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Original Research Article

Evaluation of Adenocarcinoma of Prostate According to new ISUP (International Society of Urological Pathology) Group Grade & it's Serum P.S.A Correlation

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Conflict of interest: Nil

Abstract

Background: Prostate cancer is the second most common type cancer in men accounting >15% of all diagnosed cancers. Early detection with early-stage disease is of very importance for patients to detect certain risk groups. New ISUP group grade is a powerful prognostic marker at time point of diagnosis. Patients are screened for prostate cancer with serum P.S.A. which shows highest specificity 96.4%.

Objective: To study of Serum P.S.A. level as screening method use for detection of prostate cancer in patients and Histopathological examination of TURP and TRUS guided core needle biopsies of prostate are the gold standard for diagnosis of prostate cancer

Material and method: It's a prospective observational study included 50 samples.

Results: 50 patients included in study. Most of the age group from 37 to 100 years, with a mean of 69+11 years. The age range of 66-75 years (36%) were the highest percentages of age group distributions among the patients in the present study. The mean serum PSA concentration is 77.98 ng/ml (range 16.02–119.82 ng/ml). New ISUP grade group 4 is most common in our study with 24 (48.0%) of our patients falling in this category while grade groups 1, 2, 3 and 5 has 7 (14.0%), 6 (12.0%), 7 (14.0%) and 6 (12.0%) respectively.

Conclusion: This study concluded that in patients with prostatic adenocarcinoma, there is a statistically significant association between serum PSA levels and newly introduced (2016) Gleason grade group of prostatic carcinomas.

Keywords: International Society of Urological Pathology Group Grade, Serum Prostatic Specific Antigen.

Introduction

Prostate cancer is the second most common type of cancer in men accounting for >15% of all diagnosed cancers worldwide. [1] Indian data 5.0-9.1 per lac per year as compared to the United States 110-180 per lac per year. [2] Prostate cancer approximately 75% of the diagnosed patients are 65 years of age or older and it is very rare at younger ages including adolescents.

The triple combination of the digital rectal examination, transrectal ultrasonography (TRUS), and serum prostate-specific antigen (PSA) are used in screening and early diagnosis. The main role of TRUS in diagnosing prostate cancer is to guide the biopsy. PSA, a proteolytic enzyme, is produced by both normal and tumoral prostatic epithelium. [3] Early detection of early-stage disease is of utmost importance for patients to detect certain risk groups, predicting the probability of remaining indolent or progressing to an aggressive form of Prostate cancer. In addition to clinical stage & serum PSA level, the new ISUP grade group is a powerful prognostic marker at the time point of diagnosis and has a major impact on therapy decisions. [4]

Previously we used Gleason Score for grading prostate cancer. But in 2014 New ISUP Group Grades system was introduced, which was widely accepted and incorporated into the WHO Classification of the tumor of Urinary System and Male Genital Tract in 2016. This New Group grading system is regarded as simpler and more accurate than the Gleason system.[5] The Gleason grading system for prostate adenocarcinoma has evolved from its original scheme established in the 1960s–1970s, to a significantly modified system after two major consensus meetings conducted by the International Society of Urologic Pathology (ISUP) in 2005 and 2014, respectively. The Gleason grading system has been incorporated into the WHO classification of prostate cancer, the AJCC/UICC staging system, and the NCCN guidelines as one of the key factors in the treatment decision. Both pathologists and clinicians need to fully understand the principles and practices of this grading system.

Table 1: 2014 ISUP consensus proposal is to group Gleason patterns as defined below into clinically important groups [6]

Risk group	ISUP group grade	Gleason score
1.Low	Grade Group 1	Gleason <6(3+3)
2. Intermediate favorable	Grade Group2	Gleason 7 (3+4)
3.Intermediate unfavorable	Grade Group 3	Gleason7(4+3)
4. High	Grade Group 4	Gleason 8(4+4)
5. High	Grade Group 5	Gleason 9-10(4+5=9,5+4=9,5+5=10)

Advantages of ISUP group grading –

Align the prostate cancer grading with the grading of other carcinomas. Eliminate the anomaly that the most highly differentiated prostate cancer as having a Gleason score of 6. To further define the clinically highly significant distinction between Gleason score 7(3+4) and 7 (4+3) prostate cancer. [7] In the early stage of prostate, cancer patients are often asymptomatic. Patients are screened for prostate cancer with serum P.S.A and clinical examination. Serum PSA is not a very accurate marker for malignancy determination. [8]

Most men without prostate cancer have PSA levels under 4 ng/mL of blood.

