ORIGINAL RESEARCH PAPER

Biochemistry

"ROLE OF TRACE ELEMENTS AND LIPID PEROXIDATION LEVELS IN ISCHEMIC HEART DISEASE PATIENTS"

KEY WORDS: Ischemic heart disease, lipid profile, lipid peroxidation, Trace elements.

Dr Ramprasad N* Tutor, Department of Biochemistry, S S Institute of Medical Sciences & Research Centre, Davangere, Karnataka. *Corresponding Author

Dr Savita Rathore Professor, Department of Biochemistry, Mahaveer Institute of Medical Sciences, Bhopal, Madhya Pradesh.

ABSTRACT

Cardiovascular diseases (CVDs) share heterogeneous pathophysiologic mechanisms, one of which includes increased oxidative stress. It occurs as a result of increased level of lipid peroxidation, decreased in the trace elements levels in IHD. Trace elements are of great importance for a multitude of cellular functions at the biological, chemical, and molecular levels and it will protect the development of IHD. In the present study our aim was to investigate lipids, lipid peroxidation and trace elements like Selenium, Zinc, copper and magnesium in IHD patients. Study was carried out in 52 patients of IHD and 61 healthy controls were randomly selected for the study. Various biochemical parameters like lipids, Malondialdehyde which is a Lipid peroxidation product and trace elements were measured. Increased levels of Cholesterol, triglycerides, LDL, MDA, Cu ($p<0.001$), whereas decreased levels of HDL, Se, Zn and Mg ($p<0.001$) in IHD patients compared to controls. The main observation of the current study indicates that an imbalance between oxidant and antioxidant molecules in IHD patients. Therefore, assessing of these biochemical parameters and trace elements may be useful in diagnosis of patients with IHD.

INTRODUCTION

Heart disease is one of the major health problems of developed as well as developing countries of the world. IHD is now the leading cause of death worldwide, responsible for more than 10 million deaths annually worldwide. The burden of IHDs will continue to grow in India due to continuous exposure of so many risk factors and addition to the traditional lipid panel and decreased activities of antioxidant enzymes and trace elements have been documented as independent risk factors for the development of IHD [1].

Oxidative stress is defined as the interruption of balance between oxidants and reductants within the body due to the excess production of peroxides, super oxides and free radicals. The progressive of IHD is closely associated with risk factors such as hypertension, obesity, smoking, and dyslipidemia. A lot of oxygenated compounds, particularly aldehydes such as Malondialdehyde (MDA) are produced during the attack of free radicals to membranes, lipoprotein and polyunsaturated fatty acids. Thus lipid peroxidation in the blood provides a useful information for the prognosis of the IHD patients. This imbalance will cause damage to cell membrane, cellular components and tissues in the body this will lead to oxidative stress and formation of free radicals as well as decreased capacity of antioxidant enzymes and trace element levels [2].

In recent years, awareness has created on the very important role of trace elements that play either beneficial or harmful in human health and disease. Trace elements are of great importance for a multitude of cellular functions at the biological, chemical, and molecular levels. They make essential biochemical reactions possible by acting as cofactors for enzymes and by serving to stabilize the three-dimensional structures of enzymes and proteins [3]. Several evidences shown that increasing number of studies point to the central role that trace elements play in the pathophysiology of symptom development and progression of the disease. Selenium (Se) is an essential trace element in the body. The Se-containing protein glutathione peroxidase exhibits central roles in regulating the physiological antioxidant status and plays additional roles in the heart diseases. Glutathione peroxidase activity could be related to the generation of toxic lipid peroxides, leading to endothelial dysfunction and arterial stiffness. Zinc (Zn) is one the essential trace elements that there are more than 300 enzymes that require Zn for their catalytic action which acts as a central role in the nucleic acids and protein synthesis. Copper (Cu) functions as a cofactor for many enzymes and is involved in neurotransmitter synthesis and energy metabolism. The Cu-metalloenzymes, multiple functions in the hematologic, vascular, antioxidant and neurologic pathologies have been described. Deficiencies or excess of Cu will linked to increased risk and severity of atherosclerosis. Magnesium (Mg) serves as a cofactor in approximately three hundred enzyme systems, important supplementation nutrient for body functions and it improves endothelial dysfunction in IHD patients [4].

