Significance of Serum Ferritin and Vitamin-D Level in Coronary Artery Disease Patients

E.Vasudevan*, B. Shanthi, Mary Chandrika Anton, Chaganti Sridevi, K. Sumathi and Nivethini

Department of Biochemistry, Sree Balaji Medical College and Hospital,
No.7 Works Road, Chrompet, Chennai, India.
*Corresponding Author E-mail: Vasukalai24@gmail.com

Coronary artery disease is one of the most common noncommunicable diseases that affects both men and women worldwide. Chronic inflammation and mineral nutrient deficiency, in addition to diet and sedentary lifestyle, contribute to this disease. The purpose of this study is to look at the relationship between serum ferritin, serum vitamin D levels, and serum lipid profile in patients with Coronary Artery Disease. The research was carried out at the Mahatma Gandhi Medical College and Research Institute in Puducherry. A standardised health questionnaire was distributed to study participants, which included 30 patients with Coronary Artery Disease (cases) and 30 healthy controls. It detailed current and previous medication use, hypertension, and coronary artery disease. Subjects were chosen based on their responses to study-related questions. For both cases and controls, means and standard deviations (SD) were computed. To determine the relationship between the parameters, ANOVA and Pearson's correlation were used, and it was used to find the statistical significance and correlation of Serum Ferritin, Serum Vitamin D, and Serum Lipid Profile among both groups. The serum ferritin levels among cases ($208.87 \pm 143.01 \mu$g/lit) were found to be high when compared to controls ($99.52 \pm 61.19 \mu$g/lit) with a significant p value of 0.0003. The Serum vitamin D value of cases (21.14 ± 12.9 ng/dl) was low when compared to controls (56.54 ± 18.88 ng/dl) with a significant p value of 0.0000. Serum LDL of cases (129.1 ± 26.91 mg/dl) were found to be higher than controls (105.1 ± 25.43 mg/dl). HDL of cases (33.83 ± 6.82mg/dl) was found to be lower than controls (49.53 ± 6.12 mg/dl). Altered lipid profile with low HDL-C, high LDL-C, and high LDL-C/HDL-C suggested an increased risk for CAD. Low vitamin D levels were also associated with a higher risk for CAD. According to this study, CAD patients had high serum ferritin levels, low serum vitamin D levels, and an altered lipid profile status.

Keywords: Coronary Artery Disease(CAD); Ferritin; HDL; LDL; Vitamin D.

Coronary disease appears to be prevalent among Indians of various geographical origins, religions, and languages. Cardiovascular disease is responsible for one-third of all deaths worldwide, with developing-country deaths accounting for two-thirds of all deaths.[1].

CAD was defined as an internal diameter reduction of more than 50% of at least one major coronary artery branch. Myocardial infarction usually occurs after a thrombotic occlusion of a previously narrowed coronary artery caused by atherosclerosis[2]. Inadequate oxygenation

caused by coronary atherosclerosis may cause transient disturbances in myocardium mechanical, biochemical, and electrical functions. Various studies in India have revealed a high prevalence of CAD, approaching 11% in the urban population and 7% in the rural population.[3]. Non-modifiable risk factors for CAD include age, gender, and family history, while modifiable risk factors include diabetes mellitus (DM), smoking, dyslipidemia, hypertension, and obesity.[4, 5].

Iron is required for many physiological processes, and iron overload has been linked to the progression of atherosclerosis. [6]. Excess iron can stimulate the progression of atherosclerotic lesions by catalysing the production of free radicals and promoting lipid peroxidation by lowering antioxidant levels in plasma; thus, it can be associated with the progression of atherosclerosis and increase the risk of ischemic cardiovascular events.[7]. Salonen et al phlebotomized men over the age of 50 to reduce their body iron stores and found that LDL susceptibility to ex vivo oxidation was significantly reduced. [8]. Serum ferritin is a 440 KD macromolecular protein, one-third of which is formed by iron. Serum ferritin levels are the most accurate way of measuring body iron stores. [9,10]. Total iron intake and serum iron concentrations were found to be inversely related to CHD incidence. [11,12]. Previous research indicates that vitamin D deficiency is linked to myocardial infarction, heart failure, diabetic cardiovascular disease, and peripheral vascular disease. Furthermore, recent research has found an inverse relationship between mean serum Vitamin D levels and blood pressure, diabetes, carotid atherosclerosis, microalbuminuria, stroke, and decreased renal function.[13,14,15]. Recent research suggests a link between vitamin D levels and cardiovascular disease, hypertension, heart failure, and fatal stroke. [16,17,18]. Several mechanisms could account for the link between vitamin D levels and cardiovascular disease. Vitamin D deficiency causes changes in the smooth muscle of the vascular wall, as well as inflammation and thrombosis, which could explain cardiovascular complications. [19,20,21]. By a mechanism other than macrophage foam-cell formation, oxidised LDL may contribute to atherogenesis and its sequelae. [22]. As a result, this study was carried out to determine whether there is a significant relationship between vitamin D and serum ferritin in coronary artery disease patients from the Puducherry population.

