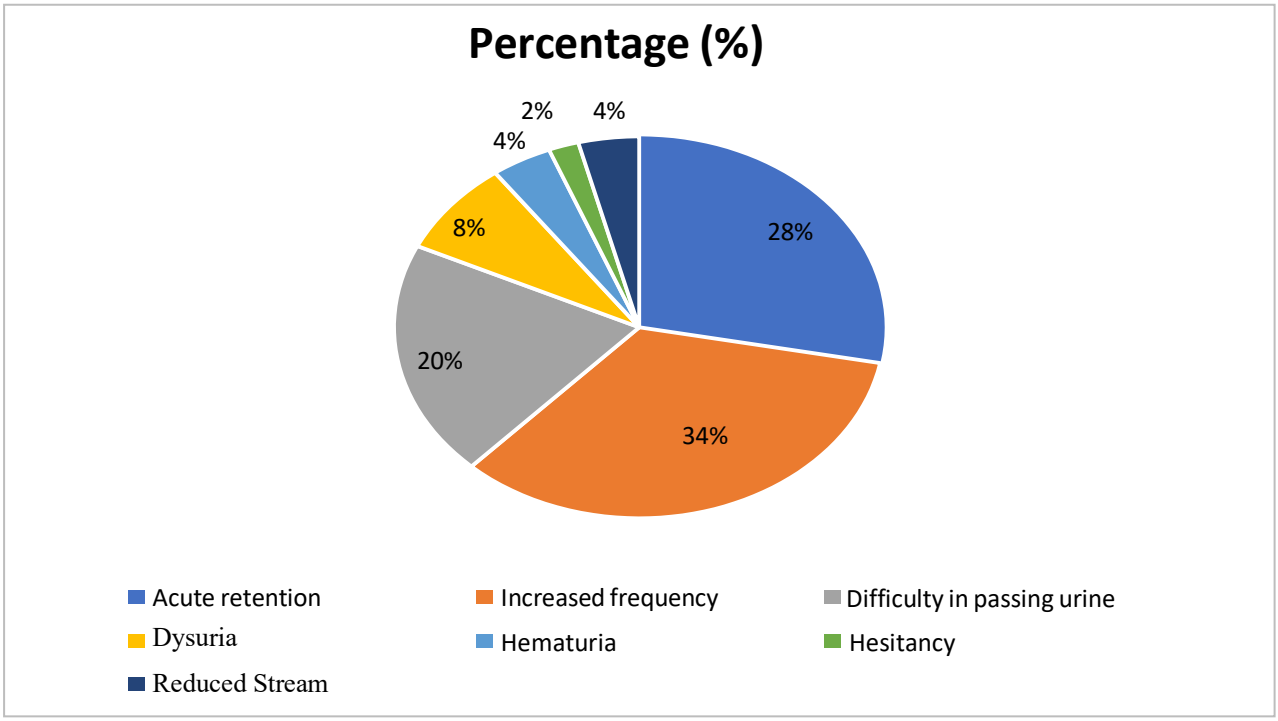

Figure 1: Distribution of cases based on clinical feature

Among 50 cases of prostatic carcinoma digital rectal examination was abnormal in 76% (38) cases.

In this study 54% (27) of patients had grade II prostatomegaly as diagnosed in ultrasonography Grade III prostatomegaly was seen in 18% (9) cases where as 28% (14)cases showed grade I prostatomegaly.

The mean PSA level was found to be 77.38±49.14 ng/ml. Among the cases the highest value of pretreatment PSA was 200 ng/ml whereas lowest value was 8 ng/ml. Majority of the patient had serum PSA level more than >50ng/ml. No patient showed serum PSA level between 0-4 ng/ml.

Bony metastasis was seen in 34% cases whereas bone scan was negative in 66% cases. Histopathologically all the cases 100% (50) were diagnosed as adenocarcinoma prostate. In this study primary scoring pattern 4 was seen in 54% cases, primary scoring pattern 5 was seen in 12% cases. Most common primary pattern was 4 and least common primary pattern was pattern 5.

