Original Article

Study of Core Biopsies of the Prostate with Emphasis on Prostate Carcinoma Detection Rate, Its Quantification and Relation to Serum PSA Level

Asha Lata Kujur*[1], Vinita Pant[2]

[1]Department of Pathology, Ranchi Cancer Hospital And Research Centre

[2]Centre of Oncopathology, Mumbai

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***Corresponding Author**:*
Dr Asha Lata Kujur
ashalata.kujur27@gmail.com

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Abstract

Background

According to the national cancer registries, there has been a noteworthy increase in the incidence and prevalence of prostate cancer in India in recent years. Elevated serum PSA level has been found to show a strong correlation with prostate cancer in multiple studies conducted worldwide. The aim of this study was (i) to determine the percentage positivity of prostate biopsies sent to our centre and compare it with national and international data (ii) to assess the number and percentage area of TRUS cores involved by adenocarcinoma and its correlation with serum PSA levels and Gleason grade.

Material and methods

A retrospective study was done in our histopathology laboratory wherein, 130 TRUS-guided biopsies received in proper fixative from different hospitals and clinics during a period of one year from 1st January 2021 to 31st December 2021, were evaluated for histopathological diagnosis. Proper detailed history and indication for biopsy were provided along with the requisition form. Statistical analysis was carried out on the data.

Results

A total of 130 biopsy samples were included in the study. Out of which 76 were malignant (58.5 %) and 54 were benign (41.5 %). It was proven that with an increase in total serum PSA level, there was an increase in the involvement of the number of cores by the tumour. A significant correlation was seen between the total serum PSA levels and involvement of cores by more than 50 per cent of tumour, proven by ANOVA and the Fischer exact test. It was also noted that the tumour volume showed a strong correlation with the grade group in accordance with the Modified Gleason grading system.

Conclusion

Total serum PSA level in conjunction with quantification of tumour provides valuable information to the clinician regarding the spread of tumour within the gland as well as the severity of the disease.Malaria and Dengue fever are the two most common arthropod-borne diseases in tropical countries like India, and endemic areas like Mangalore. Since they share a similar clinical presentation, identifying the hematological parameters, can help differentiate between patients of malaria and dengue fever and can help with its prognosis and early treatment. This study aims to find a link between diagnostic markers that are used to discriminate between the infections, occuring in malaria-endemic areas, such as Mangalore, Karnataka.

Keywords:

Prostate carcinoma, biopsy, PSA

Introduction

Prostate cancer is the second most frequently diagnosed cancer in men worldwide. According to the Global Cancer Statistics 2020, out of the 19.3 million new cancer cases diagnosed in the year 2020, prostate cancer accounted for 7.3% of all newly diagnosed cancer cases [1]. It was also listed as the fourth most common cause of cancer-related deaths occurring amongst new cancer cases in 2020 by the WHO [2]. In India, data regarding the true incidence of prostate cancer is limited mainly because there are only a handful of population-based cancer registries in India. However, a recent report from the National Cancer Registry Program suggests that the prevalence of prostate cancer when compared to other cancers has significantly increased over the last two decades [3].

In 1966, Donald Gleason first introduced a unique grading system for prostatic carcinoma derived by adding the sum of the two most common morphological patterns and the clinical stage. The clinical stage was later removed, and the grading system came to be based purely on the architectural pattern of the tumour [4]. In 1977, Gleason added that "Grading is performed under low magnification" (x 40- 100) [5]. In 2005 International Society of Urological Pathology (ISUP) Consensus Conference was held at San Antonio, Texas in which Gleason grading system for prostate cancer underwent its first major revision and thus came to be known as Modified Gleason Grading System [6]. The 2014 International Society of Urological Pathology (ISUP) grading conferences held in Chicago further attempted to resolve controversial areas relating to the Gleason Grading System establishing the fact that Gleason pattern 4 included cribriform, fused, and poorly formed glands [7]. The 2019 publications from ISUP and GUPS (Genitourinary Pathology Society) further put forward recommendations which dealt especially with reporting of tertiary pattern 5 component occupying <5 % of tumour volume in radical prostatectomy specimens [4].