Aim

To investigate the significance of serum ferritin and serum vitamin D levels in patients with coronary artery disease.

MATERIALS AND METHODS

This analytical case-control study was conducted at the Mahatma Gandhi Medical College and Research Institute, Pillayarkuppam, Puducherry [MGMCRI], a tertiary health care institution under the jurisdiction of Sri Balaji Vidyapeeth University Puducherry, in collaboration with the Departments of General Medicine and Cardiology. Both the Institutional Research Committee and the Institutional Human Ethical Committee approved the project. A standardised health questionnaire was distributed to study participants, which included 30 Coronary Artery Disease patients (cases) and 30 healthy controls. It contained information on current and previous medication use, hypertension, and coronary artery disease. Subjects were chosen based on their responses to study-related questions.

Inclusion criteria

Patients with newly diagnosed coronary artery disease in the General Medicine and Cardiology Outpatient Departments at Mahatma Gandhi Medical College and Research Institute. Healthy volunteers who were employed in MGMC&RI [for controls]

Exclusion criteria

1. Patients who had Tuberculosis, Type-1 diabetes mellitus, Anemia, Chronic bone pain, Renal failure, and Endocrine disorders
2. Pregnant women
3. Patients who are already on calcium, vitamin-D, multivitamin, haematinics, steroid, and hormonal treatment

Sample collection

Under aseptic precautions, venous blood (5ml) was drawn from all the subjects after overnight fasting of 10-12hours. Serum was separated for analysis of serum Ferritin and serum vitamin-D levels

Study parameters

1. Serum Ferritin
2. Serum Iron

3. Hemoglobin % in whole blood
4. Serum Vitamin-D
5. Serum cholesterol
6. Serum Triglycerides
7. High density lipoprotein(HDL)
8. Low density Lipoprotein(LDL)

Statistical analysis

The mean and standard deviation (SD) of cases and controls were computed. The statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS) version 17 software. To determine the relationship between the parameters, ANOVA and Pearson's correlation were used, and it was used to find the statistical significance and correlation of serum ferritin and Vitamin D among the groups.P d" 0.05 was considered significant.

RESULTS

This study included 30 control and 30 Coronary artery disease [CAD] patients after appropriate screening. Table 1 shows the mean and standard deviation of biochemical parameters of controls and cases, as well as the age and gender distribution among 30 controls and 30 coronary artery disease [CAD] patients.Table 1: Mean And Standard Deviation Of Biochemical Parameters Of Cases and Controls

DISCUSSION

Because lipids are crucial in the pathogenesis of CAD, most research has focused on measuring lipid levels. Hyperlipidemia is now well recognised as one of the most important risk factors for CAD. Earlier research focused on individual lipids, but recent research in lipoprotein profile suggests that the association with serum lipids is not only coincidental, but that regression of an abnormal lipid profile may be therapeutic and prognostic.[23,24]

The current study attempted to investigate the relationship between serum ferritin levels and Vitamin D in CAD patients. The serum ferritin pattern in CAD patients and healthy controls was studied and the variations were compared. The mean total ferritin level of CAD patients (208.87±143.01) was significantly greater than that of controls (99.52±61.19) with p<0.0003. Iron has

Table 1. Mean And Standard Deviation Of Biochemical Parameters Of Cases and Controls

Parameters	Case	Control	t-test	p-value
Ferritin µg/lit	208.87±143.01	99.52 ± 61.19	3.8504	0.0003
Iron µg /dl	153.47 ± 52	110.57 ±23.22	4.1260	0.0001
Hb%	16.36 ± 1.69	14.77 ± 1.1	4.3076	0.0001
Vitamin D ng/dl	21.14 ± 12.9	56.54 ± 18.88	8.4776	0.0000
Cholesterol mg/dl	193.33 ± 59.2	154.53 ± 27.07	3.2645	0.0018
TAG mg/dl	126.73±44.89	99.77 ± 26.23	2.8410	0.0062
HDL mg/dl	33.83±6.82	49.53±6.12	0.717	0.479
LDL mg/dl	129.1 ± 26.91	105.1 ± 25.43	3.5508	0.0008

Table 2. Correlation Between Vitamin D and Serum ferritin

Correlation between Vitamin D & Ferritin	
Pearson Correlation	-0.18755
Sig. (2-tailed)	0.151299
N	60

**. Correlation is significant at the 0.01 level (2-tailed). * . Correlation is significant at the 0.05 level (2-tailed).The Pearson correlation between vitamin D and Serum Ferritin in CAD patients showed a negative correlation [r=30.387, P Value=0.15] was statistically significant.

been proposed as an atherogenic agent primarily due to its ability to initiate severe oxidative stress, which is supported by epidemiologic and experimental research. Ferritin levels were higher in CAD patients than in controls, according to our findings. As a result, elevated ferritin levels may be an additional risk factor for atheromatic plaque formation and subsequent CAD development.[25].

