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Oxidative stress in Left bundle branch block patients determined by serum malondialdehyde and ceruloplasmin levels

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Abstract

Introduction Left bundle branch block (LBBB) can occur when there is a delay in or a block of conduction at several locations in the intraventricular conduction system. These locations include the main left bundle branch or in each of its two major fascicles; the distal conduction system of the left ventricle; the fibers of the bundle of His, which develop into the main left bundle branch; or the ventricular myocardium. Aim Serum levels of malondialdehyde (MDA) and ceruloplasmin (Cp) will be evaluated to understand more about the process of oxidative stress and its relationship to LBBB. Material and methods: Seventy patients with LBBB were compared to a control group of seventy healthy individuals. Groups were compared based on their MDA and Cp levels. Results Patients with LBBB had significantly higher MDA levels than healthy controls ($p < 0.05$). Furthermore, the levels of MDA in the study group were significantly higher than those in the control group ($p < 0.0001$). In addition, the LBBB group had a significantly greater concentration of ceruloplasmin ($p < 0.0001$). Conclusions High amounts of MDA were found in patients with LBBB, which may contribute to haematological degradation when exposed to free radicals. These findings support the idea that oxidative stress may play a role in the etiopathogenesis of LBBB by showing the presence of anbalance in the oxidant-antioxidant system.

Key words

Left Bundle Branch block, conduction system, oxidative stress, antioxidants.

Left bundle branch block (LBBB) can occur when there is a delay in or a block of conduction at several locations in the intraventricular conduction system [1]. These locations include the main left bundle branch or in each of its two major fascicles; the distal conduction system of the left ventricle; the fibers of the bundle of His, which develop into the main left bundle branch; or the ventricular myocardium[2]. The left bundle branch block can also occur when His bundle is aberrant. Although people with severe cardiac disease are more likely to have LBBB, the condition has also been observed in those with no outward signs of sickness. This is because hypertrophy, strain, and myocardial damage are all potential causes of LBBB [3]. High blood pressure, aortic valve disease, cardiomyopathy, and left bundle branch block are all associated with an increased risk of cardiovascular morbidity and mortality. In addition, LBBB is a common sign of coronary heart disease (typically with decreased left ventricular function)[4].

Although patients with previous heart disease have a higher risk of developing LBBB, as many as 12 percent of those diagnosed with LBBB had no apparent heart disease [5]. This is because Malondialdehyde (MDA) increases in the body due to lipid peroxidation, which is triggered by the hypoxia that causes ischemia [6]. Byproducts of arachidonic acid and polyunsaturated

fatty acid metabolism produce MDA, a highly reactive molecule. DNA, proteins, and lipoproteins are just a few examples of substances where MDA can rapidly react with functional groups. From polyunsaturated fatty acid peroxides, MDA is formed through further reactions. For example, in most biological samples, MDA is generated when lipids are peroxidized[7].

Oxidative stress has been shown to play a role in the aetiology of cardiovascular diseases. Several studies have related Atherosclerosis and ischemia-reperfusion damage to oxidative stress over the past 20 years [8]. Oxidative stress may have a role in the aetiology of cardiovascular problems rather than only being a consequence of these diseases. For example, myocardial perfusion is impaired when individuals with coronary heart disease (CHD) develop coronary artery blockage [9].Atherosclerosis is the leading cause of blockages because it causes the lumen of the blood vessel to narrow. Because of the reduced blood flow, the area receives less oxygen and fewer metabolic precursors [10]. Ischemic illness, or low-flow ischemia, is a common name for this condition. But if the vascular lumen closes because of vascular spasms or a blood clot in the coronary artery, no-flow ischemia may occur. Ischemia-reperfusion injury may be characterized primarily by the formation of chronic pathological alterations in the heart[11]. In cardiomyocytes, oxidative stress manifests primarily as the oxidation of phospholipid membranes. Lipid peroxidation products (LPPs) are created when electrophilic ROS and reactive nitrogen species react with lipids. The mitochondrial membrane phospholipid bilayer is the primary target of lipid peroxidation [12]. In the presence of coronary heart disease (CHD), an imbalance develops between the production of reactive oxygen species (ROS) and the availability of endogenous antioxidants, significantly disrupting the heart's redox status. Exogenous antioxidants, on the one hand, can protect the heart by decreasing the risk of oxidative damage to cells and boosting the availability of endogenous antioxidants [9].

