Journal of Advances in Medical and Pharmaceutical Sciences

16(2): 1-7, 2018; Article no.JAMPS.40194
ISSN: 2394-1111

C-reactive Protein, Trace Element and Lipid Profile in Cardiovascular Disease

Olooto E. Wasiu[1*], Amballi A. Adetola[1], A. Aiyedun[1], Onayemi A. Adedeji[1] and Olawale O. Oladipupo[1]

[1]Department of Chemical Pathology and Immunology, Olabisi Onabanjo University, Sagamu Campus, Nigeria.

Authors' contributions

This study was done with the collaboration of all authors. Authors OEW, AAA and AA designed the study. Authors AA, OAA and OOO collected the data and authors OAA and OOO handled the statistical analyses of the study, authors OEW and OOO wrote the draft of the manuscript, while authors AA and OAA wrote the results. All authors contributed to writing and proof reading of the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2018/40194
Editor(s):
(1) Erich Cosmi, Department of Woman and Child Heath, University of Padua, Italy.
Reviewers:
(1) Naufal Zagidullin, Bashkir State Medical University, Russia.
(2) Oguz Ozcelik, Firat University, Turkey.
(3) Essam A. El-Moselhy, Al-Azhar University, Egypt.
(4) John Osaigbovoh Imaralu, Babcock University, Nigeria.
Complete Peer review History: http://www.sciencedomain.org/review-history/23938

Original Research Article

Received 15th January 2018
Accepted 29th March 2018
Published 2nd April 2018

ABSTRACT

Background: The increase in consumption of industrial processed food, economic instability consequent to global economic recession; job losses; increase incidence of diabetes and chronic kidney disease; increase steroids use; dyslipidemia; and obesity has been implicated in the global increase in hypertension and corresponding heart diseases. This study evaluates the pattern of C-reactive protein, trace element and lipid profile in cardiovascular disease between January 2016 and August 2017.
Method: The study was a cross-sectional. A total of one hundred participants (consisting of 50 patients and 50 control subjects mean age 56.12±11.4 and 59.8±10.8 yrs respectively) attending medical outpatient clinic of Ogun state general hospital Abeokuta on account of hypertensive heart diseases and other cardiovascular related illness were recruited for the study. Relations that

**Corresponding author: E-mail: olotoenny@yahoo.com;*

accompanied the patients to the clinic and some workers of the hospital were recruited as controls. A structured questionnaire was administered to obtain some demographic data from all the participants. Blood pressure was measured using mercurial sphygmomanometer. Venous blood was collected from all the participants, allowed to clot and centrifuged at 3000 rpm for 5 min to obtain the serum. Serum C-reactive protein, total cholesterol, triglycerides, HDL-C, Zinc, Magnesium and Selenium were measured.

Results: Result showed no significant differences in age and height ($p > 0.05$); a statistically significant increase in weight, BMI, SBP, DBP, serum total cholesterol, LDLC, VLDLC, triglyceride, AI, CRI and CRP ($p < 0.05$); and a statistically significant decrease in serum HDLC, trace element (Zn, Mg, and Se) ($p < 0.05$) among the hypertensive patients when compared with the control subjects.

Conclusion: Base on the result obtained from this study, CVD is associated with abnormalities in inflammatory markers, lipid profile, and antioxidant micronutrients.

Keywords: Cardiovascular disease; hypertension; lipid profile; micronutrient; antioxidants.

1. INTRODUCTION

Hypertension is defined as systolic blood pressure higher than 130 mmHg and diastolic blood pressure higher than 80 mmHg [1]. It is a measure of pressure differences between the effect of blood flow on vascular walls and resistance from the vascular walls. Hypertensive heart disease refers to heart conditions caused by high blood pressure. The heart is working under increased pressure and this can cause different heart disorders such as heart failure, thickening of the heart muscle, coronary artery disease, and other conditions. The high blood pressure makes it difficult for the heart to pump blood through the vessels thus necessitating regular hard work against resistance and causes compensatory but detrimental hypertrophic changes in the left atrium, left ventricle and coronary arteries. There is thus myocardial dysfunction with the involvement of proinflammatory cytokines and inflammatory pathways in both repair and adverse remodelling of the infarcted heart [2].

The global increase in the incidence of hypertension and corresponding heart diseases may be connected with increase in the consumption of industrial processed food which has increased the amount of salt in diets worldwide; economic instability consequent to global economic recession; job losses; increase incidence of diabetes and chronic kidney disease; increase use of steroids; dyslipidemia; and overweight or obesity as a result of physical inactivity.

