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CORRELATION BETWEEN AGE AND HISTOLOGICAL GRADE OF PROSTATE CANCER AT A TERTIARY HOSPITAL, SOUTH -SOUTH NIGERIA

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ABSTRACT
Prostate cancer is the third leading cancer in men. There is paucity of data in Nigeria on prostate cancer vis-a-vis the new International Society of Urological Pathology (ISUP) grading system for prostate cancer started in 2014. The objective of the study is to examine the age of the patients diagnosed of prostate cancer in University of Port Harcourt Teaching Hospital between January 2019 and June 2022, the histological type, Gleason scores and ISUP grade of the prostate cancer cases and to correlate these with age. Histopathological slides were retrieved and reviewed; relevant data were extracted from the Laboratory Information Systems, Laboratory Requisition Forms and the departmental ledger where necessary. The data were statistically analysed. A total of 208 patients were diagnosed of prostate cancer during the study period. The meanage of the patients at diagnosis was 68.54 years, with the lowest recorded age being 49 years, while the highest age was 91 years. The most common age bracket was 60 – 69 years(35.1%). All the cases reviewed were acinar type of prostatic adenocarcinoma with commonest primary score jointly been 3 and 5 while the commonest secondary score was 4. Grade 5 was the major ISUP grade representing 44.7% of the cases. There is no correlation between age and either the Gleason scores or the ISUP grades.

KEYWORDS: Prostatic adenocarcinoma, Gleason score, International Society of Urological Pathology (ISUP) Grade.

INTRODUCTION

Cancer is one of the leading causes of mortality globally accounting for about 10 million deaths in 2020.[1]Prostate cancer is the third leading cancer in men affecting about 1.41 million men globally.[1]

The vast majority ofprostatic cancer are of epithelial origin and are adenocarcinomas.[2] There are less common malignant neoplasms in the prostate such as sarcomas and lymphomas. Prostatic adenocarcinoma has many subtypes that include ductal, acinar, atrophic, microcystic, foamy gland, pleomorphic giant cell, mucinous and signet ring variants. Acinar subtype of prostatic adenocarcinoma is by far the commonest subtype.[3.4]

The Gleason score is the sum of the two most prevalent Gleason grades. When one pattern only is present, the primary and secondary patterns are given the same grade. In radical prostatectomy when the less prevalent pattern is less than 5%, the pattern is mentioned as a minor (tertiary) pattern while any higher grade minor pattern that is 5% or more is incorporated into the Gleason score and ISUP group as the secondary pattern.[5]

Gleason grade 3 consists of single, separate glands that are infiltrative. They retain some stroma intervening between the glands. These glands could be small sized with very tiny lumina, medium sized glands with undulating luminal contours or large glands with pseudoatrophic appearance or branching.[5,6]

Gleason grade 4 show fused glands with more than one lumina and no intervening stroma.Features here include cribiform glands, glomeruloid pattern andhypernephroid arrangement of glands.[6,7] Intraductal carcinoma when admixed with invasive carcinoma should be counted as Gleason 4.[8]Gleason grade 5 are glands that show comedonecrosis or single cells that do not form glands.[6.8,9]

International Society of Urological Pathology (ISUP) put these Gleason grades to five tiers[10]. The ISUP grade one is Gleason score 3+3. The ISUP grade two is Gleason score 3+4 while ISUP grade three is Gleason scores 4+3. The ISUP grade four include Gleason score 4+4, 3+5 and 5+3. Finally, ISUP grade five include Gleason score 5+4, 4+5 and 5+5.

The objective of the study is to characterise the histological subtypes of prostate cancers,access the age group with the highest frequency of cancer of the prostate, and determine the commonest Gleason scores and ISUP grade. We will also determine the association between Gleason score and ISUP grade withpatient's age.

