

Distribution of Serum 25-Hydroxyvitamin D Levels in Hypertensive Heart Disease Patients with Atrial Fibrillation in a Secondary Medical Facility in Edo State, Nigeria

Kenneth Atoe^{1,2,3}; Ayinboumwan Ekiye⁴

¹Dept. Chemical Pathology, Edo State University, Uzairue, Nigeria

²Phytomedicine and Drug Discovery Unit, Department of Plant Biology and Biotech., Univ. of Benin, Benin City

³Applied Environmental Bioscience and Public Research Group, University of Benin, Benin City, Nigeria

⁴Dept. Chemical Pathology, University of Benin, Nigeria

Corresponding email: atoe.kenneth@edouniversity.edu.ng

DOI: 10.47760/cognizance.2023.v03i06.001

Abstract

Background: Vitamin D deficiency has been implicated in the pathogenesis of hypertension and other cardiovascular diseases which are common risk factors for atrial fibrillation (AF). It also exhibits anti-inflammatory and antioxidant properties. This study aimed to estimate the level of vitamin D in hypertensive heart disease patients who had atrial fibrillation.

Materials/Methods: A total of 100 participants which consisted of 47 non-hypertensive individuals in the control group and 53 hypertensive heart disease patients who had AF were involved in this study. All participants were within the age range of 40 to 70years. Blood pressure measurements were taken and 5millilitres of blood was drawn from each participant for estimation of serum vitamin D levels using the Enzyme Linked Immunosorbent Assay (ELISA) technique. P-value < 0.05 was considered significant.

Results: There were more males than females in both groups and the mean age of the controls was 58.3years and the subjects, 59.5years. The subjects, being hypertensive, had higher blood pressures. The mean concentration of vitamin D was significantly lower in the subjects (48.43nmol/L) than the controls (60.68nmol/L) ($P < 0.05$) though it was not indicative of vitamin D deficiency but rather vitamin D insufficiency. We found significant vitamin D insufficiency in the female subjects (45.04nmol/L) when compared with the males (51.46nmol/L) ($P < 0.05$).

Conclusion: This study highlighted significantly low vitamin D levels amongst hypertensive heart disease patients with atrial fibrillation. We recommend further studies to justify the role of vitamin D in the etiology of atrial fibrillation.

Keywords: Hypertensive heart disease, Atrial fibrillation, 25-Hydroxyvitamin D.

Introduction

The prevalence of cardiovascular disorders is on the increase worldwide and hypertension is a major and notable contributor.¹ In Nigeria, the prevalence of hypertension has been found to be about 30.6%.² Atrial fibrillation is the most common arrhythmia in hypertensive heart disease, associated with a high morbidity and mortality³ and though the etiology of atrial fibrillation is not completely understood, inflammation has a crucial role in its pathogenesis.⁴ Another mechanism involved in the pathogenesis of atrial fibrillation (AF) is the renin-angiotensin-aldosterone system (RAAS) which is involved in the structural and electrical remodeling of the atrium⁵

Vitamin D is important in regulating calcium metabolism, has antioxidant and anti-inflammatory properties and also has electromechanical effects in the left atrium. From previous

studies, vitamin D deficiency has been known to play a key role in the pathogenesis of coronary artery disease, left ventricular hypertrophy and AF which is associated with the decrease in anti-inflammatory effects in cardiac myocytes. The main mechanisms responsible for atrial fibrosis and thus AF, are oxidative stress, inflammation and activation of the RAAS.⁶ Vitamin D is a negative endocrine regulator of the RAAS and in deficient states, there is an up-regulation of the RAAS. Experimental animal studies showed that vitamin D could inhibit the RAAS system.^{7,8} Also, clinical researches showed that the use of Angiotensin converting enzyme inhibitors was associated with less atrial fibrosis, and the blockade of angiotensin II has been shown to have beneficial effects on electrical remodeling in human atrial tissue.⁹ The findings in these studies confirm that vitamin D deficiency may increase the risk of AF. However, some researchers found that vitamin D supplementation in hypertensive patients with low vitamin D has no significant effect on the blood pressure and several other cardiovascular disease (CVD) risk factors. They did not observe a benefit for higher 25-hydroxycholecalciferol concentration in relation to AF.^{10,11,12} There is paucity of studies on the relationship between vitamin D and AF in our climate. We therefore, aimed to estimate serum vitamin D levels in hypertensive heart disease patients with atrial fibrillation.