Out of 50 cases, secondary scoring pattern 3 was seen in 56% cases, secondary scoring pattern 4 was seen in 32% and pattern 5 in 12 % cases. Most common secondary pattern was pattern 3 and least common secondary pattern was pattern 5. Out of 50 cases Grade group 1[Gleason score 6(3+3)] was seen in 5(10%) cases, Grade Group 2[Gleason score7(3+4)] in 11(22%) cases, grade group 3[Gleason score 7(4+3)] in 22(44%) cases, Grade group 4[Gleason score 8(4+4; 3+5; 5+3)] in 5(10%) cases and grade group 5[Gleason score 9(4+5) in 5 cases and Gleason score 10(5+5) 2 cases] in 7(14%) cases.

Table 1: Distribution of cases based on Gleason Grade group

Gleason grade group	Number of cases	Percentage (%)
1	5	10 %
2	11	22 %
3	22	44 %
4	5	10 %
5	7	14 %
Total	50	100 %

Perineural invasion was seen in 11(22%) cases. Lympho vascular invasion was seen in 4% cases

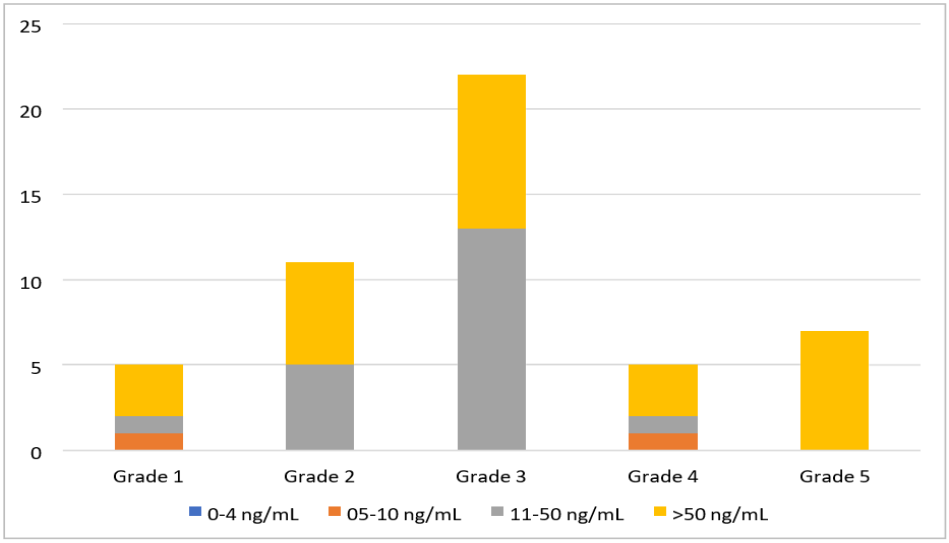

Figure 2: Distribution of cases based on pretreatment serum PSA levels and Gleason grade group

The distribution of pretreatment PSA levels in different categories of Gleason grade groups showed that 3 cases (6%) o f Grade I tumors had serum PSA < =50ng/ml.

One case (2%) between 5-10 ng/ml, one case (2%) between 11-50ng /ml.

Grade 2 tumors had PSA level between 11-50ng/ml in 5 cases (10%) and > 50ng/ml in 6(12%) cases.

Grade 3 tumors had PSA level between 11-50ng/ml in 13(26%) cases whereas 9(18%) showed serum PSA level > 50ng/ml.

In case of grade 4 tumors 1(2%) case had serum PSA level between 5-10ng/ml, another1(2%) case had serum PSA between 11-50ng/ml, 3 cases (6%) had serum PSA more than >50ng/ml.

All the grade 5 tumors had serum PSA > 50ng/ml.

Table 2: Distribution of pre-treatment serum PSA level in relation to Gleason grade group

Gleason Grade Group	PSA level (ng/mL)					P value
	0-4	5-10	11-50	>50	Total	
Grade 1	0	1	1	3	5	0.0278
Grade 2	0	0	5	6	11	
Grade 3	0	0	13	9	22	
Grade 4	0	1	1	3	5	
Grade 5	0	0	0	7	7	
Total	0	2	20	28	50	

A Statistically significant association was found between Gleason grade group and pretreatment serumPSA (P = 0.0278). The mean serum PSA level of Gleason grade group 1was 47±26.6ng/ml, group 2 was 60.36±38.56ng/ml, group 3 was 71.54±38.21ng/ml, group 4 was 79.5±45.41ng/ml and group 5 was142±53.88ng/ml.