Keeping in mind the above facts, hence in the present study was planned and conducted to evaluate the role of lipids, lipid peroxidation as a marker and measured as a MDA and important trace elements like Se, Zn, Cu and Mg were measured in IHD patients and compared with healthy normal controls.

METHODS AND MATERIALS

Study Design And Area

As randomized study was case controlled in design. The patients were included in the study were all admitted to in the Intensive Cardiac Care Unit (ICCU) / Intensive Care Unit (ICU) and some are admitted in medicine unit or attending OPD block of the Index medical college hospital & research centre Malwanchal University Indore. The study carried out 2024 to 2025.

Study Population

Consecutive 52 IHDpatients of both the sexes and 61 healthy age matched controls will be selected for the study. The criteria for the diagnosis of IHD was made on the basis of clinical history, history of myocardial infarction, 12 leads electrocardiogram (ECG), Echocardiography and Coronary angiography findings. Those patients whose body mass index (BMI) was > 25 were considered as obese. Subjects suffering from diabetes mellitus, renal disease, hepatic disease, strokes, chronic / acute inflammatory illness, pregnancy and lactating mothers were excluded from the study. None of the subjects were on antioxidant supplementation or lipid lowering drugs.

Collection Of Blood Samples & Biochemical Analysis

12 hours overnight fast. 5 ml of plain blood was collected from each subject, the serum was carefully separated by centrifugation at 3500 RPM for 15 minutes. The lipid profile was done by fully automated analyzer (Beckman AU 480 fully

autoanalyser, USA). The concentration of serum total cholesterol was estimated by CHOD- PAP method [5], Triglycerides level was estimated by GPO tinder method [6], while HDL- C estimation was done by phosphotungestic method [7], LDL- C levels by direct enzymatic methods [8]. The lipid peroxidation marker serum MDA levels were measured by thiobarbituric acid (TBA) method [9]. Trace elements like serum Se, Zn, Cu, and Mg were determined by flame atomic absorption spectrophotometer with deuterium background correction (Perkin – Elmer model 5000) [10].

Statistical Analysis:

The statistical analysis of data was performed by using SPSS version 24.0 software. All values are expressed as mean ±SD. For the comparison of values between the groups, student t-test was used. The statistical significance was considered at a 'p' value of < 0.05.

RESULTS:

The clinical features of IHD patients and controls are presented in table 1. In the present study number of BMI, smokers, and hypertensive were more in the IHD patients compared controls. Biochemical parameters like serum TC, TG, LDL and MDA levels were significantly increased whereas HDL levels decreased in IHD patients when compared to controls ($p<0.001$) as shown in table 2. Whereas serum trace elements like Se, Zn and Mg levels were significantly decreased in IHD patients ($p<0.001$). But serum Cu levels showed a significant elevation in IHD group when compared to control group ($p<0.001$) respectively.

Table 1 The Demographic Features Of Controls And IHD Patients

Particulars	Controls (n= 61) Mean ± SD	IHD (n= 52) Mean ± SD
Age (yrs)	45.8 ± 6.4	54.6 ± 8.9*
Sex (Male/ Female)	31 / 30	29 / 23*
BMI (Kg/m^2)	22.3 ± 3.4	27.4 ± 2.1*
HTN (%)	9 %	44 %*
Smokers (%)	10 %	49 %*
Family history of IHD (%)	3 %	40 %*

* P <0.001, Highly significantly compared to controls.
IHD= Ischemic heart disease,
BMI= Body mass Index,
HTN= Hypertension.

Table: 2 Various Biochemical Parameters Of The Study Subjects

Parameters	Controls (n= 61) Mean ± SD	IHD (n= 52) Mean ± SD
T. Cholesterol (mg/ dl)	140.3 ± 14.1	220.3 ± 10.4*
Triglycerides (mg/ dl)	98.2 ± 10.1	188.2 ± 10.1*
HDL- C (mg/ dl)	49.4 ± 3.5	36.4 ± 3.6*
LDL –C (mg/ dl)	84.1 ± 10.4	181.1 ± 12.0*
MDA (nmoles/ml)	3.4 ± 0.4	6.1 ± 1.1*

*P<0.001, Highly statistically significantly vs controls.
HDL-C= High density lipoprotein cholesterol,
LDL-C= Low density lipoprotein cholesterol,
MDA= Malondialdehyde.

