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Vitamin D Deficiency Prevalence and Correlates in Patients Attending the Cardiology Clinic in a Tertiary Centre in Southern Nigeria

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Abstract: *Background:* Vitamin D is an important vitamin that helps in many bodily functions. Its deficiency has been found to play a role in cardiovascular diseases like hypertension, heart failure, ischemic heart disease etc. 1α, 25-dihydroxyvitamin D, the active metabolite of vitamin D, binds major receptors found in all the major cardiovascular cells including arteries and cardiomyocytes to exert its protective effects. Darker skinned individuals have been found to be more vitamin D deficient than their Caucasian counterparts. This study sought to determine the prevalence and correlates of vitamin insufficiency and deficiency among patients attending the cardiology clinic in a major referral centre in southern, Nigeria. *Methods:* This is a descriptive cross-sectional study of a total of 192 study participants attending the cardiology out-patient clinic of the university. Informed consent was sort, and a questionnaire administered to all recruited patients and blood drawn for vitamin D assay. *Results:* There were more female study participants 55.7% as compared with their male counterparts at 44.3%. Hypertension (62.0%) as well as diabetes (33.3%) were the most common co-morbidity in the participants. Vitamin D deficiency was found in 7.8% of the study participants and 24.5% of all participants had below normal serum Vitamin D concentration i.e. <30ng/ml. A statistically significant association was noticed between the presence of comorbidities and vitamin D deficiency (F=65.87; p=0.03). Inadequate consumption of red meat was also found to be associated with insufficient and deficient serum vitamin D level (P=0.009). *Conclusion:* Vitamin D deficiency and insufficiency was found to be prevalent in patients attending the cariology out-patient clinic and linked with the presence of hypertension, hypertensive heart disease and diabetes mellitus. The need for dietary supplementation of Vitamin D should be of public health importance in not only paediatric population and maternal health, but the general adult population as well.

Keywords: Vitamin D, Deficiency, Cardiovascular, Insufficiency, Hypertension, Risk Factors

1. Introduction

Serum Vitamin Status and Cardiovascular Health

Vitamin D is a steroid hormone found in the human body through its production in the skin or its absorption through the small intestine [1]. It is required for the metabolism of calcium and phosphorous [2]. The vitamin D present in the human body is of two forms; vitamin D_2 (ergocalciferol) which is gotten from plant-based foods, and vitamin D_3 (cholecalciferol) which is produced in the human epidermis or gotten from oily fish. Vitamin D is then metabolized by the liver to 25-hydroxy-Vitamin D and further metabolized to 1, 25, dihydroxy Vitamin D which is important for muscle function, bone function, and calcium metabolism [3]. Serum levels of 25-hydroxy Vitamin D correlates with vitamin D status and as such is measured to determine deficiency state, while serum levels of 1,25 dihydroxy vitamin D despite being the active form does not correlate with vitamin D status and as such has no clinical utility. However, it is this active form that circulates throughout the body and exerts its wide range of effects [3].

1,25, dihydroxy vitamin D binds to Vitamin D receptor (VDR) which is found in the nucleus of cells where it acts as a transcription factor, inducing protein synthesis [4].

Transcriptional feedback mechanism controls renal 1,25, vitamin D production. This mechanism involves parathyroid hormone and fibroblast growth factors [5].

Vitamin D deficiency has been linked with a variety of cardiovascular diseases and various observational studies has recognized it as an important cardiovascular risk factor [6]. Low serum Vitamin D levels have been constantly linked with increased risk of cardiovascular diseases such as hypertension, coronary artery disease, ischemic heart disease, heart failure, stroke and type 2 diabetes mellitus. However, vitamin D deficiency has not been associated with cardiovascular disease as a causative factor [7].

Vitamin D deficiency is defined as serum 25-hydroxy vitamin D level less than 20ng/ml (50nmol/L) and has an inverse association with parathyroid hormone level. The prevalence of vitamin D deficiency varies widely based on age (more prevalent in elderly and young adult population), geographical location, sex (more in female than males) etc. people who live near the equator with high sun exposure have lower prevalence of vitamin D deficiency [4].