Epidemiological studies mostly support the correlation between ceruloplasmin expression and the onset of HF in humans. Furthermore, evidence from the Atherosclerosis Risk in Communities study confirmed ceruloplasmin's prognostic usefulness for the emergence of HF. Another study found that patients with greater Cp concentrations had a higher incidence of HF throughout a 22-year follow-up period [13]. Patients hospitalized with ST-segment elevation myocardial infarction with greater ceruloplasmin levels had a higher chance of developing acute HF and an elevated LV ejection percent [14]. In addition to myeloperoxidase, high-sensitivity C-reactive protein (hs-CRP), and leukocyte counts, ceruloplasmin has been related to an elevated risk of cardiovascular disease (CVD) as an acute-phase reactant [15]. This supports the hypothesis that ceruloplasmin contributes to the onset of cardiovascular disease.

Aim

This study aims to investigate oxidative stress in LBBB patients and healthy controls by comparing serum levels of malondialdehyde and ceruloplasmin.

Material and methods

This is a case-control study which comprised of both (70) healthy people to serve as a control group (36 males and 34 females), as well as (70) patients diagnosed with left bundle branch block (31 males and 39 females) serves as cases, all of whom had completed health care at AL-Rabeea Heart Center. This study was carried out in Nasiriyah, in southern Iraq. All cases were undergone Echo study by cardiologist. The groups were not different significantly from one another in regards to age or BMI. Seventy patients with LBBB (39 women, 31 men, mean age 65.63 (range 35-80 years) and 70 healthy controls (36 men, 34 women, mean age 44.53 (range 30 to 72 years) participated in the study. The control group consisted of everyone who were previously healthy show no signs of LBBB on ECG. Authorization to conduct this research was granted by both Al-Hussein Teaching Hospital and AL-Rabeea Private Hospital. Every patient and member of their family received support. Before any testing, they either signed an informed consent form or gave verbal approval.The ceruloplasmin concentration was evaluated using a colorimetric assay (Roche, Cobas e 311). While, the human enzyme-linked immunosorbent test kits (Human malondialdehyde kit) from SunLong Biotech Co., LTD with product catalogue number: SL1135Hu China were used to measure serum malondialdehyde concentrations. The standard curve (figure -1) was used to determine the MDA concentration.

Sample collection

After collecting 5 ml of blood samples and allowing the clots to form in the plain tubes, centrifugation was carried out on the blood. Hemolysis of the blood samples needed to be avoided in all circumstances. After separating it, the clear serum was used in tests to determine the serum ceruloplasmin and MDA levels.

Statistical Evaluation

The SPSS program (Version 26) was used to analyze the results, and the values were presented as

mean, standard deviation, tables, graphs, and other items, Microsoft Word and Microsoft Excel were utilized. The comparisons were two-tailed, with p-values of 0.05 or below considered significant.

Results

table 1 shows the levels of MDA and Ceruloplasmin in serum samples presented in Mean±SD, indicted that each of oxidative stress (MDA) and antioxidants in sera of LBBB patients were significantly higher than that of healthy control ($p < 0.0001$). The correlation between oxidant marker (MDA) and antioxidants (Ceruloplasmin) in the patients with LBBB and healthy control group as in Table 2, figure-2 and figure - 3.

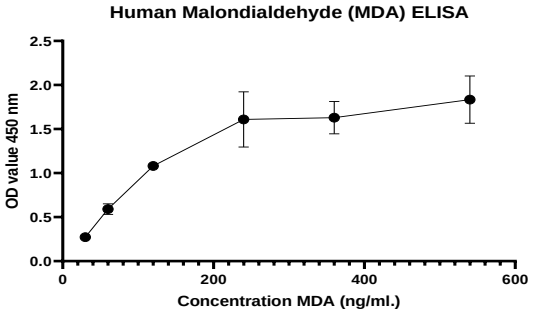

Figure-1: Standard Curve of Human Malondialdehyde (MDA)

Table-1: The levels of oxidant marker (MDA) and antioxidants (Ceruloplasmin) in serum samples of LBBB patients and healthy control groups.