MATERIALS AND METHODS

The tissue blocks and slides of all prostate specimens received in the department of Anatomical Pathology, University of Port Harcourt Teaching Hospital between January 2019 and June 2022 were selected for the study. These include prostatic specimens from in hospital patients and those from peripheral hospitals within Rivers and Bayelsa State. These tissue blocks were sectioned and stained with standard haematoxylin and eosin and viewed using a DM500 Leica light microscope. The patients' age and clinical diagnosis were obtained from the laboratory request form and departmental tissue register. Those whose tissue sections were not sufficient for diagnosis were excluded from the study. All data collected was imputed in Microsoft Excel® version 2010 spread sheet and transferred into the statistical package for social sciences version 23 (SPSS Inc., Chicago, USA) for analysis. Data are presented as frequencies and percentages using tables.Ethical approval for the study was sought and gotten from the hospital's ethical committee.

RESULTS

A total of 208 prostate cancerdiagnoses were made in the Department of Anatomical Pathology Department at University of Port Harcourt Teaching Hospital Rivers State over a 5 year period between January 2018 and December 2021.

Among the participants sampled for the current study, the mean age at presentation is 68.54years. A majority (73) of the participants (35.1%) were aged between 60 – 69 years, followed by participants aged between 70 to 79 years (34.6%) (Table 1). Worthy of note is that only 1 (0.5%) participant aged 49 years belonged to the 40 to 49 age category which happens to be the youngest age. The oldest age at diagnosis was 91years.

Table 1: Age characteristics of participants.

VARIABLE	FREQUENCY	PERCENT (%)	MEAN	SD	MODE
AGE					
40 - 49	1	0.5	49.00	0.00	49
50 - 59	37	17.8	55.46	2.80	57
60 - 69	73	35.1	64.95	3.12	69
70 - 79	72	34.6	73.78	2.78	70
≥ 80	25	12.0	84.08	3.57	80
Overall	208	100.0	68.54	9.20	69

Prostatic adenocarcinoma (acinar variant) was the only type of prostate cancer diagnosed. The commonest primary score was jointly 5 and 3 with mean ages of 69.07years and 69.39years. The least primary score is 4 with a mean age of 66.98years (table 2). The commonest secondary score is 4 with a mean age of 67.35years and the least score is 4 with a mean age of 67.35years.

Table 2: Age characteristics of Gleason-specific primary and secondary scores.

GLEASON SCORE	FREQUENCY	MIN	MAX	MEAN	SD
PRIMARY					
3	72	51	91	69.39	9.67
4	64	52	90	66.98	7.85
5	72	49	90	69.07	9.76
SECONDARY					
3	61	51	88	68.39	9.68
4	80	49	90	67.35	8.86
5	67	50	91	70.09	9.05

A spearman rank correlation test conducted to ascertain the relationship between age and Gleason scores revealed that Gleason's scores (primary, secondary, and overall) were not related to age (p = 0.991, 0.314, and 0.475) respectively (table 3).

Table 3: Correlation between Gleason's score (primary, secondary, and overall) with age.

VARIABLE	n	MEAN	SD	r_s	P-VALUE
Age	208	68.54	9.20	-0.001	0.991
Primary Score	208	4.00	0.83		
Age	208	68.54	9.20	0.07	0.314
Secondary Score	208	4.03	0.79		
Age	208	68.54	9.20	0.05	0.475
Overall Score	208	8.03	1.41		

SD = standard deviation; r_s = Spearman rank correlation coefficient

The commonest ISUP grade of prostate cancer is Grade V (44.7%) followed by Grade I (22.1%). Also highlighted is the fact that Grade III cancer was the least common among the participants (table 4).

Table 4: Prevalence of prostate cancer.

VARIABLE		FREQUENCY N = 208	PERCENT (%)
ISUP GRADE	GRADE I	46	22.1
	GRADE II	21	10.1
	GRADE III	9	4.3
	GRADE IV	39	18.8
	GRADE V	93	44.7

The mean ± Standard Deviation (SD) age of participants classified as either ISUP grade I, II, III, IV, or V are 69.33 ± 9.52, 69.81 ± 9.46, 64.67 ± 8.32, 66.18 ± 8.67, 69.23 ± 9.19 respectively (table 5). While grade I, II, and V are multimodal with equal frequencies in age across five, four, and three ages, grade III and IV were bimodal.

Table 5: ISUP grade-specific age characteristics.