This study aims to determine the prevalence of Vitamin D insufficiency / deficiency in adults attending the cardiology out-patient clinic at the University of Port Harcourt Teaching Hospital and determine risk factors associated with vitamin D deficiency.

2. Methods

2.1. Study Design

This is a descriptive cross-sectional study.

2.1.1. Study Site

This study was carried out at the cardiology out-patient clinic of the University of Port Harcourt Teaching Hospital (UPTH). The hospital is in Alakahia, Rivers State in southern Nigeria. Nigeria is located in West Africa, longitude 9.0820°N, latitude 8.6753°E and 690.93miles (1.111.95Km) north of the equator [8]. The cardiology clinic serves as a referral point for Rivers State and attends to about 200 patients per month.

2.1.2. Study Population

This study consisted of all adults attending the cardiology clinic of UPTH with a primary diagnosis were hypertension, heart failure, ischemic heart disease, cardiomyopathies, venous thromboembolism, arrhythmias and dyslipidemia. About 10 – 15 patients (of 40 – 50 patients seen per week) who met the eligibility criteria were recruited into the study per week. Informed consent was gotten from all participants. Random sampling was used with every third patient meeting the eligibility criteria were approached for recruitment into the study. The study period was between September 2021 and March 2022. A total of 192 study participants were recruited during the study period into the study.

2.2. Vitamin D Assay Procedure

Following the collection of socio-demographic and medical information from each study participants, 5mls of venous blood was collected from each study participant. Venous samples were collected without preference to fasting state, dietary restrictions or diurnal variations. Collected venous blood samples were allowed to clot at room temperature, refrigerated and transported to the chemical pathology laboratory of UPTH under cold chain for the analysis of serum vitamin D level. 25-hydroxy vitamin D was analyzed using the CALBIOTECH 25 (OH) vitamin D (enzyme linked immunoassay) ELISA. 50µl of serum was extracted from each venous sample and used for the assay of 25 (OH) vitamin D.

2.3. Statistical Analysis

Data was collected using Microsoft excel and transferred to SPSS version 24. Socio-demographic data was presented for the sample using measures of central tendencies, frequencies and percentages, and presented graphically using pie charts. Vitamin D status (deficiency vs non-deficiency) was compared amongst the study participants using chi-square and fishers exact and analysis of variance. Statistical significance was set at 95% and power at 80%.

Ethical clearance was obtained from the UPTH hospital research ethical committee.

3. Results

Patients attending the cardiology unit of the department of internal medicine at the University of Port Harcourt Teaching Hospital were recruited into this study. About 230 patients were approached with 192 completing the study making a study completion rate of 83.5%. About 44.3% of the study participants were male and 55.7% were female, the participants were composed mainly of Christians (99.0%) and majority of them ran their own businesses. (Table 1). Most participants had hypertension (62.0%) and the most common co-morbidity associated with patient diagnosis was diabetes which occurred in about 33.3% of the participants (Table 2). Vitamin D deficiency was found in 7.8% of the study participants and 24.5% of all participants having below normal serum Vitamin D concentration i.e. <30ng/mol (Table 3). When comparing the age and anthropometric parameters between the deficient and non-deficient group, systolic blood pressure was seen to be higher as vitamin D status worsened, though this was not statistically significant, there was also no significant difference in the prevalence of vitamin D deficiency based on gender (p value=0.687). Participants with low Vitamin D concentration (insufficient and deficient) tended to have a diagnosis of hypertension or hypertensive heart disease (Table 2). The study participants had a wide range of comorbidities including medical, surgical and mental health conditions. These co-morbidities were compared as regards Vitamin D status. While there was a statistically significant association between the presence of comorbidities and vitamin D status deficiency (F=65.87; p=0.03) this significant association cannot be said to be causal in nature.

Exposure to sunlight (defined as about 15 – 30 minutes of sunlight for dark- skinned individuals between 10am and 2pm) and nutritional details of study participants were examined to

determine if a relationship existed between these factors and Vitamin D deficiency. This study was able to associate lack of red meat in participants diet with suboptimal serum Vitamin D level (Table 5).