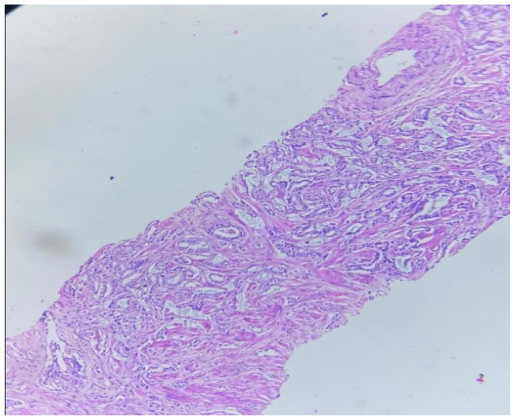

Figure 4: Photomicrograph showing Gleasonpattern3 (10X10) view

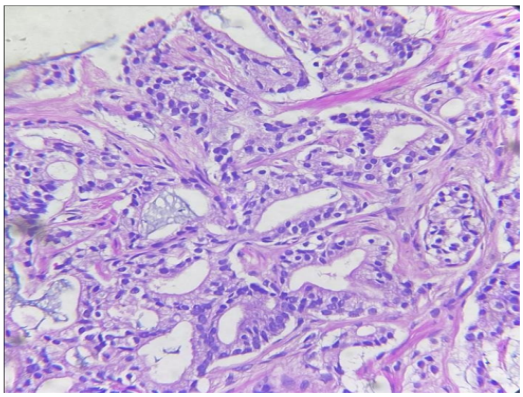

Figure 5: Photomicrograph showing Gleasonpattern3 (10X40) view

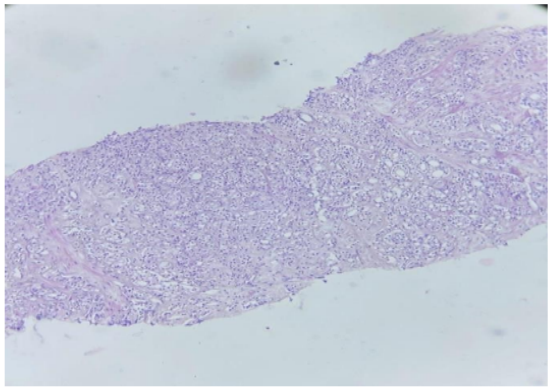

Figure 6: Photomicrograph showing GleasonPattern 4(fused glands) (10X10) view

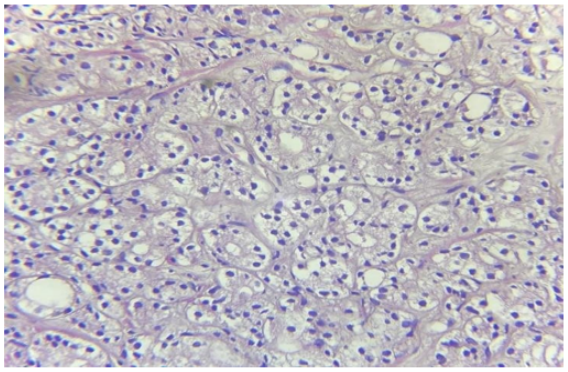

Figure 7: Photomicrograph showing GleasonPattern 4(fused glands) (10X40) view

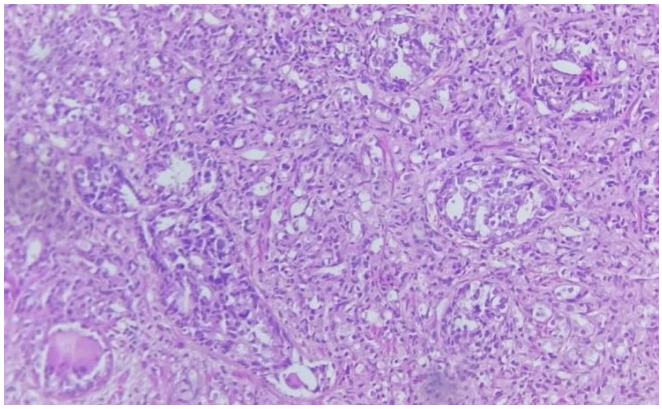

Figure 8: Microphotograph showing ciribriform and fused glands (10X 40) view, Pattern 4 (H&E)