The current study found a decrease in vitamin –D [21.14±12.9ng/dl] than the control group i.e., [56.54±18.88 ng/dl]. However, the drop in vitamin D concentration was statistically

significant. (P<0.0001) when compared to the control group. Previous epidemiological research has linked vitamin D deficiency to myocardial infarction, heart failure, diabetic cardiovascular disease, and peripheral vascular disease. Individuals with vitamin D deficiency who were followed for 4 to 5 years had a 53% to 80% higher rate of cardiovascular complications such as death from myocardial infarction or heart failure. Furthermore, recent research has linked the average serum level of Vitamin D to hypertension, diabetes, and atherosclerosis. Vitamin D has a longer half-life and can more precisely show food intake, skin production, and period of deficiency, with levels ranging from 20-30ng/ml as insufficient and higher than 30ng/ml as desirable. Vitamin D receptors are found in the majority of body cells, including cardiomyocytes, vascular smooth muscles, and vessel endothelium26. The risk of cardiovascular disease was nearly four times higher in vitamin D deficient individuals compared to those with a normal level of vitamin D. 27 Vitamin D levels fluctuate, causing changes in the smooth muscles of the vascular wall and inflammation, which could explain cardiovascular complications. [28.] Vitamin D deficiency, possibly in conjunction with low calcium intake, has been linked to impaired fasting glucose and an increased risk of type 2 diabetes mellitus, both of which are risk factors for CAD.

CONCLUSION

To summarise, high ferritin levels in CAD patients may be an additional risk factor for atheromatous plaque formation and subsequent CAD development. Low vitamin D levels are also linked to an increased risk of CAD. Evidence suggests that maintaining normal serum ferritin and vitamin D levels in the body can help prevent CAD.

ACKNOWLEDGEMENT

Authors contribution

Mr. E.Vasudevan conducted this research under the supervision of Dr. B. Shanthi. The discussion was written by Dr. Mary Chandrika Anton, Dr. Chaganti Sridevi, and Dr. Sumathi. K, Miss Nivethini.

Ethical Standards

The study involved human participants following the ethical standards of the tertiary health care institution where the study was conducted.

Conflict of Interest

Declared none by the authors.

Funding Sources

REFERENCES

1. P.M.Mckeiuge, G.J. Miller, M.G. Marmot, Coronary heart disease in South Asia overseas: a review. Department of community medicine , University College & Middle sex school of medicine, England

2. Burke, Allen & Virmani, Renu. (2007). Pathophysiology of Acute Myocardial Infarction. The Medical clinics of North America. 91. 553-72; ix. 10.1016/j.mcna.2007.03.005.

3. Geevar Zachariah, S. Harikrishnan, M.N. Krishnan, P.P. Mohanan, G. Sanjay, K.Venugopal, K.R. Thankappan, Prevalence of coronary artery disease and coronary risk factors in Kerala, South India: A population survey – Design and methods, Indian Heart Journal, Volume 65, Issue 3, 2013,Pages 243-249, ISSN 0019-4832, https://doi.org/10.1016/j.ihj.2013.04.008.

4. Sowers JR. Obesity as a cardiovascular risk factor. Am J Med. 2003 Dec 8;115 Suppl 8A:37S-41S. doi: 10.1016/j.amjmed.2003.08.012. PMID: 14678864.

5. Hajar, Rachel. "Risk Factors for Coronary Artery Disease: Historical Perspectives." Heart views : the official journal of the Gulf Heart Association vol. 18,3 (2017): 109-114. doi:10.4103/HEARTVIEWS. HEARTVIEWS_106_17

6. Pourmoghaddas A, Sanei H, Garakyaraghi M, Esteki-Ghashghaei F, Gharaati M. The relation between body iron store and ferritin, and coronary artery disease. ARYA Atheroscler. 2014 Jan;10(1):32-6. PMID: 24963311; PMCID: PMC4063519.

7. Lobo, V et al. "Free radicals, antioxidants and functional foods: Impact on human health." Pharmacognosy reviews vol. 4,8 (2010): 118-26. doi:10.4103/0973-7847.70902

8.   Salonen JT, Karpela H, Nyyssonen K, Porkalla E, Tuomainen TP, Belcher JD,et al. Lowering of body iron stores by blood letting and oxidation resistence of serum lipoproteins: a randomised crossover trail in male smokers. J Intrn Med 1995; 237:161-8.