Table 1. *Sociodemographic characteristics of all study participants.*

Variable	Frequency (n=192)	Percent (%)
Sex		
Male	85	44.3
Female	107	55.7
Occupation		
Professional	26	13.5
Civil servant	28	14.6
Business	85	44.3
Student/Housewife	4	2.1
Retired	49	25.5

Variables	Mean ± SD	Minimum	Maximum
Age (Years)	55.91 ± 13.65	20.0	85.0
Weight (Kg)	75.28 ± 16.37	42.0	125.2
BMI (Kg/m^2)	27.29 ± 5.70	14.5	44.7

Table 2. *Clinical information of study participants.*

Variables	Frequency (n=192)	Percentage (100%)
Cardiac diagnosis		
Hypertensive Heart Failure	35	18.2
Hypertension	86	44.8
Valvular heart disease	4	2.1
Peripartum Cardiomyopathy	6	3.1
Ischaemic heart disease	4	2.1
Infective endocarditis	2	1.0
Congenital Heart disease	1	0.5
Deep Venous thrombosis	2	1.0
Arrythmias	3	1.6
Dyslipidemia	4	2.1
Thyrotoxic heart disease	2	1.0
No response	43	22.4
Co-morbidities		
Anxiety disorder	3	1.6
Benign prostatic hyperplasia	5	2.6
Diabetes	38	19.8
Hyperthyroidism	2	1.0
Stroke	9	4.7
PUD	6	3.1
Hepatic steatosis	1	0.5
Osteoarthritis	14	7.3
Parkinson's disease	1	0.5
Seizure disorder	1	0.5
Inguinal hernia	1	0.5
HIV	11	5.7
Haemorrhoids	1	0.5
Pan-ophthalmitis	1	0.5
Cancer	2	1.0
Schizophrenia	1	0.5
Infertility	1	0.5
Obesity	1	0.5
No response	93	48.4

Table 3. *Prevalence of vitamin D deficiency among study participants.*

Vitamin D Class	Frequency (n)	Percentage (%)
Deficient (<20)	15	7.8
Insufficient (21-29)	32	16.7
Adequate (>30)	142	75.5
Total	192	100.0

Table 4. *Relationship between patient's diagnosis and vitamin D deficiency.*

Variable	Vitamin D Status			Total
	Deficient (<20) n (%)	Insufficient (21-29) n (%)	Adequate (>30) n (%)	N (%)
Cardiac diagnosis				
Hypertensive Heart Failure	9 (60.0)	10 (31.3)	16 (11.0)	35 (18.2)
Hypertension	2 (13.3)	18 (56.3)	66 (45.5)	86 (44.8)
Valvular heart disease	0 (0.0)	2 (6.3)	2 (1.4)	4 (2.1)
Peripartum Cardiomyopathy	1 (6.7)	0 (0.0)	5 (3.4)	6 (3.1)
Ischaemic heart disease	0 (0.0)	0 (0.0)	4 (2.8)	4 (2.1)
Infective endocarditis	0 (0.0)	1 (3.1)	1 (3.1)	2 (1.0)
Congenital Heart disease	0 (0.0)	0 (0.00	1 (0.7)	1 (0.5)
Deep Venous thrombosis	0 (0.0)	0 (0.0)	2 (1.4)	2 (1.0)
Arrythmias	0 (0.0)	0 (0.0)	3 (2.1)	3 (1.6)
Dyslipidaemia	0 (0.0)	0 (0.0)	4 (2.8)	4 (2.1)
Thyrotoxic heart disease	1 (6.7)	0 (0.0)	1 (0.7)	2 (1.0)
No response	2 (13.3)	1 (3.1)	40 (27.6)	43 (22.4)
		Fisher' Exact=49.557	*p-value=0.001**	

Table 5. *Comparison of vitamin D intake and nutrition among vitamin D deficient participants and non-vitamin D deficient participants.*