- When prostate cancer develops, the PSA level often goes above 4. About 15% of men with a PSA below 4 will have prostate cancer if a biopsy is done.
- Men with a PSA level between 4 and 10 (often called the "borderline range") have about a 1 in 4 chance of having prostate cancer.
- If the PSA is more than 10, the chance of having prostate cancer is over 50%.[9]

Therefore, this study aimed to determine serum P.S.A level as screening method use for detection of prostate cancer in patients at NSCB Medical college, Jabalpur (M.P), and also the histopathological study TURP (Transurethral) and TRUS (Transrectal Ultrasound) Guided core needle biopsy of prostate as gold standard for diagnosis of prostate cancer.

Material & Methods

This is the prospective observational study was conducted at department of Pathology N.S.C.B. Medical College & Hospital, Jabalpur (M.P.) and Urology Department of Super Speciality Hospital, Jabalpur (M.P). Duration of study was from 1st March 2021 to 31st September 2022. The sample size was 50 with inclusion criteria as male over the age of middle age groups and elderly patients clinically suspicious for prostate cancer, Patients who gave consent, abnormal Digital Rectal examination (DRE), PSA > 4.0 ng/ml and lower PSA value with other risk factors for prostate cancer (Eg. Family history). Exclusion criteria was the patients who not give consent, symptoms of dysuria, positive urine culture and abnormal coagulation parameter. Source of data was patients who came to urology OPD super speciality hospital with complaints of frequent urination, haematuria, lower UTI, need to strain for emptying the bladder.

On clinical examination of these patients if pointing towards the suspicion of prostate cancer, then go for serum PSA investigation. For further confirmation of prostate cancer, biopsy done and then they sent tissue section with proper fixation (10% Formalin) in our histopathology section department of Pathology, N.S.C.B. Medical College and Hospital Jabalpur (MP). The tumors were then graded using the 2016 New ISUP Group Grades system.

Analysis of the collected data was carried out using Microsoft Office Excel 2010 and Statistical Program for Social Sciences Version 20. Frequencies of variables were determined and cross-tabulated. Continuous variables were summarized using means and standard deviations. Pearson's correlation coefficient was also employed to test the relationships between serum PSA and study population. The level of statistical significance was set at $P \leq 0.05$. Results were presented using figures and tables, and the findings were compared with similar studies done locally and internationally.

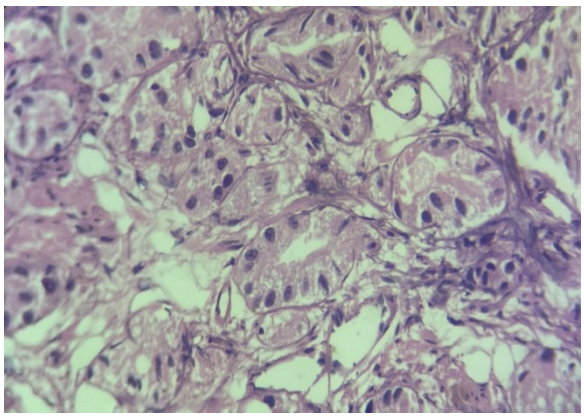


Figure 1: Microphotograph, showing ISUP group grade 1 prostate cancer (H&E, X40)

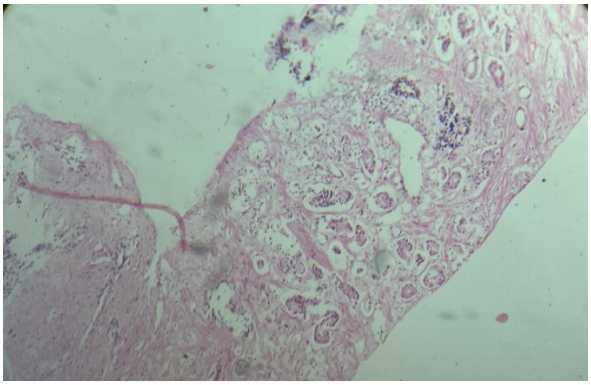


Figure 2: Microphotograph, showing ISUP group grade 2 prostate cancer (H&E, X10)