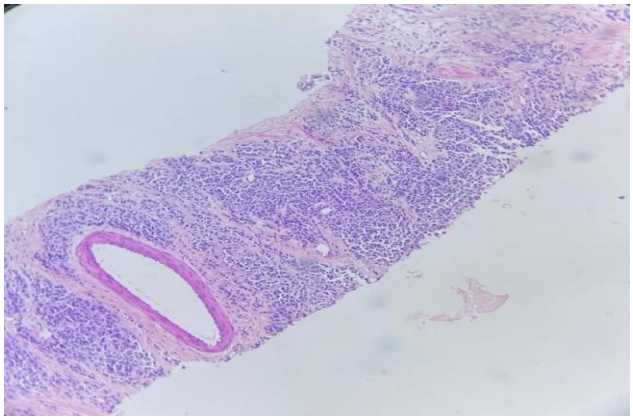

Figure 9: Photomicroghraph showing Gleason pattern 5, (10x10) view (solid sheetsof cell) (H&E)

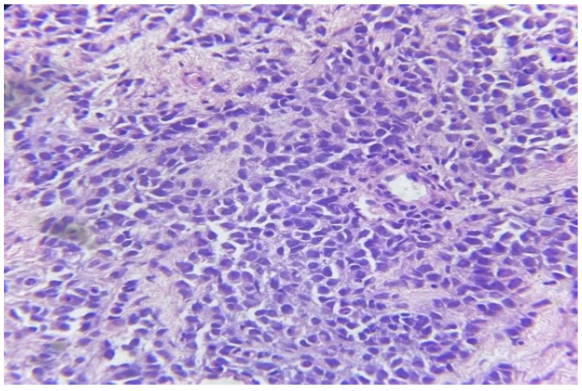

Figure 10: Photomicrograph showing solid sheetsof cell (Gleason pattern 5) 40X view (H&E)

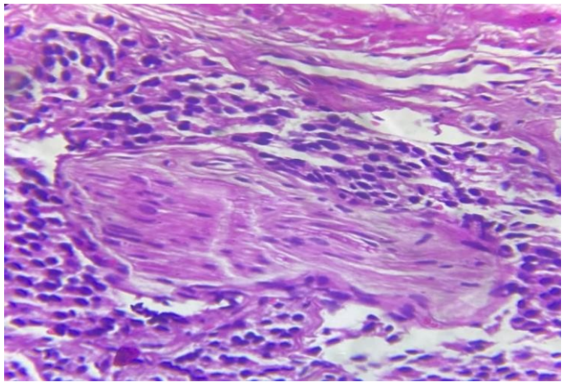

Figure 11: Photomicrograph showing pattern 5 withperineural invasion 40X view (H&E)

Discussion

The incidence of carcinoma of prostate in Indian population is less as compared to the Western population. However, this malignancy is being increasingly detected in India especially in the urban population[10]. In the present study 50 cases of prostatic carcinoma cases who underwent TRUS guided biopsies were studied and their serum PSA levels were correlated with the histopathological Gleason Grade group.

Adenocarcinoma of the prostate is a disease of the middle aged and elderly males being rare below the age of 50 years. [11]

In this study the predominant age group of carcinoma diagnosis is 70-79 years which contributes 17 cases (34%) followed by 60-69 years with 14 cases (30 %). The mean age of the patient is 69.66±10.62years with range of 39-87 years. These findings are comparable with the study conducted by C A Okolo et al [12], Madani et al [13], Gopinath Barui et al [14] who reported the mean age 67.4±10.8year, 74.5±8.34years, and 66.7±4.9 years respectively.