Prostate-specific antigen (PSA) is a protein produced by normal as well as malignant cells of the prostate gland. PSA levels act as an important diagnostic tool in the screening of prostate cancer. An elevation in free or total serum PSA level is a strong indicator of prostate cancer. The PSA test was first approved by the FDA in 1986 for monitoring and surveillance purpose in men who had already been diagnosed with the disease [8,9]. In 1994, FDA approved the PSA test to be used in conjunction with a digital rectal exam (DRE) to aid in the detection of prostate cancer in men over 50 years of age [8].

In recent years the majority of patients with prostate cancer are diagnosed by transrectal needle core biopsies. The indication for biopsy in most cases is raised serum PSA level and rarely symptoms related to the disease. Treatment choices ranging from surveillance to radical prostatectomy or radiation therapy are largely driven by the pathologic findings in the biopsy specimen as the management of prostate cancer relies primarily on histopathological parameters such as Gleason score and grade evaluated on the tissue obtained by needle biopsies [10]. Thus, the onus falls on the pathologist to report all the findings precisely and accurately. The quantification of tumours in needle biopsy specimens is a powerful predictor of the pathologic stage at radical prostatectomy and outcome after treatment of essentially any type. It is also a factor in determining patient suitability for management on a surveillance protocol [11]. Quantification of tumours for surveillance uses multiple parameters such as the absolute number of cores involved, the percentage of cores involved, and the greatest percentage of any core involvement [11].

Inclusion criteria

All TRUS-guided core needle biopsies received in proper fixative comprising of linear cores wherein sufficient clinical details including the age, serum PSA levels and indication for biopsy had been provided. The cases where serum PSA level was not available have been included in the demographic analysis as in to evaluate the benign or malignant nature of tissue obtained for

histopathological examination but not in the correlation analysis with the serum PSA level.

Exclusion criteria

Any biopsy tissue which was not received in proper fixative or was in fragmented tiny bits less than 1 cm has not been included in the study. Also, the cases where serum PSA level was not available have been excluded from the correlation studies, however, the data has been used for demographic analysis.

Materials and Methods

A retrospective study was done in our centre, wherein 130 TRUS-guided biopsies received in proper fixative during a period of one year from 1st January 2021 to 31st December 2021, were evaluated for histopathological diagnosis. The processing of formalin-fixed tissue was done on the Leica tissue processor according to the protocol for small biopsies. Hematoxylin and Eosin stained sections were prepared and histological examination was done. All cases diagnosed as prostatic adenocarcinomas were graded according to Modified Gleason's grading system [12] and along with it, tumour quantification was done [13]. Those cases where there was a small focus suspicious for adenocarcinoma were subjected to immunohistochemistry such as PSA, NKX3.1, AMACR, HMWCK etc for confirmation of diagnosis. The various clones used were as follows, Er-Pr-8(BIOGENEX) for PSA, Poly(Biocare) for NKX3.1, 13H4 DAKO) for AMACR and 34betaE12(DAKO)for HMWCK. Appropriate controls were taken in every case. The number of cores taken and the number of cores involved were also correlated with the Gleason grade and serum PSA level. A thorough history of each patient was obtained which included patient identification number, age, the purpose of undergoing the biopsy whether screening or diagnostic, total PSA level etc. The histological examination was done by the pathologist with emphasis on the number of cores taken, the number of cores involved, Gleason score and Gleason grade based upon modified Gleason grading system , tumour volume, percentage of pattern 4 and pattern 5 in the biopsy and any perineural involvement noted. The reporting format used was in accordance with the CAP guidelines [14].

Results

A total of 130 biopsy samples were included in the study. Out of which 54 were benign (41.5 %) and 76 were malignant (58.5 %). Two out of the 76 malignant cases were diagnosed as small cell carcinoma whereas the remaining 74 cases were those of adenocarcinoma of the prostate. Thus, the overall cancer detection rate of TRUS-guided core biopsy in our study was 58.5 %. In our study, the age group between 60-80 years constituted 78.5 % of the patients who were biopsied [Table -1]. The mean age for benign conditions resulting in elevated serum PSA level was 67.4 years whereas the mean age for malignant conditions was 72.6 years. In the age group of patients less than 60 years it was seen that 66.7% of the conditions were benign and 33.3 % were malignant, whereas in patients between 61 to 80 years 44.1% of the cases were benign and 55.9% were malignant [Table -1]. In patients who were more than 80 years of age 93.8% of the cases were malignant [Table-2]. This strong correlation was proved using the Chi-square test. The p-value for correlation between age and nature of the disease whether benign or malignant was 0.002 and thus statistically significant.

