DETERMINATION OF CARDIOVASCULAR DISEASES (CVD) WITH IMPORTANCE BIOMARKERS: REVIEW

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ABSTRACT

Cardiovascular disease (CVD) is classified as heart or blood vessel disease. CVD is a term used to describe many associated pathologies, commonly referred to as coronary heart disease, cerebrovascular disorder, peripheral arterial disease, rheumatologically and congenital heart disorders and venous thromboembolism. The most common chronic condition is cardiovascular disease. CVDs remain the world's largest cause of death. The chronic inflammatory disease of the artery wall is considered atherosclerosis. The positive growth of CVD atherosclerosis. The major causes of disability and death in modern society are the complications of atherosclerosis, such as myocardial infarction (MI) or ischemic stroke. Within this analysis the essential biochemical markers are clarified that early CVD predictors are used to diagnose the illness and to avoid complications.

I. INTRODUCTION

Cardiovascular disease (CVD) can be defined as a disease actually effect the Cardiovascular system involve heart and blood vessels. Types of cardiovascular diseases involved coronary artery diseases (CAD) such as angina and myocardial infarction. Other CVDs include stroke, heart failure, hypertensive heart disease, rheumatic heart disease [1]. Cardiovascular disease causes for one third of deaths in 2017 [2] and the problem is expected to increase aging of the population, poor diet, and poor diet [3]. Heart failure describe as a one types of cardiovascular disorders that understanding the heart unable to provide oxygenated blood to other site of body. The heart failure known when person needed high oxygen during exercise. The symptoms of heart failure include shortness of breath, fatigue, and swollen legs (edema), the causes of heart failure different therefore, the diagnosis also different [4]. There are many risk factors may lead to CVD in both man and women involved age, sex, tobacco use, excessive alcohol consumption, unhealthy diet, physical inactivity, high blood sugar (diabetes) and high blood sugar (hypertension) [5].

Atherosclerosis applies as the chronic inflammatory condition leading to cause death in worldwide. The atherosclerosis progressive to myocardial infraction or stroke, the clinical not from narrowing the lumen but due to thrombotic events associated with acute rupture or erosion of an unstable plaque [6]. The characteristic of atherosclerosis is lipid deposition in the vessel wall that leads to an inflammatory and proliferative cascade involving smooth muscle, endothelial, and immune cells. Despite substantial improvements in our understanding of mechanisms contributing to atherosclerosis and overall reduction in cardiovascular mortality, the absolute disease burden remains substantially high [7]. Primarily result of atherosclerosis is damage to the inner lining of the artery (endothelium), atherosclerosis due to lipid deposition in vessel which known as plaques, leading to narrow of artery and obstruct the flow of blood to the heart [8]. After time, artery become narrow the blood supply to heart reduce result angina. The plaque may be split to form clot leading to blocked other arteries in heart [9].

Angina pectoris refer as a clinical syndrome characterized by inadequate blood supply to the coronary arteries, sudden myocardial ischemia, and hypoxia, with episodic chest pain or chest discomfort [10]. The disease is most common in men than 40 years [11]. The initially symptoms of angina are pain result from heart's ischemic which reflex to body. It is characterized by paroxysmal anterior chest and compression pain [12]. The mainly location of pain in the back of the sternum and can be radiated to the anterior and left upper limbs [13], Or emotional excitement

often occurs, each episode lasts for 3 to 5 minutes, can be done once a few days, or several times a day, rest or disappear with nitrate preparations [14].

Myocardial infraction (MI) can refer as myocardial cell death due to prolonged ischemia. Clinically, the term MI is used when there is evidence of myocardial necrosis in a clinical setting, consistent with acute myocardial ischemia and with a rise in cardiac troponin [15]. Other define to MI is the result of occlusive coronary thrombosis; as a result of exposure of blood to atherosclerotic plaque contents, Myocardial infarction is a relevant cardiovascular worldwide event for morbidity and mortality [16].