Materials and Methods

Study Location and Methodology

A case-control study of 100 individuals consisting of 47 non-hypertensive individuals who served as the control group and 53 patients with hypertensive heart disease with associated atrial fibrillation. The same age range was shared by the subjects and the control group. The individuals



were chosen from the Metabolic clinic of the State General Hospital in Auchi, Edo State. After receiving the written consent of every study participant, relevant information was acquired. Following ECG results, those with atrial fibrillation were chosen as subjects. For all participants, a general physical examination was done. Using a sphygmomanometer, blood pressure was measured while the patient was seated..

Under aseptic settings, 5 ml of venous blood was drawn from the antecubital vein and dispensed into a plain sample bottle. The samples were allowed to clot and retract before being centrifuged at 3000 rpm, the sera were transferred with a Pasteur pipette into plain bottles, and stored at -80 °C until analysis. Enzyme-Linked Immunosorbent Assay technique was used to estimate the serum 25 (OH) vitamin D levels.

Data Analysis

Version 21 of SPSS was used for the analysis. The student "t" test was used to find the difference between the means of the different variables. The significance level was set at $P < 0.05$

Ethical Consideration

All procedures involving human participants in this study were carried out in compliance with the Institutional Research Committee's ethical standards, as well as the 1964 Helsinki Declaration and its most recent revision. All participants provided informed consent as well prior to the study.

Results

Figure 1 presents the percentage occurrence of male and female participants in the study. 52.8% of the subjects were males, while 47.2% were females. Mean age of the control group was 58.3 years, compared to 59.5 in the study group (Table 1). Mean systolic BP within the control group was 108mmHg, compared to 142mmHg within the subject group. Similar increase in diastolic BP was reported in the subject group. Mean Vitamin D level in the control group was 60.7nmol/L, compared to 48.4nmol/L in the subject group ($p<0.05$).

Serum Vitamin D levels were determined on the basis of gender. Vitamin D levels in the male participants were significantly higher ($p<0.05$) than in the females whether in the control or in the subject groups (Table 2). Results showed that Vitamin D levels in male participants was significantly reduced in the subject group (51.46nmol/L) when compared to the control group (63.29nmol/L). This was similar in the female population.

Discussion

Vitamin D deficiency has been found to be associated with atrial fibrillation and makes it more difficult to prevent or terminate.¹³ We found lower vitamin D levels in the hypertensive heart disease patients with atrial fibrillation than in the controls. The mean concentration of vitamin D in the males in both groups showed no deficiency while the female subjects had a mean vitamin D concentration which indicated vitamin D insufficiency. Subjects having plasma concentration of vitamin D below 30nmol/L were considered to be vitamin D deficient while those with a concentration of vitamin D between 30 and 50nmol/L were considered to be vitamin D

insufficient and a plasma concentration above 50nmol/L, normal or sufficient.¹⁴ Forman *et al*,⁸ found in their study on the incidence of atrial fibrillation, that the lower the concentration of vitamin D, the more likely to develop AF. Another study by Verdia *et al*,¹⁵ showed that gender affects vitamin status. They observed a lower level of 25-hydroxyvitamin D compared to males who had AF and it played a relevant role in the severity of AF. The finding of vitamin D insufficiency in female patients in our study, may therefore, infer poorer prognosis in females than in males.

