Serum Bilirubin, Protein, and Ceruloplasmin in Acute Myocardial Infarction

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Abstract:

Objective: A prospective study carried out to assess serum levels of bilirubin, protein, and ceruloplasmin of 50 consecutive patients of myocardial infarction (AMI) with age ranges between 35-74 years (49.54±8.17),45 were males and 10 were females.

Patient and methods: Fifty consecutive cases with symptoms and signs suggestive of AMI admitted to ICCU their age ranges between 35-74 year (49.54 ± 8.17), 41 were males and 9 were females. These patients supported by ECG and cardiac markers. Blood samples (5ml) were collected for analysis during 72 hours of admission at 9 a.m. Forty of healthy Iraqi volunteers of age- and sex-matched as a compared groups without any disease were enrolled.

Results: Results showed that serum bilirubin and ceruloplasmin were significant higher among patient group (P=0.005) and (P<0.001) than that of control group, respectively, while serum protein was significant lower among patient group (P<0.00 1) than that of control group.

Conclusion: Intravascular antioxidant i.e., serum total bilirubin and serum ceruloplasmin were significantly higher in Iraqi's patients with AMI than those of control group. Conversely, serum total protein concentrations were lower than those of control group. Therefore, serum bilirubin and serum ceruloplasmin may be considered biochemical risk factors for AMI.

Key words : Serum billirubin, protein, ceruloplasmin ,acute myocardial Infarction

Introduction:

Myocardial infarction is the leading cause of death and remains the major cause of morbidity and mortality in all developed and developing countries[1]. According to the American Heart Association, coronary heart disease (CHD) causes 12 million deaths in the word each year[2]. Lipids and lipoproteins are important risk factors for CHD. Other risk factors include smoking, hypertension, diabetes mellitus, obesity, but there is no direct evidence that either of these factors can adequately explain the increase vulnerability to CHD[3].

Acute myocardial infarction (AMI) is defined as death or necrosis of myocardial cells (part of acute coronary syndrome), characterized by a typical clinical syndrome consisting of chest pain, dyspnoea with rise and fall in troponin or creatine kinase-MB(CK-MB) to values greater than 99% of a normal reference population[4,5].

Occlusion of coronary artery deprives the myocardium oxygen, caused reduced fatty acid utilization with free radical formation which damage the myocardium further.

Oxidant stress is a condition in which oxidant metabolites exert their toxic effect because of an increased production or an altered cellular mechanism of protection[6]. Increased oxidative stress and the generation of the free oxygen radicals can

result in modification of low density lipoprotein (LDL) to oxidized LDL that could lead to atherosclerosis, which is underlying cause of AMI[7].

The antioxidant property of ceruloplasmin is through its oxidase activity as well as towards ferroxidase activity by catalyzing the oxidation of Fe^{2+} to Fe^{3+}. It also inhibits ferrous ions stimulated lipid peroxidation and is known to be involved in the decomposition of lipid peroxide and it also scavenges superoxide anion radical $(\cdot O_2^-)^2$ [8,9].

Bilirubin is a naturally occurring antioxidant and could as such have a role in protecting lipids and lipoproteins against oxidation and against plaque formation in human beings[10]. The antioxidant protection of LDL by endogenous metabolic production of bilirubin from hemoglobin breakdown has been elucidated[10].

The aim of this prospective study is undertaken to evaluate the serum level of bilirubin, protein, and ceruloplasmin in patients with AMI, and to correlate these biochemical parameters with various diagnostic and prognostic tools of AMI.

Patients and methods:

This prospective study had been conducted between November 2007 and March 2008. In this study, fifty consecutive cases with signs and symptoms suggestive of AMI admitted to intensive coronary care unit (ICCU) their age ranges between 35-74 year (49.54 ± 8.17), 41 were males and 9 were females. These patients supported by ECG and cardiac markers. Blood samples (5ml) were collected for analysis during 72 hours of admission at 9 a.m. Forty of healthy Iraqi volunteers of age- and sex-matched as a compared group without any disease were enrolled.

5 ml of venous blood were collected from both control and patient groups and the serum kept frozen for few days till analysis. Laboratory data were obtained by using commercial available kits. Samples were analysed for blood sugar, urea, and creatine levels were done to rule out diabetes, liver, and renal diseases respectively. Blood pressure was also assessed to exclude hypertensive patients.

Ceruloplasmin estimation was done by commercial kit; APTEC diagnostic nv (Belgium). Reference value is 22-61 mg/dL. Total creatine kinase (total CK) and creatine kinase MB (CK-MB) estimation were done by DiaSys Diagnostic Systems GmbH (Germany). The reference value for total CK in women was < 145 U/l and in men was < 171 U/l. CK-MB activity is between 6-25% of total CK activity. So patients with clinical evidence of AMI (chest pain and dyspnoea), ECG changes (S-T elevation), and whom showed high total CK and CK-MB values (above the mentioned reference value) were included in our study as cases. Total bilirubin and total protein were estimated by linear chemical S.L., (spain) their reference values are up to 1.0 mg/dL and 6.6-8.7g/dL respectively.

