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Correlation of Level of Serum 25-Hydroxy Vitamin D and Gleason Score as a Measure of Aggressiveness of Prostate Cancer in Black Africans

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Abstract:-

➢ ***Background***

Cancer of the prostate (CaP) is the second most commonly diagnosed cancer worldwide and the sixth leading cause of death from cancer in males. . Black men of African descent have higher risk for developing prostate cancer and are most likely to present at a younger age with more advanced disease and a poorer disease prognosis.

➢ ***Objective***

To determine if there is a relationship between the level of serum 25 hydroxy vitamin D and aggressiveness of prostate cancer using the Gleason score in black Africans in Jos.

➢ ***Methods***

A cross sectional study conducted among fifty patients presenting at the urological surgical out-patient clinics of the Jos University Teaching Hospital who were evaluated to have a clinical diagnosis of prostate cancer and scheduled for prostate biopsy. Blood samples for serum 25-hydroxy vitamin D were assayed using the ELISA technique, prostate biopsy was done and only those histologically confirmed to be prostate cancer were analysed. Data was collected using a proforma with statistical analysis done using SPSS$^{(R)}$ version 23 and Spearman's rank correlation test used with a *p*-value < 0.05 considered significant.

➢ ***Results***

Fifty patients with histologically proven prostate cancer was studied whose age ranged from 50-89 years with a predominant age group 70-79 years (70.0±7.9).The mean level of serum 25-hydroxy vitamin D was 37.90ng/ml±17.92. All patients in the study had adenocarcinoma as the histologic type with a mean Gleason score of 9.36±13.14. A Spearman's rank order correlation was statistically significant (r_s (50) = -0.423, p = 0.002).

➢ ***Conclusion***

A Spearman's rank order correlation shows a moderate negative correlation between the serum 25-hydroxy vitamin D and Gleason score (r_s (50) = -0.423, p = 0.002.Thus, serum 25-hydroxy vitamin D assay can be used to prognosticate in patients with cancer of the prostate.

Keywords: *Serum 25-Hydroxy Vitamin D, Prostate Cancer, Gleason Score*

I. INTRODUCTION

Cancer of the prostate (CaP) is the second most commonly diagnosed cancer worldwide and the sixth major cause of mortality due to cancer in males.[1] Among men living today, it has been noted that 1 in 7 (15.3%) will be diagnosed with prostate cancer and 1 in 38 (2.6%) will die from the disease.[2] Black men of African descent have been reported to be at especially high risk for developing cancer of the prostate and worse is the finding that these men of African origin are most likely to present at a younger age with more advanced disease associated with a poorer disease prognosis.[3]

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One of the most important information obtained from prostate needle biopsy is the histologic grade and the most commonly used prognostic marker is the Gleason grading system. For most carcinomas, the finding of poor differentiation (high grade) offers a reliable and powerful index of aggressive biologic behavior, including high risk of metastasis. The most aggressive tumour found in a prostate biopsy, even if it is the smallest component may determine the prognosis of the patient's tumour.[4]

The complexity in tumour biology, natural history, and outcomes among patients with prostate cancer has remained a global challenge. African-American men have a higher incidence and chance of death from prostate malignancy. African men found with cancer of the prostate are more likely to be diagnosed at a younger age, have larger tumour volume at the time of diagnosis and are more than twice likely to die from the disease due to metastasis. Although, demographic characteristics such as family history, socio-economic status, access to medical care , other co-morbidities, diet, and lifestyle have been shown to contribute to increased burden of cancer of the prostate among African-Americans, recent studies have focused on differences in serum 25-hydroxy vitamin D (25(OH) D) concentrations as the source for the unusual trend observed in this disease.[5,6]

The role played by serum 25-hydroxy vitamin D and its analogues in epithelial proliferation, differentiation and angiogenesis is known. Supported by studies this has been linked to prostate tumour growth and prostate cancer aggressiveness.[5,7] Unfortunately, few studies directly linking serum vitamin D with either prostate cancer prognosis or measures of prostate cancer aggressiveness has been done and non to the best of my knowledge has been done among black Africans and Nigerians in particular, where there is an almost equal distribution of sunlight and melanin pigment as well as high burden of aggressive disease with abysmal outcomes.