Although gender influenced Vitamin D levels both in the control and in the subject group, incidence of atrial fibrillation significantly reduced Vitamin D levels in both groups. This is similar to previous findings by Schneider *et al*⁷ and others¹⁶ but different from the observations of Alonso *et al*, who did not find a clinically relevant association of circulating vitamin D with AF. However, a meta-analysis concluded a weak but positive association between vitamin D and atrial fibrillation.⁶

Conclusion

This study found an association between vitamin D insufficiency and atrial fibrillation. However several researchers have published studies with conflicting results and unlike skeletal disease, the evidence for serum vitamin D deficiency and the risk of AF has been inconclusive. Hence our study supports the hypothesis that vitamin D status may play a role in the etiology of Atrial fibrillation in patients with hypertensive heart disease. Hence, vitamin D supplementation in hypertensive patients with low vitamin D may be useful.

Acknowledgements

The authors are grateful to Prof. B. Ikhajiagbe of the Department of Plant Biology and Biotechnology, University of Benin, Benin City, for assisting with statistical design and analyses.

Conflicts of Interests

The authors declare no conflicts of interests.

REFERENCES

- [1]. Vos T, Lim SS, Abbafati C, Abbas KM, Abbas M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396:1204-22.
- [2]. Adeloje D, Owolabi EO, Ojji DB, Auta A, Dewan MT, Olarenwaju TO, et al. Prevalence, awareness, treatment and control of hypertension in Nigeria in 1995 and 2020: A systematic analysis of current evidence. *J Clin Hypertens*.2021;23:963-77.
- [3]. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation.: 20-year follow-up of the Renfrew/Paisley study. *Am J Med*.2002;113(5):359-64.
- [4]. Katričis DG. Is atrial fibrillation an inflammatory disorder? *Eur Heart J*. 2006;27:136-49.
- [5]. Y-jen C, Yao-Chang C, Chind-Tai T, Hung-IY, Cheng-I L, Shih-Ann C. Angiotensin II and angiotensin II receptor blocker modulate the arrhythmogenic activity of the pulmonary veins. *Br J Pharmacol*. 2010;147:12-22.
- [6]. Zhang Z, Yank Y, Ng CY, Wang D, Wang J, Li G et al. Meta-analysis of Vitamin D deficiency and risk of atrial fibrillation. *Clin Cardiol*. 2016;39:537-43.
- [7]. Schneider MP, Hua TA, Bohm M, Wachtell K, Kjeldsen SE, Schneider RE. Prevention of atrial fibrillation by Renin-Angiotensin system inhibition: a meta-analysis. *J Am Coll Cardiol*. 2010;55: 2299-307.
- [8]. Forman JP, Williams JS, Fisher ND. Plasma 25-hydroxyvitamin D and regulation of the renin-angiotensin system in humans. *Hypertension*. 2010;55:1283.
- [9]. Boldt A, Scholl A, Garbade J, Resetar ME, Mohr FW, Gummet JF et al. ACE-inhibitor treatment attenuates atrial structure remodeling in patients with lone chronic atrial fibrillation. *BasicRes Cardiol*. 2006;101:261-7.
- [10]. Pilz S, Gaksch M, Kienreich K. Effects of vitamin D on blood pressure and cardiovascular risk factors: a randomized controlled trial. *Hypertension*. 2015; 65(6):1195.
- [11]. Vitezova A, Cartolano NS, HEERINGA J, ZILLIKENS MC, HOFMAN A, FRANCO OH, et al. Vitamin D and the risk of Atrial fibrillation- the Rotterdam study. *PLoS One*. 2015;10(5)e0125161.
- [12]. Alonso A, Misialek JR, Michos ED, Eckfeldt J, Selvin E, SolimanEZ, et al. Serum 25-hydroxyvitamin D and the incidence of atrial fibrillation: the atherosclerosis Risk in Communities (ARIC) study. *Europace*. 2016;18(8):1143-1149.
- [13]. Hanofy DA, Chang SL, Lu YY. Electromechanical effects of 1,25-dihydroxyvitaminD with antiatrial fibrillation activities. *J Cardiovasc Electrophysio*.2014;25:317-323.