About the PSA level, the majority of patients who were advised to undergo the biopsy procedure had a total serum PSA level between 4.0 to 20.0 ng/ml (61.5 valid per cent). In our study, 32.4 % of the malignant cases belonged to Gleason grade group 4, followed by 27.0 % and 24.3 % of grade group 1 and grade group 3 prostatic adenocarcinomas respectively. Another important finding which was statistically proven in our study was that with an increase in total serum PSA level there was an increase in the percentage of malignant cases based upon increasing serum PSA levels [Table no.-2]. Thus the percentage of malignant cases

which was found to be 25% at a total serum PSA level of less than 4.0 ng/ml in our study became a 100 % when the total serum PSA levels were more than 100 ng/ml.The p value for this observation was 0.001 and thus statistically very significant.

The mean of number of cores taken for evaluation of pathologic condition was 14.2 and the mean value for number of cores involved at various serum PSA levels was found to be 8.92. The mean value of percentage of cores involved was 64.4 %. This calculation was based on applying tools for group statistics primarily ANOVA test to compare variances across the means for different groups.

The main emphasis of this study was to do quantification of tumours obtained by core needle biopsies and their correlation with serum PSA levels. Thus in our study a mean of 10.8% of cores showed less than 5 per cent involvement by tumour, a mean of 34.3% of cores showed 5 to 50% involvement by tumour and a mean of 55.0% of cores showed more than 50 % involvement by tumour [Table 3]. This was statistically analysed using Levene's Test for Equality of Variances. Thus it was proven that with an increase in total serum PSA level there was an increase in the involvement of the number of cores by tumour. There was also a significant correlation seen between the total serum PSA levels and involvement of cores by more than 50% of tumour as proven by ANOVA and Fischer exact test. The p value for correlation between numbers of cores involved and per cent of cores involved was <0.001 and thus statistically significant.

Table 1 Frequency Distribution

		Number of cases	Percentage of cases
Age (years)	<=60	12	9.2
	61-80	102	78.5
	>80	16	12.3
PSA Level	<=4	8	6.6
	4.1-10.0	39	32.0
	10.1-20.0	36	29.5
	20.1-40.0	16	13.1
	40.1-100.0	14	11.5
	>100.0	9	7.4
Diagnosis	Benign	54	41.5
	Malignant Adenocarcinoma Small Cell Ca	76 74 2	58.5 56.9 1.5
Gleason Grade group	Grade 1	20	27.0
	Grade 2	9	12.2
	Grade 3	18	24.3
	Grade 4	24	32.4
	Grade 5	3	4.1

Table 2 Association with Benign/Malignant

		Benign		Malignant		P value
		N	%	N	%	
Age (years)	<=60	8	66.7	4	33.3	0.002*
	61-80	45	44.1	57	55.9	
	>80	1	6.3	15	93.8	
PSA Level	<=4	6	75.0	2	25.0	<0.001**
	4.1-10.0	25	64.1	14	35.9	
	10.1-20.0	17	47.2	19	52.8	
	20.1-40.0	1	6.3	15	93.8	
	40.1-100.0	1	7.1	13	92.9	
	>100.0	-	-	9	100.0	