Oxidized LDL (oxLDL) is a low-density lipoprotein (LDL) oxidation which plays an important role in pathogenesis, independently of LDL cholesterol. The consequence of oxLDL is the modification of native LDL The first hypothesis to demonstrate oxLDL induced damage to endothelial cells was linked to oxidization and atherogenesis [17]. MicroRNAs (miRNAs) may be referred to as endogenous, small, non-coding RNA molecules (18-22 nucleotides) that can be regulated at post-transcriptional gene expression, by binding to targeted mRNA, resulting in mRNA degradation or translation [18]. MiRNAs are relatively stable in blood circulation and can be useful in the diagnosis of disease as biomarkers. Inflammatory autoimmune diseases, MiR-146a is a relatively well-known miRNA and plays an important role in pathogenesis for several autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis [19]. Also in vascular endothelial cells, smooth muscle cells and monocytes / macrophages, miRNA-146a was found. It plays a role in regulating the development of atherosclerosis through the use of various target genes [20].

Human afamine is defined as a serum glycoprotein and is a presumably vitamin E binding protein responsible for vitamin E that circulates in body fluids [21]. Preptin is a new hormone secreted from proinsulin -like growth factor I-which has an essential function in the metabolism of minerals. It is synthesized with cell insulin in pancreatic β cells [22]. Preptin considers a 34-amino acid peptide hormone, which is consecrated by insulin, amylin and pancreastatin from b cell pancreas sideways [23]. Preptin, the first peptide identified in 2001. Males have lower levels of preptin than females [24]. Preptin is believed to be a glucose-induced enhancer of physiological insulin emissions [25].

II. METHODOLOGY

In recent years, cardiovascular disease mortality has increased as a result of a late diagnosis of the disease, so many researchers are working to detect biochemical markers and use the early disease predictors. A number of studies showing biochemical markers in cardiovascular disease in table (1) have been shown in other studies in this study.

In this study of 200 blood samples from adults with atherosclerosis, Abdulfattah et al. [26] comprised 100 patients who were subdivided into 20 mg of atorvastatin (n = 52) and 40 mg of atorvastatin (n = 48) and 100 safe control subjects. The number of years between 30- and 60 years old. The disease activity of patients' groups to determine by vessel disease affected. OxLDL determined by competitive ELISA, relative quantification (RQ) of miRNA146a expression, in whole blood was estimated using reverse transcriptase quantitative real time polymerase chain reaction.

Hasan et al. [22] in the total sample were 60 patients subdivided into 30 men and women and 30 patients subdivided into healthy groups. Their age ranged between the ages of 35-65 years, the estimates for patients and control groups with the use of competitive ELISA of biochemical parameters (Afamin and Preptin).

Omnia et al. [27], This study is cross-sectional study, designed to measure the NLR\PLR (Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio) as a marker for systemic inflammation in CVD patients. The number of patients in study (100) were performed for laboratory investigation, also questioner was conducted in this study. Hundred samples from patients diagnosed with cardiovascular diseases (regarding of age, gender and type of disease and exclude Patients who are diabetic, renal disease patients and diseases other than cardiovascular diseases) and other 100 samples from normal healthy individuals were used as control. NLR was calculated as the ratio of neutrophil count to lymphocyte count, and PLR was calculated as the ratio of platelet count to lymphocyte count.

Table (1): Methodology in studies

Studies	Biochemical markers	Methods
Abdulfattah et al (2020)	Oxidized LDL (oxLDL) miRNA146a	Competitive (ELISA) real time polymerase chain reaction.
Hasan et al. (2020)	Afamin Preptin	Both Competitive (ELISA)
Omnia et al. (2020)	Lymphocyte count Platelet count Neutrophils count (NLR\PLR)	Counts of blood cells by complete blood count (CBC)

III. RESULTS AND DISCUSSION

The study of Abdulfattah *et al*. [26] shows that the ox-LDL level in patients with atorvastatin has increased significantly ($P < 0.05$) in comparison of control. In contrast, there are no significant ox-LDL differences between 40 mg and control patients. The mean of $\pm Ct$ of miRNA146a was significantly higer compared to 20 mg atorvastatin (-0.67 ± 0.85 vs -2.84 ± 1.80) but the gap between it and the patient's atorvastatin was negligible (-0.67 ± 0.85 vs -1.72 ± 1.69).