Variables	Vitamin D Status			Total
	Deficient (<20) n (%)	Insufficient (21-29) n (%)	Adequate (>30) n (%)	N (%)
Adequate sunlight				
No	3 (20.0)	2 (6.3)	15 (10.3)	20 (10.4)
Yes	12 (80.0)	30 (93.8)	130 (89.7)	172 (89.6)
		Fisher's exact=2.095	*p-value=0.382*	
Vitamin D supplement				
No	15 (100.0)	32 (100.0)	143 (98.6)	190 (99.0)
Yes	0 (0.0)	0 (0.0)	2 (1.4)	2 (1.0)
		Fisher's exact=0.707	*p-value=1.000*	
*Oily fish				
No	4 (26.7)	8 (25.0)	19 (13.1)	31 (16.1)
Yes	11 (73.3)	24 (75.0)	126 (86.9)	161 (83.9)
		Chi square=4.071	*p-value=0.131*	
Liver meat				
No	10 (66.7)	13 (40.6)	62 (42.8)	85 (44.3)
Yes	5 (33.3)	19 (59.4)	83 (57.2)	107 (55.7)
		Chi square=3.356	*p-value=0.187*	
Red meat				
No	11 (73.3)	19 (59.4)	57 (39.3)	87 (45.3)
Yes	4 (26.7)	13 (40.6)	88 (60.7)	105 (54.7)
		Chi square=9.414	*p-value=0.009**	
Egg yolk				
No	9 (60.0)	17 (53.1)	69 (47.6)	95 (49.5)
Yes	6 (40.0)	15 (46.9)	76 (52.4)	97 (50.5)
		Chi square=1.042	*p-value=0.594*	
Cheese				
No	13 (86.7)	28 (87.5)	129 (89.0)	170 (88.5)
Yes	2 (13.3)	4 (12.5)	16 (11.0)	22 (11.5)
		Chi square=0.411	*p-value=0.786*	
Fortified food				
No	8 (53.3)	10 (31.3)	42 (29.0)	60 (31.3)
Yes	7 (46.7)	22 (58.8)	103 (71.0)	132 (68.8)
		Chi square=3.757	*p-value=0.153*	

*Oily fish is defined as Mackerel, Tuna, Salmon, Sardine and Catfish

4. Discussion

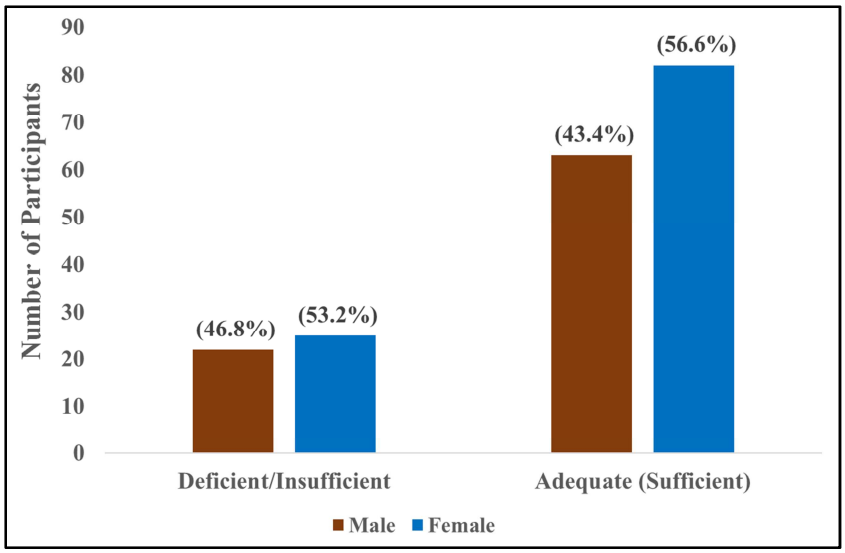
4.1. Main Findings

This study found that about a quarter of the patients attending the cardiology clinic of UPTH on an out-patient basis had serum Vitamin D levels below the normal limit and 7.8% of them were deficient in Vitamin D. Having a diagnosis of hypertension and hypertensive heart disease has an association with being deficient in Vitamin D, as well as having a medical comorbidity.