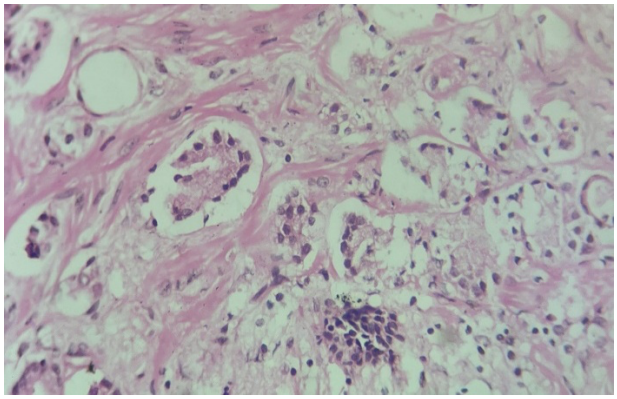


Figure 3: Microphotograph, showing ISUP group grade 2 prostate cancer (H&E, X40)

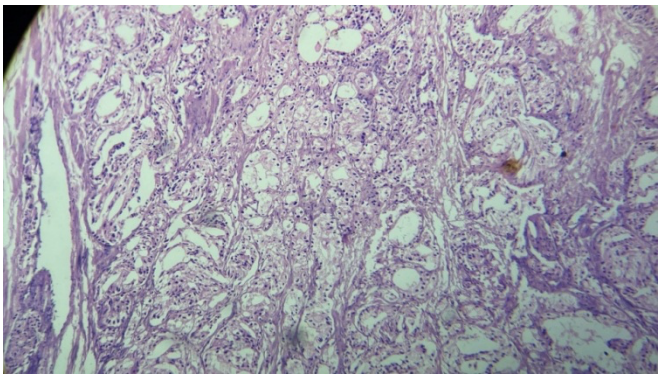


Figure 4: Microphotograph, showing ISUP group grade 3 prostate cancer (H&E, X40)

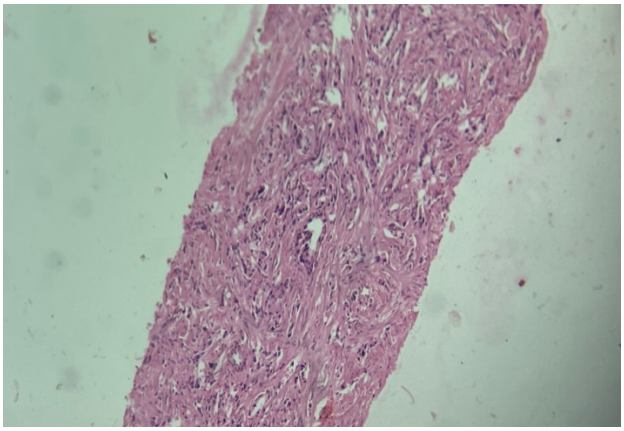


Figure 5: Microphotograph, showing ISUP group grade 4 prostate cancer (H&E, X10)