Parameter	LBBB patients	Healthy control	P-value
MDA (ng/ml.)	220.981±94.636	51.401±114.899	<0.0001
Ceruloplasmin (mg/dl)	32.829±8.236	22.072±5.521	<0.0001

Table 2: The correlation between oxidant marker (MDA) and antioxidants (Ceruloplasmin).

Groups			Ceruloplasmin
LBBB patients	MDA	r	0.4360
		p-value	0.0002
Healthy control	MDA	r	- 0.1223
		p-value	0.313

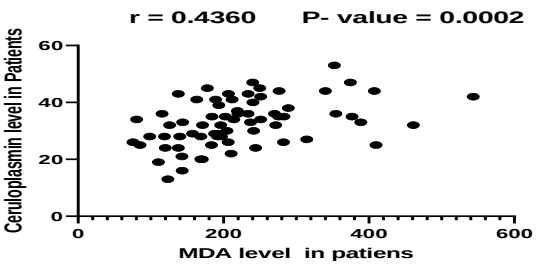

Figure-2: Correlation MDA vs Ceruloplasmin among patients group

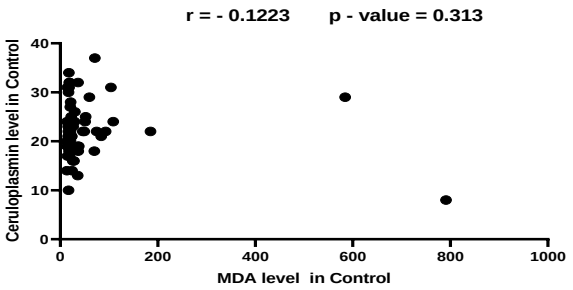

Figure-3: Correlation MDA vs Ceruloplasmin among control group

Discussion

Malondialdehyde (MDA) and ceruloplasmin (Cp) concentrations were examined in the present study. Seventy LBBB patients and seventy healthy-looking controls had their blood drawn for this study.Ischemia-reperfusion damage, atherogenesis, and cardiac remodelling have been related to oxidative stress for many years, and all are biomarkers of cardiovascular disease. Indicators of oxidative stress may be utilized in modifying risk assessments and therapeutic plans for patients suspected of having a myocardial infarction (MI) or coronary artery disease.[16]. Many studies have associated oxidative stress with heart disease[17][6]. Several studies suggest that elevated levels of oxidative stress play a significant role in the development of cardiovascular disease.[17].

Patients with left bundle branch block had their antioxidant defense system assessed by measuring their levels of MDA and Ceruloplasmin. Malondialdehyde is a byproduct of a radical chain reaction that occurs during the breakdown of polyunsaturated fatty acids in cell membranes. More malondialdehyde (MDA) is produced when more free radicals are in the body.[17][6]. Malondialdehyde is a common and extremely reliable indicator of oxidative stress in medical conditions. There is evidence that plasma MDA levels were higher in patients with LBBB compared to the control group. Malondialdehyde is measured to assess the degree that free radicals are damaging plasma membranes and is used as a marker of oxidative stress. Patients with cardiovascular diseases have been shown to have abnormally high levels of lipid peroxidation products, indicating an oxidative process imbalance. [18]. Increased oxidative stress and changes in ion channels have been associated with the development of plaques in the coronary arteries [19]. As a result, the current analysis supports prior findings. Furthermore, it indicates that lipid peroxidation may play a role in the pathophysiology of left bundle branch block due to the significantly