The study participants who had below normal serum Vitamin D levels were noted to have diabetes mellitus and cerebrovascular accident (stroke) as comorbid medical conditions. The effect of environmental factors such as sunlight exposure and dietary intake of foods rich in vitamin D were also examined. Nigeria being above the equator has adequate amount of sunlight and as such participants

subjective response to sunlight exposure was not found to influence their serum vitamin D status. Concerning dietary intake of foods rich in Vitamin D, the study found that inadequate consumption of red meat was associated with insufficient and deficient serum vitamin D level.

This study was a cross sectional study and as such causal relationships could not be determined for the associations found.



Chi Square=0.162; p value=0.687

Figure 1. *Vitamin D levels among male and female participants of the study.*

4.2. Strengths and Limitations

This study has the strength of being the first study of its kind to determine the relationship between serum vitamin D level and medical and social factors affecting patients in the south-south region of Nigeria. Despite this, it has the limitation based on being unable to determine a causal relationship between these factors and Vitamin D level.

This study also has the limitation of being unable to identify the effect of Vitamin D deficiency on medical outcome of the participants. This could have been determined if a prospective approach was used.

4.3. Comparison with Other Literature

The findings from this study when compared with literature shows that vitamin insufficiency and deficiency is present globally. In the United States of America, vitamin D deficiency was found in 41.6% of study participants with minority groups having relatively higher level (blacks had a prevalence rate of 82%) [9]. Their study also found that hypertension and poor nutritional intake of foods rich in Vitamin D (daily mild consumption) was associated with vitamin D deficiency. This is similar to findings from our study as hypertension and poor red meat consumption were associated with Vitamin deficiency and insufficiency. Several prospective as well as meta-analysis of observational studies have found vitamin D deficiency to be associated with high blood pressure. [10] [11] Vitamin D supplementation have been shown to lower systolic blood pressure by 2–6 mmHg but more studies are required before concluding on its effect on blood pressure and cardiovascular risk reduction. [11]

In countries with high sunlight exposure (that is countries above the equator), vitamin deficiency was also found to be highly prevalent [12]. Pakistan had a deficiency rate of 53.5% and an insufficient rate of 31.2% despite high levels of sunshine [13]. This indicates dietary cause of Vitamin D deficiency. Hovsep an et. al., [14] in their study of Vitamin D in an out-patient setting in Iran found prevalence of mild Vitamin D deficiency (20-30ng/ml) of 19.6%, moderate Vitamin D deficiency (10-20ng/ml) of 23.9% and severe Vitamin D deficiency (10ng/ml) of 26.9%. contrary to our study, they found associations between vitamin D deficiency and gender (being more in women) and age (younger age group having higher prevalence of Vitamin D deficiency) [14]. The prevalence of Vitamin d deficiency varied with the seasons being higher in winter and less in spring/summer seasons.

The Fulani population in Nigeria are nomadic cattle rearing tribe who are exposed to high amounts of sunlight and whose diet is generally centered around their cattle. A study by Glew et. al., [15] found below normal serum Vitamin D serum level (≤30ng/ml) of 83% in females and 45% in males.

These studies as well as our study highlight the role dietary sources of Vitamin d have to play in serum Vitamin d levels and as such dietary fortification should be promoted both in out-patient clinics and at the community levels.

While we were unable to find a causal relationship between Vitamin level and medical diagnosis and co-morbidity, we found that hypertension, hypertensive heart disease and comorbid diabetes mellitus were associated with Vitamin D level. Other literature has been able to link Vitamin D deficiency with acute myocardial infarction (MI). Lee et. al., [9] found that 96% of patients with acute MI have abnormally low serum Vitamin D (75% having insufficient Vitamin D

level and 21% being deficient in Vitamin D). as with our study, the presence of co-morbid diabetes mellitus was associated with Vitamin D deficiency.

5. Conclusion

Vitamin D deficiency and insufficiency is prevalent in patients attending the cariology out-patient clinic and linked with the presence of hypertension, hypertensive heart disease and diabetes mellitus. The need for dietary supplementation of Vitamin D should be of public health importance in not only paediatric population and maternal health, but the general adult population as well.

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