Fisher Exact Test : *p<0.05; Significant; **p<0.001; Highly significant

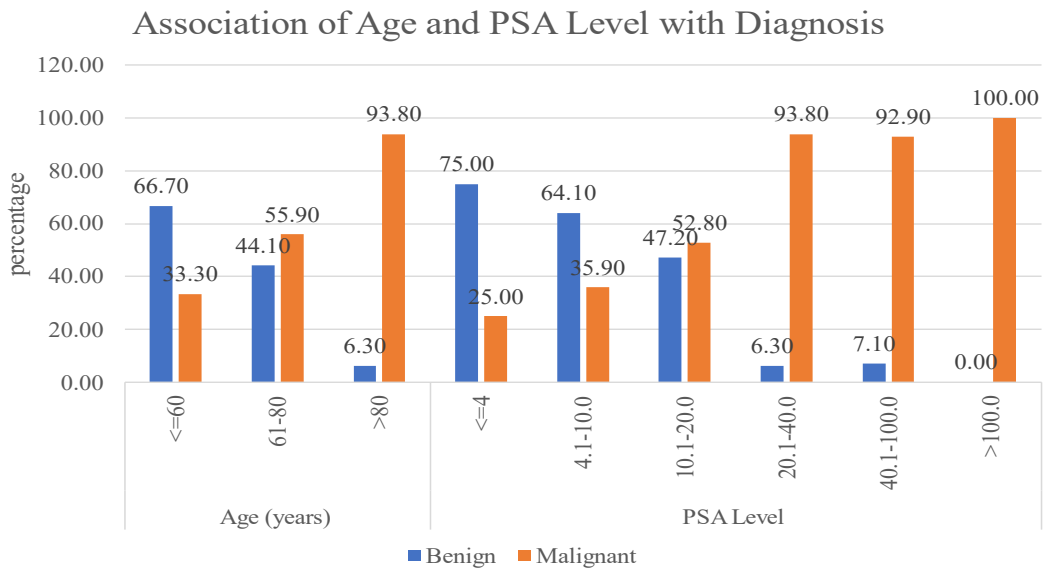

Figure 1 Association of Age and PSA Level with Diagnosis

Table 3 Association with PSA levels

	PSA level												P value
	<=4 (n = 2)		4.1 – 10.0 (n = 14)		10.1 – 20.0 (n = 19)		20.1 – 40.0 (n = 15)		40.1 – 100.0 (n = 13)		>100.0 (n = 9)		
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	
No. of cores taken	8.00	5.66	14.147	3.42	14.16	2.93	15.33	4.30	14.08	4.92	15.89	5.44	0.241
No. of cores involved	2.50	2.12	5.43	2.90	8.00	5.23	8.13	4.70	12.23	4.38	15.11	5.28	<0.001**
% of cores involved	54.17	64.82	41.19	24.65	57.19	34.48	55.40	33.32	87.27	12.03	95.23	6.51	<0.001**
Mean (%) cores <5%	0.00	0.00	18.16	27.77	13.48	25.33	7.24	12.24	9.50	13.42	4.04	5.84	0.496
Mean (%) cores 5-50%	0.00	0.00	56.56	37.27	32.06	31.29	40.95	25.95	23.26	17.75	25.83	17.42	0.013*
Mean (%) cores >50%	100.0	0.00	25.28	32.80	54.45	38.62	51.80	27.77	67.83	19.94	70.12	18.86	0.001*