elevated levels of blood MDA observed. Human malondialdehyde (MDA) concentrations, an indication of oxidative stress and antioxidants (ceruloplasmin), were considerably greater in the patient's group ($p< 0.0001$), as shown in Tables (1) and (2). Our results agree with Pablo Castro et al. 2005 [20] and Aura Mongirdiene et al. 2023 [21], who also discovered significantly increased MDA levels in patients with chronic heart failure. Furthermore, elevated serum MDA levels have been connected to a greater incidence of AMI and coronary artery disease [22]. Ceruloplasmin is an acute-phase protein that is a reliable diagnostic indicator of conditions involving disruption of system homeostasis. Although ceruloplasmin levels increase in response to acute inflammation and during pregnancy, it is widely employed as an acute-phase reactant in clinical practice. [23]. The activity of this enzyme is mostly responsible for the high concentration of copper oxidase in the circulatory system. At the same time, it supports protecting the body from harm by influencing the body's anti-oxidant capacities, making them more effective against free radical activities. Ceruloplasmin (Cp) is a peroxidase that breaks down various chemicals. The various catalytic activities, including glutathione peroxidase action, have also been demonstrated.[24][25]. Table (1) illustrates the statistical analysis results showing that ceruloplasmin levels in serum samples of LBBB patients when compared to the healthy controls (32.829 ± 8.236 mg/dl vs 22.072 ± 5.521) were statistically highly significant ($p< 0.0001$).

Consistent with our results, May Khalil Ismail et al. 2018 [26] found individuals with a wide range of cardiovascular disorders had elevated blood levels of ceruloplasmin, which may be connected to ceruloplasmin's function as an acute-phase reactant. Copper and ceruloplasmin may be additional risk factors for cardiovascular disease [27]. An imbalance between the oxidants and the antioxidants produced by the body, as shown by an elevated concentration of ceruloplasmin in cases of LBBB. In addition, as shown in Table (2) and Figure (2), a positive association existed between plasma MDA and Cp concentrations. This relationship, identified among the patients who participated in the study, may be additional evidence of the disturbance of the oxidative-antioxidative balance and the role of oxidant stress in the pathogenesis of LBBB. A similar investigation was conducted by Keith et al., on patients with cardiac conditions with various degrees of participation.In this study, indicators of oxidative damage, such as malondialdehyde, along with protective antioxidants, such as the amount of glutathione levels, indicated an obvious connection between these markers and the severity of the condition[28]

Conclusions

Patients with LBBB had significantly higher levels of MDA, which could lead to haematological degradation when combined with free radicals. These results demonstrate an imbalance between oxidants and antioxidants, supporting the hypothesis that oxidative stress contributes to the etiopathogenesis of LBBB.

References

J. W. Hurst, “Left Bundle-branch Block—Pathophysiology, Prognosis, and Clinical Management,” Clin. Cardiol., vol. 30, no. 10, p. 535, 2007.

M. H. Nikoo, A. Aslani, and M. V. Jorat, “LBBB: state-of-the-art criteria,” 2013.

A. C. Jain and M. C. Mehta, “Etiologies of left bundle branch block and correlations with hemodynamic and angiographic findings,” Am. J. Cardiol., vol. 91, no. 11, pp. 1375–1378, 2003.

“The Relationship Between Left Bundle Branch Block And The Presence Of Coronary Artery Disease And Left Ventricular Dysfunction 1 Asaad Hassan Kata Alnwessry, 2 Kassim M Al-doori,” 2005.

D. Gurzău et al., “Major left bundle branch block and coronary heart disease—are there any differences between the sexes?,” J. Clin. Med., 2021, doi: 10.3390/jcm10112284.

S. Gaweł, M. Wardas, E. Niedworok, and P. Wardas, “Malondialdehyde (MDA) as a lipid peroxidation marker,” Wiad. Lek. (Warsaw, Pol. 1960), vol. 57, no. 9–10, pp. 453–455, 2004.

A. Ayala, M. F. Muñoz, and S. Argüelles, “Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal,” Oxid. Med. Cell. Longev., vol. 2014, 2014.

A. Kibel, A. M. Lukinac, V. Dambic, I. Juric, and K. Selthofer-Relatic, “Oxidative stress in ischemic heart disease,” Oxid. Med. Cell. Longev., vol. 2020, 2020.

T. Senoner and W. Dichtl, “Oxidative stress in cardiovascular diseases: Still a therapeutic target?,” Nutrients. 2019, doi: 10.3390/nu11092090.