There is convincing evidence that oxidative stress play important roles in the development of cardiovascular disease (CVD) [3]. Oxidative stress increases low density lipoprotein cholesterol (LDLC) peroxidation, thereby increasing its uptake by macrophages with increased foam cell formation and atherosclerosis. The connection between the various heart disease risk factors and the clinical features of CVD such as congestive cardiomyopathy, myocardial ischemic injury and hypertensive heart disease is oxidative stress [4,5]. Consequently, there is inflammatory response which is an important factor in the initiation and progression of atherosclerosis and atherothrombosis [6].

Variations in the levels of several trace elements and their roles in the pathogenesis of CVD have been reported [7]. Low serum Zn levels have been reported to be associated with increased cardiovascular mortality [7].

To evaluate the disease and status of emerging risks in patients, various physical factors and other biomarkers alone or in combination are used as risk predictors. Traditional risk factors and biophysical factors commonly used to estimate cardiovascular risk include hypertension, diabetes, cigarette smoking, heavy alcohol ingestion, elevated total cholesterol, elevated LDLC, reduced high-density lipoprotein cholesterol (HDLC), elevated triglycerides and family history, each can predict early coronary heart diseases [8]. Pro-inflammatory risk factors include oxidized LDLC, cytokines (interleukin-1, tumour necrosis factor-α), intercellular adhesion molecule-1, selectins, interleukin-6 and C-reactive protein (CRP) [9]. The aim of this study is to determine the contributory role of CRP, trace elements and lipid either solely or in various combinations in CVD.

2. MATERIALS AND METHODS

2.1 Location

This study is a cross-sectional study and was carried out at the Ogun State General Hospital, Sokenu, Ijaye, Abeokuta, Ogun State, Nigeria. The patients were drawn from those attending medical outpatient clinics (MOP) of the hospital.

2.2 Inclusion and Exclusion Criteria

Included in the study are newly diagnosed patients with cardiovascular related illness and also hypertensive patients. Excluded from the study are non-hypertensive, active cigarette smokers, chronic alcohol consumers, obese patients, patients on steroids, patients with chronic renal diseases, and those who do not give their consent.

2.3 Informed Consent and Ethical Consideration

After explaining details of the study to both the patients and control subjects, informed consent was obtained from each of them before the commencement of the research. Ethical approval was also obtained from the Health Research Ethics Committee of the hospital.

2.4 Patients and Control Selection

A total of one hundred participants (consisting of 50 patients and 50 control subjects; both male and female inclusive) were obtained using Armitage technique for sample size determination at 5% probability level of significance [10]. The participants were randomly selected among patients and people attending medical outpatient clinic (MOP) of the hospital on account of hypertensive heart diseases and other cardiovascular related diseases. The controls were non-hypertensive, non-active cigarette smokers, and non-chronic alcohol consumers selected from relations that accompanied the patients to the clinic and among workers of the hospital. Patients and control subjects were matched for age and sex.

A structured questionnaire was self-administered on both the patients and the control subjects to obtain some demographic data such as age, sex, and social habits (cigarette smoking and alcohol intake). Anthropometric measurements (height and weight) were carried out, and the body mass index (BMI) was computed using the formula: BMI = Weight/Height^2 (kg/m^2).

Blood pressure was measured in both the patients and control subjects using mercurial sphygmomanometer while participants were sitting with their arm rested. The systolic and diastolic blood pressure was determined using the first and fifth phases of korotkof sound respectively. Hypertension was described as systolic and diastolic blood pressure greater than 130 mmHg and 80 mmHg respectively [1,11].

2.5 Collection and Storage of Samples

Ten milliliter (10 ml) of fasting venous blood (8-10 hr overnight fast) was aseptically collected from antecubital fossa vein of both the patients and controls. The blood sample was dispensed into sterile plain bottles and allowed to clot. The samples were then centrifuged at 3000 rpm for 5 minutes and serum separated into sterile plain bottles. Two mililiter (2 ml) of serum sample was used to analyse for C-reactive protein immediately after collection while the remaining serum sample was stored at -20°C until analysed (for total cholesterol, triglycerides, HDL-C, Zinc, Magnesium and Selenium).