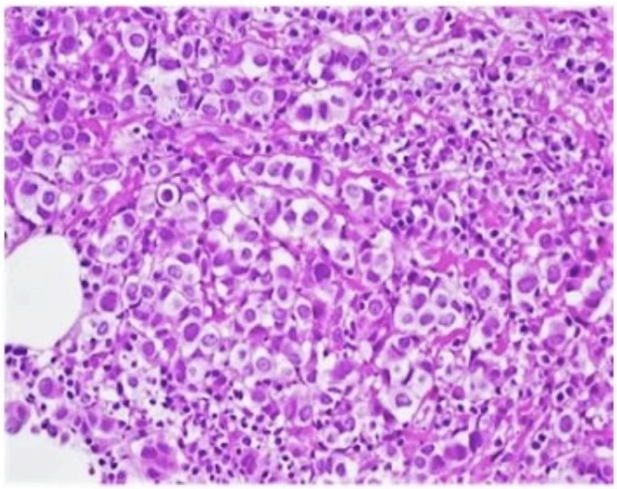


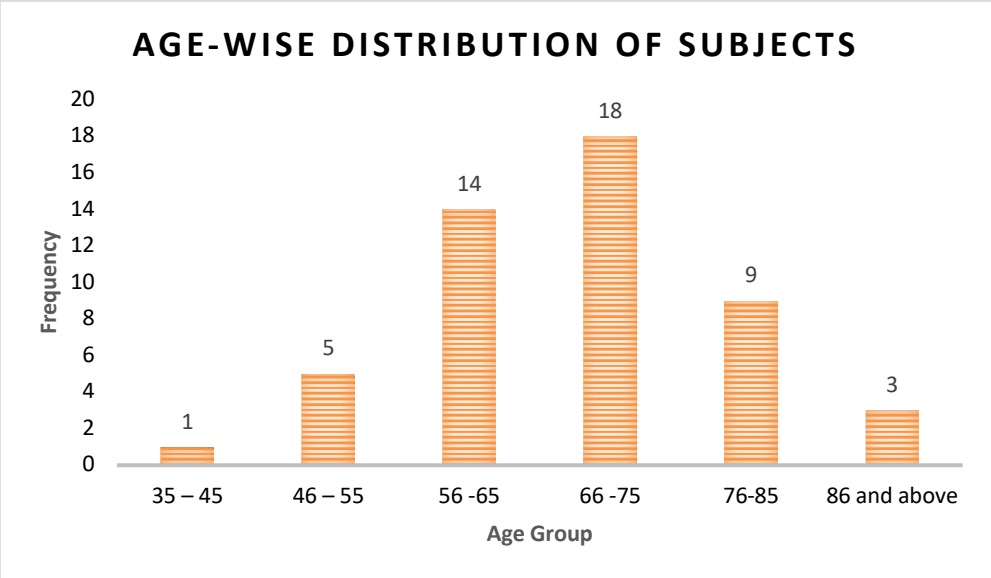
Figure 6: Microphotograph, showing ISUP group grade 5 prostate cancer (H&E, X40)

Results

Table 1: Age-wise distribution of subjects (n= 50)

Age group (years)	Frequency (%)
35 – 45	1 (2.0)
46 – 55	5 (10.0)
56 -65	14 (28.0)
66 -75	18 (36.0)
76-85	9 (18.0)
86 and above	3 (6.0)

In table no.1 shows the mean age of study participants was observed to be 69 ± 11 years. The age wise distribution depicts that maximum distribution of patients belongs to 66 -75 years (36%) while minimum distribution (2.0%) of the patients were below the age of 45 years.

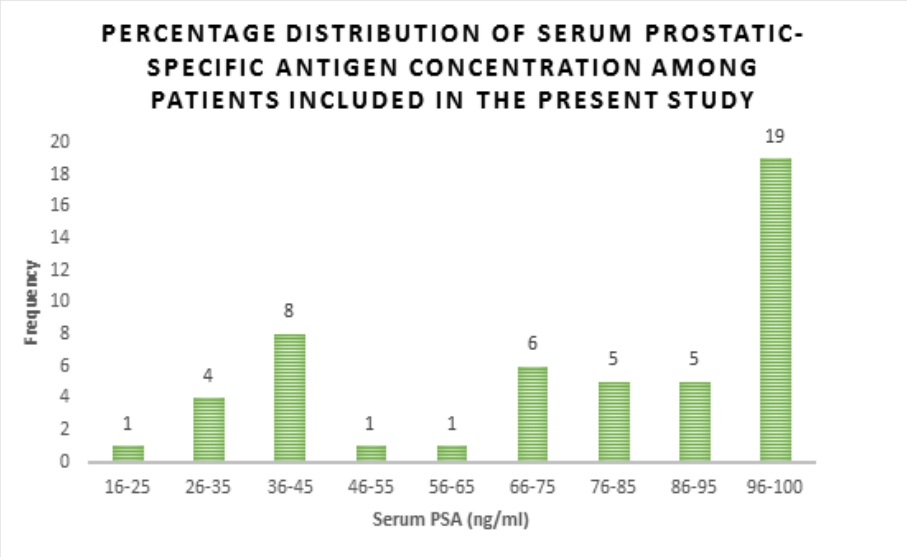


Graph 1: Age Group Wise Distribution

Table 2: Percentage distribution of serum prostatic-specific antigen concentration among patients included in the present study (n= 50)

Serum PSA (ng/ml)	N (%)
16-25	1 (2)
26-35	4 (8)
36-45	8 (16)
46-55	1 (2)
56-65	1 (2)
66-75	6 (12)
76-85	5 (10)
86-95	5 (10)
96- >100	19 (38)
Total	50 (100)

In above table no. 2 shows maximum (38%) patients were fall into serum PSA level 96 - >100 ng/ml, while minimum (2%) patients were fall into serum PSA level 16-25 ng/ml, 46-55 ng/ml and 56-65 ng/ml respectively.