This is the rationale for this research which seeks to ascertain the value of serum 25-hydroxy vitamin D measurements for determining aggressiveness of cancer of the prostate using the Gleason score in black Africans in Jos metropolis, Nigeria. Establishment of this, or any relationship may help to appropriately counsel patients on possible rate of disease progression, likely outcome of disease irrespective of stage at diagnosis as well as individualize patients treatment options in a bid to maximize benefits and minimize adverse effects.

II. MATERIALS AND METHODS

- *Study Site*

This research was conducted in the urology division of the department of surgery at the Jos University Teaching Hospital, a tertiary health care providing hospital located in Jos, the capital city of Plateau state, Nigeria.

- *Study Design*

This was a prospective cross-sectional study carried out over a one year period spanning October 2020 to September 2021.

- *Study Population*

The study participants were new patients presenting to the Urology Surgery Outpatient clinics with clinical diagnosis of prostate cancer, who had a prostate biopsy with histologic confirmation of the diagnosis.

- *Data Collection Procedure*

The subjects were new patients who presented to the Urology Surgery Outpatient Department with clinical diagnosis of prostate cancer, who had a prostate biopsy with histologic confirmation of the diagnosis. On the morning of prostate biopsy procedure,4.5mls of blood was collected in the fasting state for serum 25-hydroxy vitamin D assay. The blood collected were centrifuged at 3000gn for 15 minutes within two hours of collection to obtain the serum. The serum was stored at -20°C to −80°C in order to preserve its physiologic state until required for use. Samples were analysed by the same chemical pathologist using the enzyme-linked immunosorbent assay (ELISA) technique. Selected patients then had digitally guided transrectal prostate biopsy done as a day case procedure. Prophylactic antibiotics (Intravenous levofloxacin 500mg and metronidazole 500mg) were given 60 to 120 minutes before the procedure. Anaesthesia was done via a caudal block using 10mls of 1% of plain xylocaine. Cores of prostate tissue were obtained using a high speed Gallini spring-loaded 18-G Tru-cut needle and a sextant biopsy was obtained under transrectal digital guidance. Prostate biopsy tissue specimens were preserved in 10% buffered formalin and examined microscopically after Haematoxylin-Eosin staining for histologic diagnosis and other characteristics. Data was recorded using a structured preform.

- *Statistical Methods*

The obtained data were collated using the Statistical Package for Social Sciences (SPSS) versions 23. Results were presented as tables and charts. The normality of the data was checked using the Kolmogorov-Smirnov test and the relationship of serum vitamin D_3 level and Gleason score was tested using the Spearman's Rank Correlation test.

P value <0.05 was considered statistically significant at confidence interval of 95%.

➢ *Ethical Considerations*

Ethical approval for this study was obtained from the Research and Ethics Committee of Jos University Teaching Hospital (JUTH). All participants gave their consent and the results of patient's evaluation were treated with utmost confidentiality. Financial obligation other than is routine for patient evaluation and care was borne by the researcher.

III. RESULTS

50 patients were studied whose age ranged from 50 years to 89 years with a mean of 70.0±7.9. It was observed that 26% of the participants had tertiary education and 22% had no formal education. 44% of participants in the study were retired civil servants and 26%were farmers. (Table 1)

It was noted that 32% of study participants had locally advanced disease while 34% had clinically metastatic disease at the time of presentation.(Table 2).

The mean serum 25-hydroxy vitamin D level in the study participants was 37.90±17.92 with a median of 31.47ng/ml. (Table 3)

All 50 patients with prostate cancer in this study had adenocarcinoma as the histologic type, with a mean Gleason score and standard deviation of 7.56±1.25.