Fasting plasma lipid profiles (triglycerides, total cholesterol, HDL-C) were assayed enzymatically with commercial test kits obtained from Randox Laboratories, Crumlin, England using standard methods [12,13,14]. LDLC was computed using the formula LDL-C = Total Cholesterol – 0.2(Triglycerides) – HDLC [12] while the atherogenic index (LDLC/HDL-C ratio) and coronary risk index (total cholesterol/HDL-C ratio) were calculated for all samples [15,16]. Serum C-reactive protein was also determined using sandwich immunodetection method [17]. Trace element (Zinc, Magnesium, and Selenium) were measured by colorimetric and atomic absorption spectrophotometric techniques using Thermo X-series 2 ICP-MS (Bremen, Germany).

2.6 Statistical Analysis

The obtained data was analysed using SPSS version 21. Continuous variables were expressed as Mean ± Standard Error of Mean (Mean ±SEM). The differences between mean values were compared using Independent student t-test. The level of statistical significance was set at $p < 0.05$.

3. RESULTS

Result on biophysical parameters shows that the mean age of the hypertensive patients and the control subjects were 56.12±11.4 and 59.8 ± 10.8 years respectively. There was no statistically significant difference ($p > 0.05$) in the mean age and height. A statistically significant increase in weight, BMI, SBP and DBP was observed among the hypertensive patients when compared with the control subjects (Table 1).

Results of biochemical parameters showed a statistically significant increase $p < 0.05$) in serum total cholesterol, LDLC, VLDLC, triglycerides, AI, CRI and CRP among the hypertensive patients when compared with the control subjects. Also, a statistically significant decrease ($p < 0.05$) in serum HDLC was observed among the hypertensive patients when compared with the control subjects.

Result of trace element showed that serum trace element (Zn, Mg, and Se) of the hypertensive patients was significantly reduced ($p < 0.05$) as compared to that of control subjects (Table 3).

Table 1 showed the biophysical parameters of the patients and controls. The level of statistical significance was considered at $p<0.05$. There was a significant difference in the weight, BMI, SBP and DBP amongst the patients and control groups. * Represent statistically significant difference at $p < 0.05$ when compared with the control.

BMI = Body mass index SBP = systolic blood pressure, DBP = diastolic blood pressure

Table 2 showed the biochemical parameters of the patients and controls. The level of statistical significance was considered at $p < 0.05$. There was a significant difference in the serum CRP, total cholesterol, HDLC, LDLC, VLDLC, triglyceride, AI, and CRI among the patients and control groups. * Represent statistically significant difference at $p < 0.05$ when compared with the control.

HDLC = High density lipoprotein, LDLC = low density lipoprotein, VLDLC = very low density lipoprotein, AI = atherogenic index, CRI = coronary risk index, and CRP = C-reactive protein

Table 1. Biophysical parameters of the hypertensive patients and control

Parameters	Case N = 50	Control N = 50	t-value	p-value
Age (Yr)	56.12 ± 11.4	59.8 ± 10.8	2.12	0.371
Weight (kg)	74.7±1.4	66.94±0.9	4.59	0.000
Height (m)	1.61±0.01	1.60±0.01	1.14	0.258
BMI (kg/m^2)	30.0±0.63	26.2±0.24	5.54	0.000
SBP (mmHg)	148.0±1.68	110.4±1.34	17.5	0.000
DBP (mmHg)	93.6±0.85	72.6±0.90	17.06	0.000

Table 2. Serum biochemical parameters of the hypertensive patients and control

Parameters	Case N = 50	Control N = 50	t-value	p-value
CRP (mg/L)	18.98±1.32*	5.96±0.15	9.83	0.000
Total Cholesterol (mg/dl)	234.8±4.33*	154,5±1.8	17.13	0.000
HDLC (mg/dl)	36.04±0.39	50.64±1.11*	12.39	0.000
LDLC (mg/dl)	175.21±4.02*	85.22±1.43	21.07	0.000
VLDLC (mg/dl)	23.58±0.47*	18.68±0.09	10.17	0.000
Triglyceride(mg/dl)	117.92±2.36*	93.38±0.47	10.17	0.000
AI	4.86±0.10*	1.73±0.05	27.89	0.000
CRI	6.52±0.11*	3.11±0.06	28.18	0.000

Table 3. Serum trace elements of the hypertensive patients and control

Parameters	Case N = 50	Control N = 50	t-value	p-value
Zn (µg/L)	68.66±1.04*	96.00±0.79	20.91	0.000
Mg (mg/L)	1.25±0.04*	2.12±0.03	17.48	0.000
Se (µg/L)	37.42±1.63*	62.10±1.39	11.52	0.000

Table 3 showed the serum trace element of the patients and controls. The level of statistical significance was considered at $p < 0.05$. There was a significant difference in the serum Zn, Mg, and Se amongst the patients and control groups. * Represent statistically significant difference at $p < 0.05$ when compared with the control.