- [14]. Munns CF, Shaw N, Kiely M, Specker BL, Thacher TD, Ozono K, et al. Global consensus recommendations on prevention and management of nutritional rickets. *J. Clin Endocrinol Metab.* 2016; 101:394 – 415.
- [15]. Verdia M, Schaffer A, Barbieri L, Di Giovine G, Marino P, Suryapranata H, et al. Novara Atherosclerosis Study Group (NAS). Impact of gender difference on vitamin D status and its relationship with the extent of coronary artery disease. *Nutr Metab Cardiovasc Dis.* 2015;25(5):464-70.
- [16]. Belen E, Aykan A, Kalay E, Sungur M, Sungur A, Cetin M. Low-level Vitamin D is associated with atrial fibrillation in patients with chronic heart failure. *Adv Clin Exp Med.* 2016;25:51-7.

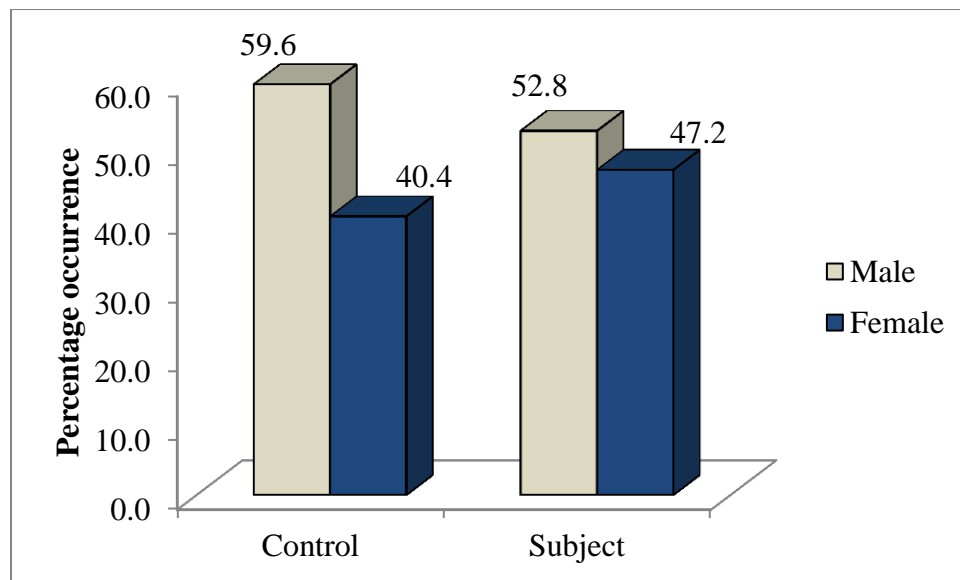


Figure 1: Percentage occurrence of male and female participants in the study

Table 1: General information of the study participants

Group	Age		Systolic BP		Diastolic BP		Vitamin D	
	(yr)	(yr)	(mmHg)	(mmHg)	(mmHg)	(mmHg)	(units)	(units)
	Control	Subject	Control	Subject	Control	Subject	Control	Subject
Mean	58.319	59.453	108.085	142.981	71.723	97.094	60.681	48.434
SD	8.837	10.020	6.763	5.183	5.020	7.458	4.904	5.986

t-value	-0.597	-29.141	-19.693	11.105
p-value	0.552	<0.001	<0.001	<0.001

Table 2: Distribution of serum Vitamin D levels according to gender in the study population

Sex	N	Mean	SD	t	Df	p-value
<u>Control</u>						
Male	28	63.29	4.618	5.765	45	<0.001
Female	19	56.84	1.834			
<u>Subject</u>						
Male	28	51.46	4.282	4.593	51	<0.001
Female	25	45.04	5.856			