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Original Research Article

Comparison of serum 25-hydroxy vitamin D amongst black African prostate cancer patients with non-aggressive versus aggressive disease using the Gleason score

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ABSTRACT

Background: Black men of African descent have higher risk for developing prostate cancer and present at a younger age with advanced disease and a poorer prognosis. Limited number of studies directly linking serum vitamin D with either prostate cancer prognosis or measures of prostate cancer aggressiveness have been done. The objective of this study is to compare serum 25 hydroxy vitamin D levels in patients with non-aggressive and aggressive prostate cancer using the Gleason score in black Africans in Jos.
Methods: A cross sectional study conducted among fifty patients who presented to the urological surgical out-patient clinic of the Jos University Teaching Hospital who had clinical diagnosis of prostate cancer and were scheduled for prostate biopsy. Blood samples for serum 25-hydroxy vitamin D assay was analysed using the enzyme linked immunosorbent assay (ELISA) technique, patients with histologically confirmed prostate cancer were analysed. Data was collected in a proforma, statistical analysis done using statistical package for the social sciences (SPSS)$^{(R)}$ version 23 and t-test was used for comparison with a p value <0.05 considered significant.
Results: Fifty patients were studied whose age ranged from 50-89 years. The mean level of serum 25-hydroxy vitamin D was 37.90 ng/ml±17.92. The mean serum 25-hydroxy vitamin D of patients with non-aggressive disease (GS≤6) and aggressive disease (GS≥7) was 48.44±17.09 and 34.57±17.08 respectively with a p value of 0.018.
Conclusions: This study showed that black African prostate cancer patients with high grade tumors (Gleason score ≥7) had significantly lower 25-hydroxy vitamin D levels compared to those with low grade tumors (Gleason score <7).

Keywords: Serum 25-hydroxy vitamin D, Prostate cancer, Gleason score

INTRODUCTION

Cancer of the prostate (CaP) is globally the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males.[1] Among men alive today, it is estimated that 1 in 7 (15.3%) will be diagnosed with prostate cancer with 1 in 38 (2.6%) dying from this disease.[2]

African American men develop prostate cancer at a rate of 1.5 to 1.9 times higher than their European American counterpart and these racial differences are further emphasized by increased diagnosis of aggressive prostate cancer.[3] 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 prostate cancer in African Americans, recent studies have focused

on differences in serum 25-hydroxy vitamin D (25(OH) D) concentrations as the source for the disparate trends seen in this disease.[3,4]

Metabolites of vitamin D have been known to control cellular growth and differentiation, which has been attributed to anti-proliferation, pro-differentiating and pro-apoptotic effects on prostate epithelial cells. The role of vitamin D in prostate tumour growth and aggressiveness has been supported by studies and these associations have been linked to sunlight exposure and melanin content of skin.[3,5] However, only a limited number of studies directly linking serum vitamin D with either prostate cancer prognosis or measures of prostate cancer aggressiveness have been done.[3,4] A comparison of serum vitamin D among prostate cancer patients with less aggressive and more aggressive disease using the Gleason score as a measure of aggressiveness especially in black Africans may be an invaluable tool in prognostication for this disease that is a huge global burden. The objective of this study is to compare serum 25 hydroxy vitamin D levels in black African prostate cancer patients with non-aggressive and aggressive prostate cancer using the Gleason score.

METHODS

Study site

This study was carried out in the Urology Division of the Jos University Teaching Hospital, a tertiary health institution located in the Plateau state capital, Jos, Nigeria.

Study design

It was a prospective cross-sectional study conducted over a period of one year between October 2020 to September 2021.

Study population

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.

The criteria for inclusion were patients with histologically proven diagnosis of prostate cancer who consented to participate in the study. conversely, criteria for exclusion was patients already on treatment for prostate cancer, those diagnosed with prostate cancer who were taking vitamin D containing supplements, patients on drugs that could affect serum 25-hydroxyvitamin D levels such as phenobarbital, isoniazid and corticosteroid, and patients with terminal diseases such as end stage liver and renal diseases.

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, 4.5 ml of fasting blood samples were collected for serum 25-hydroxy vitamin D assay. The sample was centrifuged at 3000 gn 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. Patients had digitally guided transrectal prostate biopsy as a day case procedure. Intravenous levofloxacin 500mg and metronidazole 500 mg were administered 60 to 120 minutes before the procedure for prophylaxis. Caudal block with 10 mls of 1% of plain xylocaine was used as a form of anaesthesia. The procedure was done with patient in left lateral position using a high speed Gallini spring-loaded 18-G Tru-cut needle. 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 proforma.

Statistical methods

All data obtained from the study subjects were subjected to statistical analysis using the statistical package for social sciences (SPSS) version 23 statistical software. Results are presented as tables and charts. Kolmogorov-Smirnov test was used to test for normality of the data and the t-test was used for comparison of the two groups. This analysis was done with the assistance of a medical statistician.

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

Ethical considerations

Permission to conduct this study was obtained from the research and ethics committee of Jos University Teaching Hospital (JUTH), Jos, Nigeria. Informed consent was obtained from all patients who met the criteria to be included in the study. The results of each patient's evaluation were treated with utmost confidentiality and financial obligation other than is routine in patient evaluation, pertaining to this study was borne by the researcher.