Zn = Zinc, Mg = magnesium and Se = selenium.

4. DISCUSSION

The etiologic role of oxidative stress and micronutrient deficiency in cardiovascular diseases are interrelated and of great importance. While oxidative stress causes endothelial dysfunction, atherosclerosis, apoptosis, increase lipid peroxidation, necrosis, and CVD; micronutrient deficiency causes autoimmunity dysfunction, accumulation of autoimmune complexes, recruitment of inflammatory cells and finally CVD, thereby acting as antioxidants, immune modulators and anti-inflammatory agent [18].

A measure of acute or chronic inflammatory activities in CVD is C-reactive protein (CRP). CRP level is reduced by drugs (e.g. aspirin, clopidogrel, statins, celecoxib, niacin, thiazolidinedione, beta blockers, ACE inhibitors derivatives [11,19]; and regular exercise [20]. The observed increase in serum CRP in CVD patients is a consequence of the inflammatory events associated with the condition and suggests high cardiovascular mortality and morbidity risk. CRP production starts during early stage of the inflammatory process, it thus has much clinical relevance and high prognostic role in the event of CVD. CRP reduces nitric oxide (NO) production, induces LDL oxidation, and destabilizes fibrous layer of atheroma thereby causing thrombus formation in the endothelial wall [21].

Abnormalities in lipid profile (dyslipidaemia) characterised by hypercholesterolemia, hypertriglyceridemia; increased LDLC, VLDLC; and reduced HDLC are risk factors for CVD. Atherogenic (AI) and coronary risk indices (CRI) had been reported to be good predictor of future cardiovascular events [22,23] and thus could be of great importance in evaluating and screening for coronary artery disease [24]. These indices are arithmetic manipulations of serum triglycerides, total cholesterol, HDLC and LDLC. The serum values of both indices was noted to increase (AI= 4.8 and CRI = 6.5; normal values are <2.5 for AI and < 4.0 for CRI) [25] in patients with hypertensive heart disease and this constitutes a predictor of complications among hypertensive patients.

Micronutrients (Zn, Mg, and Se) had form integral part of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase. Abnormalities of these trace elements therefore affect their free radicals scavenging power. The degree of oxidative stress and inflammatory status in CVD can be indirectly measured by considering antioxidant status and inflammatory responses of individuals with the disease condition. Selenium and Zinc acts as a biological antioxidant by scavenging free radicals thereby decreasing lipid peroxidation and stabilizes the membrane [26]. Serum level of antioxidant microelements (zinc, magnesium, and selenium) was observed to be reduced in hypertensive heart disease. Similar reduction in serum Zn and Se had been reported in CVD [26,27]. Though conflicting results are available on serum magnesium in coronary heart disease (CHD) and the pathway is unclear but low serum magnesium has been implicated in cardiovascular mortality [28]. The observed hypomagnesaemia in this study also corroborates earlier finding of reduced serum magnesium level in cardiovascular diseases [28].

5. CONCLUSION

The result obtained from this study showed that CVD is associated with abnormalities in inflammatory markers, lipid profile, and micronutrients. The risk factors or markers of impending CVD in hypertensive patients demonstrated by these patients include obesity ($BMI \geq 30 kg/m^2$), high systolic and diastolic blood pressure, high serum marker of inflammatory involvement, dyslipidaemia, high atherogenic and coronary risk indices, and reduced antioxidant micronutrient level. Considering the observed reduction in serum Zn, Mg and Se in hypertensive heart disease, dietary supplementation with Mg, Zn and Se may be of great impact in improving the morbidity and mortality associated with CVD.

CONSENT AND ETHICAL APPROVAL

After explaining details of the study to both the patients and control subjects, informed consent was obtained from each of them before the