VARIABLE		MIN	MAX	MEAN	SD	MODE
ISUP GRADE	GRADE I	51	88	69.33	9.52	60, 64, 65, 69, 71, 72
	GRADE II	54	89	69.81	9.46	60, 66, 67, 73, 82
	GRADE III	53	76	64.67	8.32	58, 76
	GRADE IV	52	91	66.18	8.67	65, 69
	GRADE V	49	90	69.23	9.19	69, 70, 75

A Fisher exact test for association showed that age category was not associated with ISUP grades.

Table 6: Association between age categories and ISUP grades.

VARIABLE		ISUP GRADE					$\chi 2$	P-VALUE
		GRADE I	GRADE II	GRADE III	GRADE IV	GRADE V		
AGE	40 - 49	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	15.414[f]	0.545
	50 - 59	6 (16.2)	3 (8.1)	4 (10.8)	9 (24.3)	15 (40.5)		
	60 - 69	16 (21.9)	8 (11.0)	2 (2.7)	18 (24.7)	29 (39.7)		
	70 - 79	17 (23.6)	6 (8.3)	3 (4.2)	10 (13.9)	36 (50.0)		
	≥ 80	7 (28.0)	4 (16.0)	0 (0.0)	2 (8.0)	12 (48.0)		

f = Fisher's exact

DISCUSSIONS

The mean ageat presentation in this study is 68.54years. This is similar to other studies that showed the mean age of diagnosis of prostate cancer to be in the seventh decade of lifeat 66years[11], 69years[12] and 64.5years.[13] On the contrary, higher mean ages were seen in the eight decade of 71.4years in a study in Ibadan[14] Nigeria and 70years in a previous study in Port Harcourt[15] Nigeria.It is known that prostatic adenocarcinoma may be asymptomatic in its early days. Thus the poor intake of screening exercise to detect early prostatic cancer may be the reason why patients presented late in our center.

Prostatic adenocarcinoma of the acinar type is the only histological type found in this study. All the studies reviewed showed acinar type to be the commonest histological type with varying proportions of 97.8%[12], 99.1%[16], 100%[15], 100%.[17]

The most common ISUP grade of prostate cancer is Grade V (44.7%) followed by Grade I (22.1%) while Grade III cancer was the least common among the participants.This is similar to the findings of Emiogun et al[12] in south-west Nigeria and Amadi et al[18] in south-east Nigeria of ISUP grade group V as the commonest . Anunobi[16]and Oluwole[13] saw Grade IV as the

commonest ISUP grade. And Nwafor[19] saw Grade III as the most common grade. A plausible reason for the higher ISUP grade at presentation here may be due to poor health seeking behaviour that lead to late presentation of patients.

The ISUP Grade V was most commonly seen between 70-79years while grade I was most commonly seen at same age interval. A Fisher exact test for association showed that age category was not associated with ISUP grades. This statistical non significance of age with histological grade is similar to the findings of Emiogun et al.[12] Pepe et al[20], in Italy, however found that the Gleason scores of prostate cancers increase with age. This difference could be due to the massive screening of men in developed countries compared to poor health seeking behaviour in Nigeria. Screening tests is still financially out of reach to many Nigerians especially those in the rural areas. In addition it is known that prostate cancer may be indolent and asymptomatic at the early stage prompting late presentation in the absence of routine screening tests for men using PSA.

CONCLUSION

This study shows that most of the prostate cancer diagnoses were seen in patient in the seventh decade of life with a mean age of 68,54years. All the cancers diagnosed were acinar type of prostatic adenocarcinoma with grade 5 been the commonest ISUP grade at presentation. This is in line with other studies that say that prostate cancer has a high grade at diagnosis and mortality in Africans. This calls for increase awareness of the burden of the disease and subsidization of the cost of serum prostatic specific antigen screening test to catch it at the earliest grade. This will better improve patient outcome and prognosis. There is no correlation between age and either gleason scores or ISUP grade grouping.

Limitations of the study

Small sample size
Retrospective study

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Statement of ethical approval

Ethical approval was sought and obtained from the Hospitals' ethical committee

Statement of informed consent

This was a retrospective study and so no informed consent was obtained from patients.

Conflict of interest

The authors confirm that there is no conflict of interest and no funding was received for this work.

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