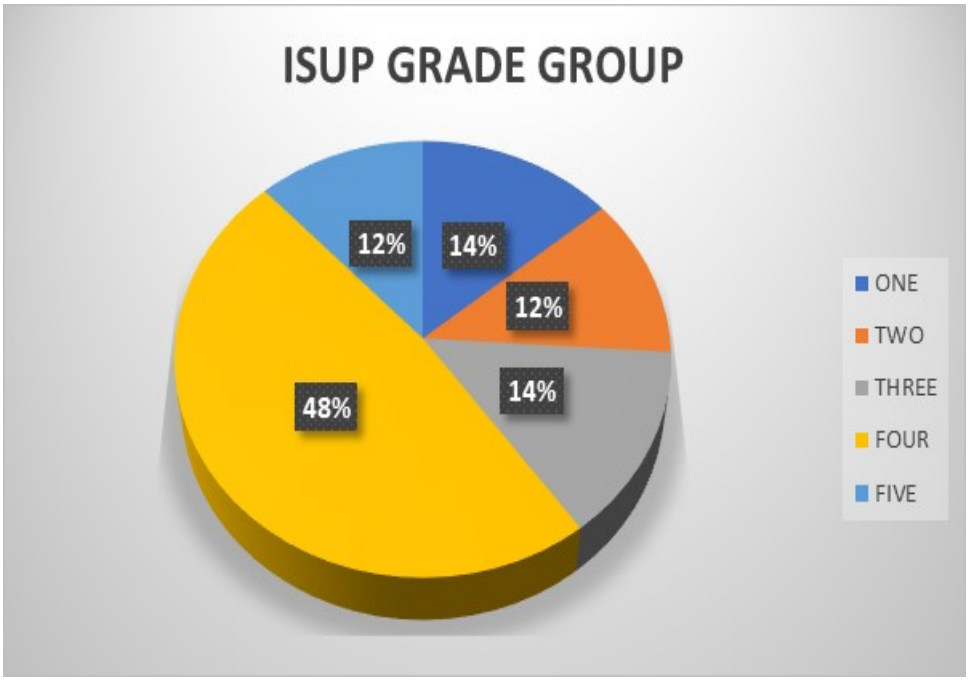


Graph 2: Percentage distribution of serum prostatic-specific antigen concentration among patients included in the present study (n= 50)

Table 3: Percentage distribution of new isup grade group among patients included in the present study (n= 50)

ISUP grade group	N (%)
1	7 (14.0)
2	6 (12.0)
3	7(14.0)
4	24 (48.0)
5	6 (12.0)

Table 3 shows Most of the patients 24 (48%) diagnosed as histopathological new ISUP grade group 4, (Most common), While least common ISUP grade group is 2 & 5, where 6 (12%) patients diagnosed in ISUP grade group is 2 and 6 (12%) patients diagnosed in ISUP grade group is 5.



Graph 3: Percentage distribution of new isup grade group among patients included in the present study (n= 50)