The data from patients and controls were compared using independent student's "t" test. Values were expressed as mean ± SD. Statistical analysis was done using the SPSS (version 12.0). "P" value <0.05 was considered to indicate statistical significance.

Results:

Biochemical data were collected from 50 patients of AMI of which 41 (82%) were males and 9 (18%) were females. Their age ranges between 35-74 year (49.54 ± 8.17).

Table 1: independent t-test of some biochemical risk factors in patients with AMI compared with those of healthy control.

Variable	Patients (mean±SD) n=50	Control (mean±SD) N=40	P-value
Total bilirubin (mg/dL)	1.72 ± 0.26	1.07 ± 1.58	0.005
Total protein (g/dL)	5.77 ± 0.97	7.33 ± 2.51	< 0.001
Ceruloplasmin (mg/dL)	76.32 ± 11.25	44.08 ± 9.94	< 0.001

Table 1 shows that serum total bilirubin concentrations in patients with AMI (1.72 ± 0.26 mg/dL) was significantly higher (P=0.005) than that in healthy controls (1.07 ± 1.58 mg/dL) and serum ceruloplasmin concentrations in patients with AMI (76.32 ± 11.25) was also significantly higher (P< 0.001) than that in healthy (44.08 ± 9.94). On other hand, table 1 shows that serum total protein concentration in patients with AMI (5.77 ± 0.97) was significantly lower (P< 0.001) than that in healthy controls (7.33 ± 2.51).

Table 2: Correlations between some biochemical variables in patient group according Pearson correlation

		Total bilirubin mg/dl	Total protein g/dl	Ceruloplasmin mg/dl
Total bilirubin mg/dl	Pearson Correlation	1	-.113	-.051
	Sig. (2-tailed)	.	.433	.726
	N	50	50	50
Total protein g/dl	Pearson Correlation	-.113	1	-.160
	Sig. (2-tailed)	.433	.	.267
	N	50	50	50
Ceruloplasmin mg/dl	Pearson Correlation	-.051	-.160	1
	Sig. (2-tailed)	.726	.267	.
	N	50	50	50

Table 2 shows no significant correlation between serum bilirubin, total protein, and total ceruloplasmin in patient group according to Pearson correlation.

Discussion:

AMI is emerging as a major health problem among the Iraqis population with male prominence. This study is an attempt to look for the diagnostic and prognostic importance of serum bilirubin, total protein, and ceruloplasmin levels in patients with AMI.

In this study, serum bilirubin among patients with AMI was significantly higher levels than among control group (P=0.005, table 1). Bilirubin is an effective intravascular antioxidant possibly protecting lipids and lipoproteins against oxidant and against plaque formation in the human beings[11]. *In vivo* and *in vitro* studies have demonstrated that bilirubin exhibits potent antioxidant properties preventing the oxidative damage triggered by a wide range of oxidant related stimuli[12]. The protective action of bilirubin therefore direct towards the prevention of such oxidation process which eventually may be protective against the process of atherosclerosis. Recent reports suggest an inverse relationship between bilirubin levels and CHD; they stated that mild increase in the circulatory bilirubin might have a protective role against CHD by suppressing atherosclerosis[10, 13].

Our data showed that total serum protein were significantly lower in patients with AMI than in controls (P<0.001, table 1). Hypoproteinemia may be due to combination of microalbunuria[14], increased loss of albumin into extravascular space[15], and increased degradation of plasma proteins by free radicals[16]. Since protein sulfurhydryls serves as sacrificial antioxidants, preventing plasma lipid peroxidation as well as being targets for oxidative damage[17].

In the present study, an increased level of serum ceruloplasmin in AMI patients (P<0.001, table 1) suggests that this molecule may act as an oxidative stress indicator, though mechanism remains unclear[18]. It is an inflammation-sensitive protein and an acute phase reactant[18]. It was shown that ceruloplasmin exhibits pro-oxidant activity and
causes oxidative modification of LDL[18]. Ceruloplasmin is an important intravascular antioxidant and it protects tunica intima against free radical injury[19]. Ceruloplasmin is an acute phase protein and is synthesized by the liver in response to tissue damage and inflammation[19]. Ceruloplasmin exhibits a cardioprotective effect and prevents oxygen free radical induced release of noradrenaline, a powerful vasoconstrictor[20].

Olusi et al[21]. and Kharb[22] showed increased serum bilirubin in MI. On other hand, Schwertner data are not agreement with our findings, who found that serum total bilirubin was an independent risk factor for MI[23]. Verma et al[24] showed increased of both bilirubin and ceruloplasmin an antioxidant in coronary artery disease [CAD]. Nusier et al[25] suggested that the increased of serum bilirubin and decreased in serum total protein in AMI patients. Patil et al[26] and Serajwala et al[27] showed increased serum ceruloplasmin in AMI.

Conclusion:

In conclusion, intravascular antioxidant i.e., serum total bilirubin and serum ceruloplasmin were significantly higher in Iraqi's patients with AMI than those of control group. Conversely, serum total protein concentrations were lower than those of control group. Therefore, serum bilirubin and serum ceruloplasmin may be considered biochemical risk factors for AMI.

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