Table 3 Serum Trace Elements Levels In Patients And Controls.

Parameters	Controls (n= 61) Mean ± SD	IHD (n= 52) Mean ± SD
Selenium (µg/ dl)	92.3 ± 8.7	69.9 ± 10.1*
Zinc (µg/ dl)	102.3 ± 6.7	88.9 ± 8.1*
Copper (µg/ dl)	78.4 ± 11.6	121.9 ± 9.2*
Magnesium (mg/ dl)	2.63 ± 1.1	1.70 ± 1.2*

*P<0.001, highly statistically significantly compared to controls.

DISCUSSION:

Cardiovascular disease is the leading cause of death worldwide including India. The relation between heart failure and vascular disease is also marked by oxidative stress, caused by ischemia, left ventricular (LV) dysfunction. The prevalence of IHD occurs by so many risk factors. Tobacco smoking is not only dangerous, but also a strong risk factors for the development of IHD patients. In our data shows number of smokers are high in IHD patients compared to controls same findings was found by several authors [2, 11]. Like other studies; nowadays, HTN, overweight and obesity are recognized as a rising pandemic in cardiac patients. In our study also, HTN and obesity was found significantly increased levels in IHD patients [12].

Hypercholesterolemia and triglyceridemia are independent risk factors that alone or together can accelerate the development of IHD and progression of atherosclerotic lesions. HDL is regarded as one of the most important protective factors against arteriosclerosis. HDL's protective function has been attributed to its active participation in the reverse transport of cholesterol. Numerous cohort studies and clinical trials have confirmed the association between a low HDL and an increased risk of IHD. Whereas LDL is a bad cholesterol it undergoes oxidation by oxidative stress and generation of free radicals can result in oxidized LDL that can lead to pathogenesis of cardiac disease. Several cohort studies revealed that lipid profile is a potent independent risk factors for IHD [13]. In the present study also we observed increased cholesterol, triglycerides, LDL and reduced HDL cholesterol in IHD patients. Lipid peroxidation is a metabolic process that causes oxidative deterioration of lipids by reactive oxygen species. This process can degrade the lipids within the cell membrane leading to cell damage and cell death. MDA is a natural product of LPO it plays an important role in ageing, diabetes and atherosclerosis. In this study we measured the MDA levels as a product of LPO. Several authors have reported that increased levels of MDA in IHD patients [2]. In our study also we observed significant increased levels of MDA in IHD patient compared to controls.

Trace elements exhibit a greater number of physiological and biochemical activities in a body. They take part in vital functions in the body, which include growth and development, some metabolic function, and tissue repair. The connection between trace elements and human healthiness has been infrequently investigated especially in reference to cardiovascular diseases. Selenium (Se) Selenium, a constituent of selenoproteins as selenocysteine, has important antioxidant properties. Selenoproteins with antioxidant functions include glutathione peroxidases, which reduce hydrogen peroxide, lipid and phospholipid hydroperoxides. In our previous studies [2] we observed deceased levels of Se in IHD patients. In the present study there is a significant decreased levels of Se in IHD patients compare to controls. Moreover, it boosts the immune system by increasing the activity of white blood cells and prevents premature aging, degenerative and inflammatory diseases, and CVD.

Zinc (Zn) is an essential trace element which acts as antioxidant and anti-inflammatory agent that support the heart function and help to prevent atherosclerosis. Several experimental models clinically and statistically support that deficiency of Zn and Cu may have some effect on pathogenesis of CVD. We observed decreased levels of Zn in IHD patients when compared to controls. Similar studies are observed that deceased Zn activities in IHD patients [14]. Zn is critical for maintaining myocardial structure and modulating oxidative stress within cardiomyocytes. Copper (Cu) is a component of antioxidant enzymes, such as Superoxide