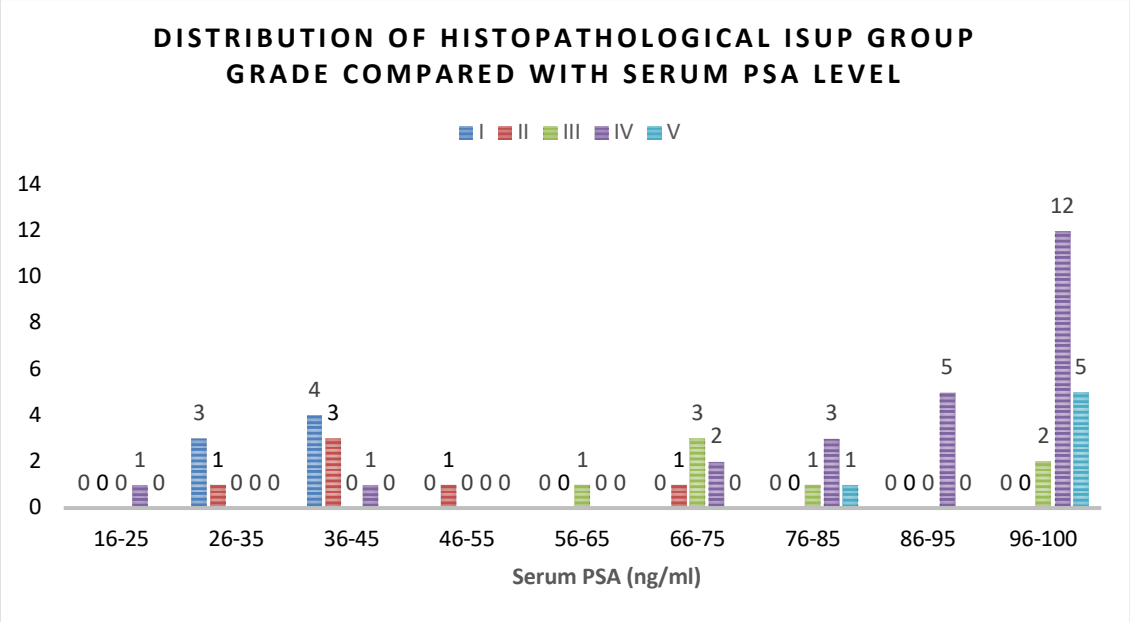
Table 4: Distribution of histopathological ISUP group grade compared with serum PSA level

ISUP group grade	Serum PSA (ng/ml)																		Total	
	16-25		26-35		36-45		46-55		56-65		66-75		76-85		86-95		96- >100			
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
1	0	0%	3	43%	4	57%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	7	14%
2	0	0%	1	16.67 %	3	50%	1	16.67 %	0	0%	1	16.67 %	0	0%	0	0%	0	0%	6	12%
3	0	0%	0	0%	0	0%	0	0%	1	14.29 %	3	43%	1	14.29 %	0	0%	2	28.4 %	7	14%
4	1	4.2%	0	0%	1	4.2%	0	0%	0	0%	2	8.34%	3	12.48 %	5	20.8 %	12	50.0 %	24	48%
5	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	1	16.67 %	0	0%	5	83.4 %	6	12%

Fisher's Exact test value = 68.64, p value = 0.001 (Significant)

In the above table shows, the Serum PSA level was elevated maximum 24 (48%) patients which was histopathological diagnosed as ISUP Group Grade 4. In ISUP Group Grade 4, highest Serum PSA level was 96 - >100 ng/ml in 12 (50%) patients among 24 patients and lowest Serum PSA levels were 16-25 ng/ml and 36-45 ng/ml in 1 (4.2%) patient each. In our study, minimum number of patients 6 (12%) was diagnosed histopathological as ISUP Group Grade 2 as well as 5.

3 (50%) patients among 6 patients. having Serum PSA level 36-45 ng/ml diagnosed as ISUP Group Grade 2. 5 (83.4%) patients among 6 patients. having Serum PSA level 96 - >100 ng/ml diagnosed as ISUP Group Grade 5.



Graph 4: Distribution of histopathological isup group grade compared with serum psa level

Discussion

Present study conducted in NSCB Medical College & hospital, Jabalpur (M.P). The aim of study to establish correlation between Serum P.S.A. (as a screening method for detecting Prostatic carcinoma) with histopathological I.S.U.P Group Grade on TURP (Transurethral) & TRUS (Transrectal Ultrasound) Guided core needle biopsies (as Prostatic biopsies are gold standard for diagnosis of Prostate cancer). Serum P.S.A and histopathological new I.S.U.P Group grades also correlate with radiological findings.

An ideal screening test should have high specificity, high sensitivity, the disease entity tested for should have an important impact on the social and economic indicators and there should be appropriate curative modalities available to treat the condition once it is detected.