R. Ross, “The pathogenesis of atherosclerosis—an update,” N. Engl. J. Med., vol. 314, no. 8, pp. 488–500, 1986.

C. N. Bairey Merz et al., “Ischemia and no obstructive coronary artery disease (INOCA) developing evidence-based therapies and research agenda for the next decade,” Circulation, vol. 135, no. 11, pp. 1075–1092, 2017.

W. Wang and P. M. Kang, “Oxidative stress and antioxidant treatments in cardiovascular diseases,” Antioxidants. 2020, doi: 10.3390/antiox9121292.

A. P. Arenas de Larriva, L. Limia-Pérez, J. F. Alcalá-Díaz, A. Alonso, J. López-Miranda, and J. Delgado-Lista, “Ceruloplasmin and coronary heart disease—a systematic review,” Nutrients, vol. 12, no. 10, p. 3219, 2020.

M. Hammadah, Y. Fan, Y. Wu, S. L. Hazen, and W. H. W. Tang, “Prognostic value of elevated serum ceruloplasmin levels in patients with heart failure,” J. Card. Fail., vol. 20, no. 12, pp. 946–952, 2014.

M. S. Ahmed, A. B. Jadhav, A. Hassan, and Q. H. Meng, “Acute phase reactants as novel predictors of cardiovascular disease,” Int. Sch. Res. Not., vol. 2012, 2012.

T. Vichova and Z. Motovska, “Oxidative stress: Predictive marker for coronary artery disease,” Exp. Clin. Cardiol., vol. 18, no. 2, p. e88, 2013.

J. Karolkiewicz, “Effects of oxidative stress and free-radical mediated damage on cell structure and function–connection to aging processes,” Gerontol Pol, vol. 2, pp. 57–69, 2011.

E. Gianazza, M. Brioschi, A. M. Fernandez, and C. Banfi, “Lipoxidation in cardiovascular diseases,” Redox Biol., vol. 23, p. 101119, 2019.

R. Zhang et al., "Myeloperoxidase functions as a major enzymatic catalyst for initiation of lipid peroxidation at sites of inflammation," J. Biol. Chem., vol. 277, no. 48, pp. 46116–46122, 2002.

P. Castro et al., "Effects of carvedilol on oxidative stress and chronotropic response to exercise in patients with chronic heart failure," Eur. J. Heart Fail., vol. 7, no. 6, pp. 1033–1039, 2005.

A. Mongirdienė, A. Liuizė, D. Karčiauskaitė, E. Mazgelytė, A. Liekis, and I. Sadauskienė, "Relationship between Oxidative Stress and Left Ventricle Markers in Patients with Chronic Heart Failure," Cells, vol. 12, no. 5, p. 803, 2023.

K. M. Venardos and D. M. Kaye, "Myocardial ischemia-reperfusion injury, antioxidant enzyme systems, and selenium: a review," Curr. Med. Chem., vol. 14, no. 14, pp. 1539–1549, 2007.

P. L. Fox, B. Mazumder, E. Ehrenwald, and C. K. Mukhopadhyay, "Ceruloplasmin and cardiovascular disease," Free Radic. Biol. Med., vol. 28, no. 12, pp. 1735–1744, Jun. 2000, doi: 10.1016/S0891-5849(00)00231-8.

A. Augustyniak and E. Skrzydlewska, "Zdolności antyoksydacyjne w starzejącym się organizmie Antioxidative abilities during aging," Postep. Hig Med Dosw, vol. 58, pp. 194–201, 2004.

J. A. Buege and S. D. Aust, "[30] Microsomal lipid peroxidation," in Methods in enzymology, vol. 52, Elsevier, 1978, pp. 302–310.

M. K. Ismail, M. Y. Samera, and S. K. Abid, "Oxidative stress markers and antioxidant activity in patients admitted to Intensive Care Unit with acute myocardial infarction," Int. J. Health Sci. (Qassim)., vol. 12, no. 5, p. 14, 2018.

V. Panichi et al., "Ceruloplasmin and acute phase protein levels are associated with cardiovascular disease in chronic dialysis patients.," J. Nephrol., vol. 17, no. 5, pp. 715–720, 2004.

M. Keith et al., "Increased oxidative stress in patients with congestive heart failure," J. Am. Coll. Cardiol., vol. 31, no. 6, pp. 1352–1356, 1998.