In the present study all of the patients, the presenting complaint was LUTS (lower urinary tract symptoms) with or without haematuria. This increased frequency of urine, urgency, hesitancy and nocturia were related to compression of the prostatic urethra due increased prostatic size. The most common chief complain was increased frequency of micturition (34%) followed by acute urinary retention (28%). Difficulty in passing urine was seen in 20% cases. These findings are comparable with Kirokaya et al [15], Patel sk et al [16] and Chouhan et al. [17] where LUTS was the most common presenting symptoms.

The gold standard triad for diagnosing prostate cancer comprised digital rectal examination (DRE), PSA level, and transrectal ultrasonography followed by TRUS guided biopsy and its histopathological examination. [18] Digital rectal examination has low sensitivity and specificity in detection of prostate cancer. In this study it was found that 76% of prostate cancer had abnormal DRE which is comparable with thestudy of Haid M et al [19] and Ojewala et al. [20] where they found 77.4% and 79.41% respectively.

PSA, a proteolytic enzyme, is produced by both normal and tumoral prostatic epithelium. A serum PSA level exceeding 4 ng/ml is abnormal and considered as a most sensitive marker for detection of prostate Carcinoma. However, this elevation is not specific to malignancy but may be due to benign prostatic hyperplasia, prostatitis, infarction and trauma (such as transurethral resection, needle biopsy). [21]

In our study maximum value of PSA is 200ng/ml and minimum is 8ng/ml. With mean serum PSA level 77.38±49.14ng/ml.

Studies done by C. A. Okolo et al [12], Goupinath Barui et al [14], Chauhan et al [17], Dr Mumtaz et al [22] found mean serum PSA level 207.9 ±221.3ng/ml, 58.47±22.19ng7/ml, 59.65 ±38.65ng/ml, 21.41±13.67ng/ml respectively. The mean PSA level in various study was different with a wide range. The wide range of variability in different study may be due to different age group, different no of cases and different grades in each study.

In this study of TRUS guided prostatic biopsy, 50 cases of prostatic carcinoma were diagnosed. All the cases (100%) were adenocarcinoma of prostate which was similar to the studies conducted by Kirokaya B et al [15], UG Ugareet al [23], Olewole op et al [24].

Histological grading of adenocarcinomas is a good prognostic index and so has been done in every biopsy report. D.F Gleason published his proposed grading system for carcinoma of the prostate in the seventies, which is now universally accepted. In this present study most common Gleason score 7 was seen in 66% cases which was comparable with the study conducted by Goupinath Barui et al. [14] In the present study most common Gleason grade group is 3 (44%), followed by grade group 2 (22%), grade group 5(14%), grade group1 (10%)

and 4(10%). A study by Gopinath Barui et al [14] in 2019 found that most tumors are grade 3 and grade 4 tumors. In the studies Mohmmad D et al [25] in 2020, Pooran Priya et al [26] 2020 found that most tumors are grade 4, grade 5 and grade 3 tumors. Our present study is comparable with these studies.

Findings of the present study showed that patients with high Gleason score and grade group had significantly higher serum PSA levels. This proved that mean PSA levels play a significant role in diagnosing prostatic adenocarcinoma. A Statistically significant association was found between Gleason grade group and pretreatment serum PSA with a P value 0.0278.

Various studies like Deepika Gurumurthy et al [27] Antony et al [28], Gopinath Barui et al [14], Mohmmad et al [25] showed that there is no statistically significant association between Gleason grade group and pretreatment serum PSA level. However our study is comparable with studies conducted by C. A. Okolo et al [12], Murtala Abu Bakkar et al [29],Mumtaz et al [22], Lovely Jose et al [30], Kavita Kumari et al [31] as they have found significant correlation between Gleason grade group and serum PSA level.

Hence we can conclude that a carcinoma associated with elevated serum PSA level is more probable to be of a high grade morphology than a carcinoma with lower PSA level.

Presence of perineural infiltration is considered a poor prognostic factor. In our study it was found that22% tumour showing perineural invasion which comparable with the study Zho et al [32].

Conclusion

Diseases of prostate has caused considerable challenges to both urologist and pathologist. Significant positive correlation between pretreatment serum PSA level and Gleason grade group was noted and carcinoma of prostate associated with an elevated serum PSA level is more likely to be of higher grade than carcinoma with normal PSA levels.

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