Age of distribution of cases Current study showed the patients' age ranges from 37–100 years, which is almost similar to reported by Murtala *et al*. (35-100 years). Also, our study reported age group of 66–75 years with the mean age of the patients is 69 ± 11 years, which is quite common to study done by Murtala *et al* (Age group was 60-69 years and mean age of patients was 66.3 years). However, single (2.0%) patient were found with the age of below 45 years, which is quite with the study done by Murtala *et al*. (0.8% patient are below the age of 40 years). [10] This study represents the mean serum PSA concentration 77.98 ng/mL (range 16.02 –119.82 ng/mL). The Serum PSA concentration for patients falling within new I.S.U.P group grade 1, 2, 3, 4 & 5 has 14%, 12%, 14%, 48% & 12% respectively. These are comparable to values previously reported by Murtala *et al.* (mean serum PSA concentration was 45.48 ±32.39 ng/mL (range 4.0–156.20 ng/mL). [10]

However, none of the patients in this study had a serum PSA concentration <4.0 ng/ml. and only single patient (2.0%) reported the serum PSA value of 16.02 ng/ml. Nineteen patients (38%) presents with the serum PSA values >94 ng/ml. So, this is supported the fact that most of the doctors only recommended prostate biopsy in the patients with a serum PSA concentration of ≥4.0 ng/ml.

New ISUP group grade 4 is the most common in our study with 24 (48.00%) patients falling within this category, while ISUP grade groups 1, 2, 3 and 5 have seven

(14.00%), six (12.00%), seven (14.00%) and six (12.00%) patients, respectively. Concerning this finding, contrast result was found with the studies done by Bahrain *et al* (Most common ISUP group grade 2 & 3) & Murtala *et al.* (Most common ISUP group grade 1). [10,11]

Gleason score 8(4+4) is the most common in the present study with 24 (48.0%) patients, who were falling within this category, while Gleason score 6, 7, 9 & 10 presented by the 7 (14.0%), 13 (26.0%), 5 (10.0%) & 1 (2.0%) patients respectively.

The Serum PSA level was elevated maximum 24 (48%) patients which was histopathological diagnosed as ISUP Group Grade 4. In ISUP Group Grade 4, highest Serum PSA level was 96 - >100 ng/ml in 12 (50%) patients among 24 patients and lowest Serum PSA levels were 16-25 ng/ml and 36-45 ng/ml in 1 (4.2%) patient each and minimum number of patients 6 (12%) was diagnosed histopathological as ISUP Group Grade 2 as well as 5. Maximum 24 (48%) patients among all included patients were diagnosed as New ISUP Group Grade 4. In this group grade, maximum 15 (63%) patients were examined digital rectal examination as firm to hard nodular prostate. Minimum 6 (12%) patients among all included patients were diagnosed as ISUP Group Grade 2 as well as 5. Although DRE and Serum PSA are complementary to some extent and their combined use may increase the overall rate of cancer detection. In a multicentre screening study of 6630 men, the prostate cancer detection rate was 3.2 percent for DRE, 4.6 percent for PSA, and 5.8 percent for the two methods combined. Just 18 percent of cancers were detected only by DRE. In another study, the PPV of a suspicious DRE with a normal PSA level was 10 percent, whereas the PPV for a normal DRE with an elevated PSA level was 24 percent. [12]

In the present study, Histomorphologically ISUP Group Grade 4 were diagnosed maximum 14 (43.75%) patients in core needle biopsy and maximum 10 (52.94%) patients in prostatic chips. The minimum 3 (9.38%) patients were diagnosed as ISUP Group Grade 3 in core needle biopsy and minimum 1 (5.88%) patient were diagnosed as ISUP Group Grade 1 & 5 each in prostatic chips.

Also, our study revealed a statistically positive correlation between the serum PSA value and the ISUP Group Grade of cancer. This is in keeping with the previous works done by Epstein *et al*. [13] and Spratt *et al*. [14] The above-cited works also demonstrated that serum PSA has a stronger correlation with the ISUP Group Grade than it does with the corresponding ungrouped GSs (Gleason score) of cancer. So, we recommend that male population over 50 years should be screened for the early detection of prostate cancer. [15]