Table 1: Demographic characteristics of 50 study participants with prostate cancer

Demographic characteristics	Frequency (n=50)	Percentage
Mean ± SD age	70.0±7.9	
Age group (yrs)		
50-59	6	12.0
60-69	15	30.0
70-79	23	46.0
80-89	6	12.0
Educational level		
None	11	22.0
Primary	12	24.0
Secondary	14	28.0
Tertiary	13	26.0
Occupation		
Retiree	22	44.0
Farmer	13	26.0
Business	7	14.0
Civil servant	4	8.0
Artisan	4	8.0

Table 2: Clinical stage at time of presentation for 50 study participants with prostate cancer

Clinical stage	Frequency	Percentage
Early disease	17	34.0
Locally advanced disease	16	32.0
Metastatic disease	17	34.0

Table 3: Mean level of serum 25-hydroxy vitamin D in 50 patients with prostate cancer according to histologic type.

Histologic type	Mean ± SD	Median
Adeno carcinoma	37.90±17.92	31.47

Table 4: Correlation of serum 25-hydroxy vitamin D and the Gleason Score in patients with prostate cancer.

			Gleason Score
Spearman's rho	Serum 25-hydroxy vitamin D level (ng/ml)	Correlation Coefficient	-0.423*
		p-value	0.002
		N	50

*. Correlation is significant at the 0.05 level

IV. DISCUSSION

In this study, fifty (50) patients with histologically proven prostate cancer were studied.Majority (46%) of them were in their eight decade of life. This finding is similar to that conducted in 16 African countries by Adeloye et al, where they found out that individuals that were 71years and above had the highest incidence of prostate cancer and this was followed by those 60 -69 years.[1] From this study, the mean age of patients with prostate cancer was 70.0 ± 7.9 years, similar to the findings by Nwofor and Oranusi conducted in the southeastern part of Nigeria with a mean of 71.0± 10.9.Also, the finding is not different from that observed by Osegbe DN, and Badmus et al, with values of 68.3± 9.4, and 68.0±9.8 years respectively.[8,9 ,10] This buttresses the point that prostate cancer is a disease common in the elderly.

This study noted that though majority (66%) of the patients had clinically advance and metastatic disease at the time of presentation, a remarkable number of patients (34%) had clinically early stage disease as at the time of presentation. This finding contrasts that obtained by Ibrahim et al at Maiduguri Northeastern part of Nigeria where 100% of the studied patients had advanced disease at the time of presentation.[11] This finding may be attributable to differences in level of awareness of prostate cancer, accessibility to appropriate healthcare facility and improvement in available diagnostic facilities.

There is a variation with regards definitions of vitamin D deficiency; hence the threshold for vitamin D deficiency is still a subject of debate. However, most authorities believe optimal level of serum 25-hydroxy vitamin D is 35–55 ng/ml and a desirable value ≥40ng/ml. [12, 13] from this study, the mean level serum 25-hydroxy vitamin D in patients with prostate cancer was 37.90±17.92 ng/ml. However, study by Adedapo et al, at the University College Hospital Ibadan, showed a mean serum 25-hydroxy vitamin D of 30.362±8.639, a value slightly lower than what this current study reports. A retrospective Study by Yatura et al among 479 patients with cancer of the prostate in the United States of America showed a mean serum 25-hydroxy vitamin D of 28.4 ± 0.54.14. This study showed that serum 25 hydroxyl vitamin D level in black African patients with prostate cancer is higher especially in the Jos metropolis and its environs. This can be attributed to relatively steady sunny weather all year round coupled with the staple diet known to be rich in basic nutrient and vitamins.

This study showed a moderate negative correlation of serum 25-hydroxy vitamin D and Gleason score, which was statistically significant (r_s (50) = -0.423, p = 0.002).This finding is similar to the Bulgarian study by Gunluska et al, which noted a moderately negative correlation of serum 25-hydroxy vitamin D level and Gleason score (Spearman r = -0.46, p <0.05).[15]. Thus, serum 25- hydroxyl vitamin D has much value that is consistent with aggressiveness of disease among patients with prostate cancer. This is supported by other studies.[16,17] This study has shown that among patients with prostate cancer, the lower the serum 25-hydroxy vitamin D level at the time of diagnosis the higher the Gleason score and by implication the more aggressive the course of the disease.

V. CONCLUSION

This study shows that in patients with cancer of the prostate, black Africans has a higher baseline serum 25-hydroxy vitamin D level at the time of diagnosis and that serum 25-hydroxy vitamin D level is a veritable marker in aggressiveness of prostate cancer.

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