commencement of the research. Ethical approval was also obtained from the Health Research Ethics Committee of the hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. American Heart Association. Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. 2017.
2. Frangogiannis NG. The inflammatory response in myocardial injury, repair and remodelling. Nat Rev Cardiol. 2014;11(5):255–265.
3. Gracia KC, Llanas-Cornejo D, Husi H. CVD and oxidative stress- a review, J. Clin. Med. 2017;6.
4. Pankuweit S, Ruppert V, Maisch B. Inflammation in dilated cardiomyopathy. Herz. 2004;29(8):788–793.
5. Shahbaz AU, Sun Y, Bhattacharya SK et al. Fibrosis in hypertensive heart disease: Molecular pathways and cardioprotective strategies. Journal of Hypertension. 2010; 28(1):S25–S32.
6. Libby P, Ridker PM. Inflammation and atherothrombosis from population biology and bench research to clinical practice. Journal of the American College of Cardiology. 2006;48(9 Suppl A):33-46.
7. Ravi KU. Emerging risk biomarkers in cardiovascular diseases and disorders-a review. Journal of Lipids. 2015;50.
8. Chobanian AV, Bkris HR, Cushman WC et al. Seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure. Hypertension. 2003;42:1206-1252.
9. Welsh P, Woodward M, Rumly A, Lowe G. Associations of plasma pro-inflammatory cytokines, fibrinogen, viscosity and C-reactive protein with cardiovascular risk factors and social deprivation: The fourth Glasgow MONICA study. British Journal of Haematology. 2008;141(6):852–861.
10. Armitage P, Berry A. Statistical methods in medical research New York John Wiley and Son's Blackwell. 1987;160-163.
11. Mitrovic V, Klein HH, Krekel N et al. Influence of the angiotensin converting enzyme inhibitor ramipril on high sensitivity C-reactive protein (hs-CRP) in patients with documented atherosclerosis. Z Kardiol. 2005;94:336-342.
12. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499-502.
13. Schettler G, Nussel E. Colorimetric determination of cholesterol. Arh Med Soz. Med Prav. Med. 1975;10-55.
14. Nagele U, Hagele EO, Sauer G. Reagent for enzymatic determination of serum otal triglycerides with improved lypholytic efficiency. J. Clin. Chem. Clin. Biochem. 1984;22:165-174.
15. Abbot RD, Wilson PW, Karvel WB, et al. High density lipoprotein cholesterol, total cholesterol severing myocardial infarction. Atherosclerosis. 1988;8:207-211.
16. Alladi S, Shanmugasundaram KR. Induction of hypercholesterolemia by supplementing soy protein with acetate generating amino-acids. Nutrition Reports International. 1989;40(5):893-899.
17. Natalie K, Armin I, Gerlinde T, et al. Determination of C-reactive protein: Comparison of three high-sensitivity immunoassays. Clinical Chemistry. 2003;49(10):1691.
18. Christopher EE. Essential trace element and mineral deficiencies and cardiovascular diseases: Facts and controversies. International Journal of Nutrition and Food Sciences. 2017;6(2):53-64.
19. Reunanen A, Knekt P, Marniemi J, et al. Serum calcium, mag-nesium, copper and zinc and risk of cardiovascular death. Eur J ClinNutr. 1996;50:431–437.
20. Hamer M, Sabia S, Batty GD, et al. Physical activity and inflammatory markers over 10 years: Follow-up in men and women from the Whitehall II cohort study. Circulation. 2012;126:928-933.
21. Cardoso IL, Paulos AT. C reactive protein and cardiovascular disease. Int Arch Cardiovasc. 2017;1(1):11.
22. Kazemi T, Hajihosseini M, Moossavi M, Hemmati M, Ziaee M. Cardiovascular risk

factors and atherogenic indices in an iranian population: Birjand East of Iran. Clin Med Insights Cardiol. 2018;12:1-6.
23. Silva D, Lacerda AP. Proteína C reativa de alta sensibilidade como biomarcador de risco na doença coronária. Revista Portuguesa de Cardiologia. 2012;31:733-745.
24. Olooto WE, Olawale OO, Amballi AA, et al. Plasma lipid profile and transaminase activities as indicator of cardiovascular disorder and hepatocellular damage in type 2 diabetes mellitus patients. African Journal of Science and Nature. 2016;3:10-16.
25. Grover SA, Levington C, Panquest S. Identifying adults at low risk for significant hyperlipidemia: A validated clinical index. J. Clin. Epidemol. 1999;52:49-55.
26. Tabaru A, Hasani E, Bushi E. Serum trace element in patients with cardiovascular disease. Albanian Journal of Biomedical Sciences. 2017;1:8-13.
27. Jagtap Vanita R, Dhanashri GK. Evaluation of effect of trace elements and antioxidants levels in patient with ischaemic heart disease. International Journal of Biotechnology and Biochemistry. 2016;12(2):145-151.
28. Matias PJ, Azevedo A, Laranjinha I, Navarro D, Mendes M, Ferreira C, Amaral T, Jorge C, Aires I, Gil C, Ferreira A. Lower serum magnesium is associated with cardiovascular risk factors and mortality in haemodialysis patients. Blood Purif. 2014;38:244–252.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/23938