Conclusion

This study concluded that in patients with prostatic adenocarcinoma, there is a statistically significant association between serum PSA levels and newly introduced (2016) New I.S.U.P Group Grade of prostatic carcinomas. Thus, from our study it has been concluded that PSA can be used as a screening method for prostatic adenocarcinomas due to its significant positive correlations, especially when the levels are high. New ISUP group grade 4 is the most common in our study with 24 (48.00%) patients falling within this category. In this group grade, maximum 15 (63%) patients were examined digital rectal examination as firm to hard nodular prostate. Such studies should also examine the relationship between the New I.S.U.P Group Grade, serum P.S.A. and stage of cancer. This will further enhance prognostication and estimation of the risk of disease progression. There is a recommendation for additional studies with mass number of patients to be conducted to further investigate of the clinical utility of the New I.S.U.P Group Grade system and serum P.S.A. in prospective clinical trials.

References

1. Ferlay et al. Cancer incidence and mortality worldwide: sources, methods, and major patterns in GLOBOCAN 2012. Int J Cancer, 2015. 136: E359.
2. Hebert JR, Ghumare SS, Gupta PC. Stage at diagnosis and relative differences in prostate cancer incidence in India: Comparison with the United States. Asian Pac J Cancer Prev. 2006; 7:547-55.
3. Epstein JI. The prostate and seminal vesicles. In: Mills SE, Carter D, Greenson JK, Oberman HA, Reuter V, Stoler MH, editors. Sternberg's diagnostic surgical pathology. 5th ed. Philadelphia: Lippincott Williams Wilkins; 2004. 2083-132.
4. Montironi R, Mazzucchelli R, Scarpelli M, Lopez-Beltran A, Mikuz G, Algaba F, et al. Prostate carcinoma2: prognostic factors in prostate needle biopsies. BJU Int (2006) 97(3):492-7.
5. Asian Pac J Cancer Prev. Prostatic Adenocarcinoma: A grading from Gleason to the new grade group system: A Historical and critical Review. 2019; 20(30):661-666.
6. AJCC Cancer Staging Manual (8th Edition) American Joint Committee on Cancer,2017. The Gleason score and Grade Groups.
7. Kane, C. J., et al. Variability in Outcomes for patients with intermediate- risk prostate cancer (Gleason Score 7, International Society of Urology Pathology Gleason Group 2-3) and Implications for Risk Stratification: A Systemic Review. Eur Urol Focus, 2017. 3: 487.
8. Loeb S et al. Pathological characteristics of prostate cancer detected through prostate specific antigen-based screening. J Urol, 2006. 175: 902.
9. American Cancer Society. Cancer Facts & Figures 2020. Atlanta, Ga: American Cancer Society; 2020.
10. A. Murtala, M. S. Sani, A.A. Saad, A.L. Almustapha, C.A. Karo, M. Ahmed, M. Umar, A. Shehu, E.S. Dauda, K. Balarabe et al. Adenocarcinoma of the Prostate: Correlation between Serum Prostate-Specific Antigen and Gleason Grade Group, Annals of Tropical Pathology. 2018; 9(2): 126-130.
11. Bahrain et al. Prostatic Adenocarcinoma: Age, Tumor Grade and Level of Serum Prostatic Antigen (PSA), Med Bull 2020; 42 (2): 104 – 106.
12. Shree Kumar Chinmayananda Mishra, Binod Kumar Sahu, Debasis Debadatta Behera, Somanath Sethi, Sanjukta Dixit, A Study on Utility of Serum Prostate Specific Antigen Level and USG of Prostate to Differentiate Most Common Benign Diseases and Carcinoma of Prostate Gland, J Res Med Dent Sci, 2022, 10 (6):137-141. 135.
13. Epstein JI, Zelefsky MJ, Sjoberg DD, Nelson JB, Egevad L, Magi-Galluzzi C, et al. A contemporary prostate cancer grading system: A validated alternative to the Gleason score. Eur Urol 2016; 69:428-35.
14. Spratt DE, Cole AI, Palapattu GS, Weizer AZ, Jackson WC, Montgomery JS, et al. Independent surgical validation of the new prostate cancer grade-grouping system. BJU Int 2016; 118:763-9.
15. Chakdoufi S., Moumen A., & Guerboub A. Dyslipidemia and Diabetic Retinopathy in Moroccans Type 2 Diabetics Patients: A Cross-Sectional Study. Journal of Medical Research and Health Sciences, 2023; 6(3): 2471–2479.