Dismutase (SOD) and ceruloplasmin, which protect the heart from oxidative damage. But deposition of Cu can cause oxidative stress and damage to cardiovascular systems which may cause risk of CAD. In our study, we observed significant increased levels of Cu in IHD patients. Similar observations were made by several authors [11]. Magnesium (Mg) is essential for maintaining proper body function. It is vital for body's immune system, CVD and musculoskeletal systems. Deficiency of this element will lead to HTN, diabetes, kidney disease and CVDs. Several epidemiological studies have shown that decreased levels of Mg in IHD patients [15]. Similarly In our study also we observed significant deceased levels of Mg in IHD patients compared to control values. Lower Mg levels may influence numerous regulatory functions of Mg^{2+} ions in hormonal, cardiovascular and immune systems; depletion of Mg in plasma induces higher susceptibility of the lipoproteins to the oxidative stress, and a possible pro-oxidant effect. It prevents vascular calcification and endothelial dysfunction, which are key factors in atherosclerosis.

This study has some limitations. First of all, it is case controlled study in small number of patients. Further epidemiological and prospective large number of studies to confirm these findings.

CONCLUSION:

In conclusion, increased levels of lipid peroxidation and role of trace element levels in the body and they may contribute to the increased susceptibility for the development of IHD. Preclinical and clinical evidence even suggests that some edible fruits can block lipid peroxidation to enhance antioxidant enzyme activities under conditions of metabolic syndrome and Heart diseases. However, as previously discussed, although supplementation with antioxidants and trace elements may be a promising strategy to alleviate oxidative stress and improve metabolic functions. The combination of diet, exercise and medication are the important for the maintenance of body weight and secondary preventive measures like control of hyperglycemia may be suggested to the IHD patients to protect them from further cardiovascular detoriation.

REFERENCES:

1. Barry Halliwell, John M.C. Gutteridege and Carrolle E. Cross. Free radicals, antioxidants, and human disease: Where are we now?. J Lab Clin Med. 2024: 119:6:598 -- 620.
2. Ramprasad N. Study of trace elements and malondialdehyde levels in cardiovascular disease patients. IJARBS. 2014: 1:9:25- 32.
3. Strong JP: Natural history and risk factors for earl y human atherogenesis. Clin Chem. 1995; 41: 138-143.
4. Wechselberger C, Barbarra M, David B. The role of trace elements in cardiovascular diseases. Toxics. 2023; 23: 11: 12: 956 – 971.
5. Richmond W. Preparation and properties of cholesterol oxides from nocardia sp. and its application to the enzymatic assay of total cholesterol in serum. Clin Chem. 1973; 19: 1350-1356.
6. McGowan MW, Artiss JD, Strandbergh DR, Zak B. A peroxidase-coupled method for the colorimetric determination of serum triglycerides. Clin Chem. 1983; 29: 538-542.
7. Rifal N, Warnick GR editors. Laboratory measurement of lipids, lipoproteins and apolipoproteins. Washington DC: American Association of Clinical Chemistry. 1994; (AACC) press; 21 – 42.
8. Pissani T, Gebski CP, Leary ET, et al. Accurate direct determination of low density lipoprotein cholesterol using an immune separation reagent and enzymatic cholesterol assay. Arch Pathol Lab Med. 1995; 119: 1127- 1135.
9. Yagi K. Lipid peroxides and Human disease. Chem Phy lipids 1987; 45: 337-351.
10. Elmer P and Conn N. Analytical methods for atomic absorption spectrophotometry. 1975; London, Oxford press. P 273-290.
11. Jan P. W Houtman. Trace elements and cardiovascular diseases. Journal of Cardiovascular risk. 1996; 3: 1: 18 –24.
12. Kharb S, Singh GP. Effect of smoking on lipid profile, lipid peroxidation and antioxidant status in normal subjects and in patients during and after acute myocardial infarction. Clin Chem Acta. 2000; 302, 213-219.
13. Kaviarasan K, Arjuna MM, Pugalendi KV. Lipid profile, oxidant- antioxidant status and glycoprotein components in hyperlipidemic patients with / without diabetes. Clin Chim Acta. 2005; 362, 49-56.
14. Wen Y, Qian X, Jia. Correlation of serum lipids, lipoproteins, lipid peroxide products and metals with coronary heart disease. Chin Med J. 1993; 106: 167-170.
15. Forrest H Nielsen. The role of dietary magnesium in cardiovascular disease. Nutrients. 2024; 16: 4223://doi.org/10.3390/nu16234223.