9.   Tuomainen TP, Punnonen K, Nyyssonen K, Salonen JT. Association between body iron stores and risk of acute myocardial infarction in men. Circulation 1998;97:1461-6

10.   Tuomainen TP, Diczfalusy U, Kaikkonen J, Nyyssonen K, Salonen JT. Serum ferritin concentration is associated with plasma levels of cholesterol oxidation products in man. Free Radic Biol Med 2003:35:922-8.

11.   Das De S, Krishna S, Jethwa A. Iron status and its association with coronary heart disease: systematic review and meta-analysis of prospective studies. Atherosclerosis. 2015 Feb;238(2):296-303.

12.   Hunnicutt J, He K, Xun P. Dietary iron intake and body iron stores are associated with risk of coronary heart disease in a meta-analysis of prospective cohort studies. J Nutr. 2014 Mar;144(3):359-66.

13.   M. C. Cure, E. Cure, S. Yuce, T. Yazici, I. Karakoyun, and H. Efe, "Mean platelet volume and vitamin D level," Annals ofLaboratory Medicine, vol. 34, no. 2, pp. 98–103, 2014

14.   Martins D, Wolf M, Pan D, Zadshir A, Tareen N, ThadhaniR,et al. Prevalence of cardiovascular risk factors and the serumlevels of 25-hydroxyvitamin D in the United States: data fromthe Third National Health and Nutrition Examination Survey.Arch Intern Med 2007; 167(11): 1159-65

15.   Kendrick J, Targher G, Smits G, Chonchol M. 25-Hydroxyvitamin D deficiency is independently associated withcardiovascular disease in the Third National Health and NutritionExamination Survey. Atherosclerosis 2009; 205(1): 255-60.

16.   Krause R, Buhring M, Hopfenmuller W, Holick MF, Sharma AM. Ultraviolet B and blood pressure. Lancet.1998;352:709–10. [PubMed].

17.   Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta celldysfunction. Am J ClinNutr. 2004;79:820–5. [PubMed]

18.   Cigolini M, Iagulli MP, Miconi V, Galiotto M, Lombardi S, Targher G. Serum 25-hydroxyvitamin D3concentrations and prevalence of cardiovascular disease among type 2 diabetic patients. Diabetes Care.2006;29:722–4. [PubMed]

19.   Targher G, Bertolini L, Padovani R, Zenari L, Scala L, Cigolini M, et al. Serum 25-hydroxyvitamin D3concentrations and carotid artery intima-media thickness among type 2 diabetic patients. Clin Endocrinol.2006;65:593–7. [PubMed]

20.   Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008; 117:503–11. [PMC free article] [PubMed]

21.   Nibbelink KA, Tishkoff DX, Hershey SD, Rahman A, Simpson RU, 1,25(OH)2-vitamin D3 actions on cell proliferation, size, gene expression, and receptor localisation in the HL-1 cardiac myocyte. J Steroid Biochem MolBiol Mar. 2007; 103:533-7 [PubMed]

22.   AhmadaliKhalili1 , Amir Ghorbanihaghjo2*, Nadereh Rashtchizadeh3 , Samad Gaffari1 Association between Serum Ferritin and Circulating Oxidized Low-density Lipoprotein Levels in Patients with Coronary Artery Disease

23.   J. H. Lee, R. Gadi, J. A. Spertus, F. Tang, and J. H. O'Keefe, "Prevalence of vitamin D deficiency in patients with acute myocardial infarction,"The American Journal of Cardiology, vol. 107, no. 11, pp. 1636–1638, 2011.

24.   Pourmoghaddas A, Sanei H, Garakyaraghi M, Esteki-Ghashghaei F, Gharaati M. The relation between body iron store and ferritin, and coronary artery disease. ARYA Atheroscler. 2014;10(1):32-36.

25.   de Godoy MF, Takakura IT, Machado RD, Grassi LV, Nogueira PR. Serum ferritin and obstructive coronary artery disease: angiographic correlation. Arq Bras Cardiol. 2007 Apr;88(4):430-433. English, Portuguese. doi: 10.1590/s0066-782x2007000400011. PMID: 17546273.

26.   Siadat, Zahra Dana et al. "Association of vitamin D deficiency and coronary artery disease with cardiovascular risk factors." Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences vol. 17,11 (2012): 1052-1055.

27.   Judd S, Tangpricha V. Vitamin D deficiency and risk for cardiovasculardisease. Circulation.2008; 117:503-11. (PMC free article) [PubMed]

28.   Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-Hydroxyvitamin D and Risk of Myocardial Infarction in Men: A Prospective Study. *Arch Intern Med.* 2008;168(11):1174–1180. doi:10.1001/archinte.168.11.1174