One-Way ANOVA: : *p<0.05; Significant; **p<0.001; Highly significant

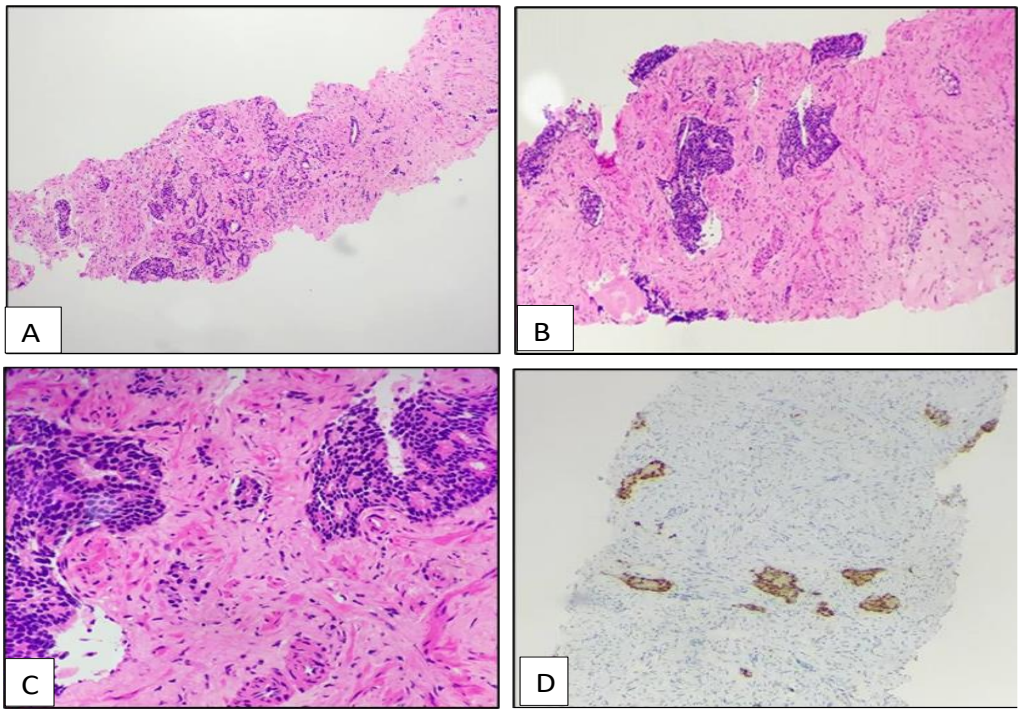

Figure 2 A, B: Hematoxylin and Eosin-stained sections of TRUS guided core biopsies for histomorphological diagnosis and tumor quantification. C: Low power view showing foci of prostatic adenocarcinoma showing pattern 4. D: Small foci showing adenoca

Discussion

Donald F Gleason in 1966 introduced a system to grade prostatic carcinoma based solely on the glandular architecture of the tumour. In 2005 and 2014, the International Society of urological pathology reviewed and revised the Gleason grading system in order to update the guidelines such that there was more concordance between the needle biopsies and radical prostatectomy specimens of prostatic carcinoma [6,7]. According to the WHO classification of tumours fifth edition, emphasis has been put on the recognition of prostatic intraepithelial neoplasia as a subtype of acinar adenocarcinoma, the correlation between androgen deprivation therapy and prostate cancers with neuroendocrine morphology and a more exhaustive description of intraductal carcinoma of the prostate (IDC-P) and atypical intraductal proliferation (AIP) [15]. In our study as well two cases of prostatic adenocarcinoma with neuroendocrine differentiation had been noted but the majority of the cases were those of acinar adenocarcinoma.

This study was done with the objective to determine the percentage positivity of prostate biopsies sent to our centre and compare it with national and international data and also to quantify the volume of the linear cores obtained through TRUS guided core biopsies and their correlation with total serum PSA levels. The incidence of prostate carcinoma in India has been reported to be between 2 to 11.1 per 1,00,000 population in various nation-based cancer registries [16].

The comparison of overall cancer detection rates of TRUS guided biopsies from other international studies have been as follows, Janbaziroudsari et al., Iran 32.4% [17]Teoh et al., Hong Kong, 27.6% [18], Lee et al. Singapore, 35.1% [19] Vida et al., Romania, 69.77% [20], Na R et al., China 47% [21], Imazu et al., Japan 54.3% [22] , Rodriguez et al., Spain 39.1% [23], Orozco et al., USA 38.3% [24], and Abril et al., Mexico 37% [25] to name a few.

In comparison studies done in India showed the following overall cancer detection rates, Agnihotri et al., 57.5% [26], Sinha et al., 24.37% [27], Patil S et al.,25.53% [28]. In our study, the overall cancer detection rate was 58.46% which was close to international studies like Imazu et al., Japan 54.3%[22] and Indian studies like Agnihotri et al., 57.5% [26].

The clinical profile of patients in most of these studies was similar wherein the patient had enlarged prostate with elevated serum PSA levels at the time of histopathological diagnosis. Quantification of tumour for surveillance protocols have used various parameters including an absolute number of cores, percentage of cores involved, and the greatest percentage of any core involvement[10]. Thus in concordance with several studies done earlier, our study also revealed that there is a strong correlation between the number of cores involved and the proportion of involvement of linear cores with the pathologic stage. The study done by Brimo et al [29], and Sebo et al etc [30] showed that tumour volume is a strong predictor of the pathologic stage of prostate cancer thus dictating the approach towards management. Other studies such as by Atsushi et al [31] and Poulos et al [32] also reiterated this fact but however were based on radical prostatectomy specimens.

Conclusion

Our study showed that the cancer detection rate for prostate cancer at our centre was 58.46 %. Also similar to Several studies done earlier which showed a significant correlation between serum PSA levels and tumour volume irrespective of the size of the prostate [33,34], our study also showed that the percentage of cores involved by tumour correlated best with serum PSA level. This correlation was highly significant when the involvement of the core by the tumour was more than 50 per cent and in patients belonging to the older age group. Thus serum PSA continues to be a powerful indicator in predicting the tumour volume and extent of prostatic involvement, as it was seen in our study that the higher the PSA value the greater is the number of cores involved as well as the greater is the percentage of involvement of each individual core by the tumour. Thus dictating the use of surveillance protocols and line of management to be implemented.

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