The study suggests that LDL oxidation may be considered criteria for oxidative pressure and endothelial dysfunction. OxLDL promotes endothelial dysfunction and helps in the formation and development of atherosclerotic plaques and also the destabilization of the gene miRNA146a, which has been shown to be miRNA146a expression. In the Abdulfattah *et al*. [26], the positive correlation between oxLDL and miRNA 146a may therefore indicate the potential role of this biomarker in the pathology of ASCAD and could be considered a reliable predictor of diagnosis and treatment.

Hasan *et al*. [22] revealed in this study the significant decrease in Afamin concentrations in the post-catheterization patient compared to control group, and no significant reduction in pre-catheterization in patients compared to patients control group. Also shown significant increase in concentration of Preptin in both pre- catheterization and post- catheterization compared to control group. The present study concluded for the first time that decreased Afamin and increased preptin levels are strongly involved in the progress of cardiovascular diseases and could independently predict the improvement of the pathogenesis of cardiovascular disease in CVD patient's treatment by catheterization. They were associated with atherosclerosis disease that was considered one of the most important leading causes of CVD.

In this study, Omnia *et al*. [27] showed an NLR value significantly higher than the control group (5.6 ± 3.3 vs. 1.7 ± 0.8; $P=0.000$). It also showed that the PLR value was significantly higher compared to the control group. The patient's age of the CVD was insignificant with both NLR ($P=0.729$) and PLR (0.40). The association between NLR and PLR with the sex of CVD patients showed that NLR was significantly higher in male than female (6.7 ± 4.7) patients (3.9 ± 2.4), and statistically significant ($P=0.008$). The PLR in males (182.5 ± 62.2) was also significantly higher than in femals (156.6 ± 67.4), and there was a statistically significant difference ($P=0.013$).

Shown above research demonstrates that there was a considerable rise in platelet counts between several CVD group in contrast to standard individuals. Enhanced platelet counts and platelet activation have an play role in thrombus formation and the atherosclerosis. The modification of platelets count referring to unusual vessel walls, can lead in arterial thrombosis. Besides that, enhanced platelets counts were indicated to helps potential and lead to a more intense course of active atherosclerosis. The present study suggested that, the lymphocytes count was greatly decreased in CVD patients when opposed to regular respondents. A lower serum lymphocyte count was shown to be linked with worse cardiovascular implications in patients with CAD and heart failure. This can be warranted by in cases of prolonged inflammation, lymphocyte counts reduction due to higher lymphocyte apoptosis.

Table (2): The value of biochemical markers in other studies

Studies	Biochemical marker	Patients with CVD		control group
Abdulfattah *et al.*(2020)	OxLDL (U/L) miRNA146a	treated with 20 mg ofatorvastatin	treated with 40mg of atorvastatin	44.50±23.00 −0.67±0.85
		79.95 ± 36.78 −2.84 ± 1.80	64.61 ± 34.00 −1.72 ± 1.69	
Omnia *et al.* **(2020)**	**NLR** **PLR**	**5.6±3.3** **162.3±83.2**		**1.7±0.8** **98.4±28**
Hasan *et al.* **(2020)**	Afamin pg/ml Preptin pglml	Pre-catheterization	Post-catheterization	1.95±0.26 41.58±23.50
		1.46±0.53 85.73±41.97	1.94±0.33 58.93±23.99	

IV.   CONCLUSION

The conclusion of this study indicates that the biochemical markers play an important role in the early detection of cardiovascular diseases and reduce the risk of disease complication. The suggestion of this study is to incorporate these biochemical markers in clinical practice in order to enhance diagnosis and positive CVDs.

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