RESULTS

A total of 50 patients who gave consent and met the inclusion criteria were recruited for the study. The age range of the subjects was 50-89 years with a mean age and standard deviation of 70.0±7.9. Twenty-two (44%) of the participants were retired civil servants, while 13 (26%) were farmers (Table 1).

It was noted that 34% of the patients had early disease, 32% of study participants had locally advanced disease

while 34% had clinically metastatic disease at the time of presentation (Table 2).

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 (years)		
50-59	6	12.0
60-69	15	30.0
70-79	23	46.0
80-89	6	12.0
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

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

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 3).

Table 3: Histologic type, frequency and mean Gleason score of 50 study participants.

Characteristics	Frequency	Percentage
Adenocarcinoma	50	100.0
Gleason Score ≤ 6	12	24
Gleason Score≥7	38	76
Mean Gleason score	7.56±1.25	

Table 4: Comparison of mean serum 25-hydroxy levels between participants with Gleason score of ≤6 and ≥7 among the 50 study participants.

Gleason score	Mean± SD 25-hydroxy vitamin D (ng/ml)	t-test	P value
≤6	48.44±17.09	2.454	0.018
≥7	34.57±17.08		

The mean serum 25-hydroxy vitamin of patients with less aggressive disease (GS≤ 6) was (48.44±17.09) and those with aggressive disease (GS ≥7) was (34.57±17.08) with a p value of 0.018 (Table 4).

DISCUSSION

Fifty (50) patients with histologically proven prostate cancer were studied. Majority (46%) of the patients presented in the eight decade of life. This finding corroborates with that conducted in 16 African countries by Adeloye et al, where the age group with the highest incidence of prostate cancer was 71 and above followed by 60 -69 years.[1] Our study showed a mean age of patients with prostate cancer of 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 and Badmus et al, which noted the mean ages for prostate cancer to be 68.3±9.4, and 68.0±9.8 years respectively.[6-8] This buttresses the fact that prostate cancer is a disease of 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 is in contrast to study done by Ibrahim et al in Maiduguri Northeastern part of Nigeria where 100% of the studied patients had advanced disease at the time of presentation.[9] 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.

Definitions of vitamin D deficiency vary, hence the appropriate threshold for vitamin D deficiency is still being debated. However, the most widely accepted optimal level of serum 25(OH) D is 35–55 ng/ml and a desirable value ≥40 ng/ml.[10,11] From this study, the mean level of serum 25-hydroxy vitamin D in patients with prostate cancer was 37.90±17.92 ng/ml. However, Adedapo et al, at the University College Hospital Ibadan, found patients with prostate cancer had a mean serum 25-hydroxy vitamin D level of 30.362±8.639 that was slightly lower than what this current study report. A retrospective study by Yatura et al among 479 patients with prostate cancer in the United States of America showed a mean serum 25-hydroxy vitamin D level of 28.4±0.54.[12] This study showed a higher serum 25 hydroxyl vitamin D in patients with prostate cancer in the Jos metropolis and its environs 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.

The mean Gleason score and standard deviation from this study was 7.56±1.25. A further look at the percentage of patients with less aggressive disease (Gleason score ≤6) and those with aggressive disease showed that while 24% of patients presented with a less aggressive disease,

majority (76%) of our patients at the time of diagnosis had aggressive disease. This finding is not so different from that observed by Nnabugwu et al among 205 patients, which had 37% with GS ≤6 and 63% having GS ≥7.[13] From this observation, it can be inferred that majority of Africans at the time of diagnosis do have an aggressive disease.

Furthermore, analysis of the serum 25-hydroxy vitamin of patients with less aggressive disease (GS≤6) and those with aggressive disease (GS≥7) showed that patients with GS≤6 had a higher mean serum 25-hydroxy vitamin (48.44±17.09) compared to those with a GS≥7 (34.57±17.08). This when subjected to the t-test showed a p value of 0.018 which is statistically significant. This finding is similar to that of the Bulgarian pilot study that involved 53 patients by Gunluska et al, they showed that patients with high grade tumors (Gleason score ≥7) showed significantly lower 25-hydroxy vitamin D levels, while those with low grade tumors (Gleason score <7) was seen to show higher 25-hydroxy vitamin D status (50.49 versus 63.17 nmol/l, $p<0.05$).[14]

Also, this finding may support the study observation by Shui et al that higher 25(OH) D levels were associated with a 57% reduction in the risk of lethal prostate cancer and that by Murphy et al, that in both European American and African American men, severe deficiency was positively associated with higher Gleason grade and tumor stage.[15,16]

Possible limitations for this study could be a reduction in the sample size due to some missed diagnoses as a digitally guided transrectal prostate biopsy was done as against an ultrasound guided prostate biopsy which is the standard due to its non-availability in the facility.

Also, this was a cross sectional study in which a one-time measurement of circulating levels of serum vitamin D_3 was obtained. It may not have sufficiently reflected a chronic deficiency state of vitamin D in these patients.

CONCLUSION

This study has shown that in patients with prostate cancer, black Africans have a higher baseline serum 25-hydroxy vitamin D at the time of diagnosis and that the serum 25-hydroxy vitamin D level is higher in those with less aggressive disease when compared to those with more aggressive disease.

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