A Comparative Study for Some Atherogenic Indices in Sera of Myocardial infarction, Ischemic Heart Disease Patients and Control

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Abstract

Cardiovascular diseases (CVD) are the first world's leading causes of death. One of the major risk factor for the development of CVD is dyslipidemia, which involve elevated plasma levels of (TG), (TCh), (LDL-C), (VLDL-C) and a low level of (HDL-C). Generally, the hyperlipidemias are at risk of Ischemic heart disease (IHD) and peripheral vascular disease. The strong association between the risk of Cardiovascular Artery Diseases (CAD), high levels of LDL-C and low levels of HDL-C has been well established. However enormous contributions of TG to CVD have been underestimated. Indeed high levels of TG have been associated with an increased incidence of CAD and an increased population of small dense LDL-C particles. The ratio of TG to HDL-C was proved as strong predictor of Myocardial Infarction (MI).Cardio Risk Ratio (CRR) and Atherogenic Coefficient (AC) have a good predictive value for future cardiovascular events. Atherogenic Index of Plasma (AIP), which indicated that plasma atherogenecity, was also a significant independent predicator of CAD.

This study was primarily to evaluate the serum lipid profile and to estimate the atherogenic indices (CRR, AC and AIP).

Results showed no significant changes in TCh, TG, and HDL-C levels in MI and HID, while LDL-C showed significant increases in MI and IHD, VLDL-C showed highly significant decreases in MI and IHD, compared to control

The atherogenic indices showed significant and no significant increases in MI and IHD respectively, compared to control. The risk factor according to AIP for MI is more in developing CVD than IHD.

Keywords: CVD, MI, IHD, AIP.

Introduction

Cardiovascular diseases (CVD) are the first world's leading causes of death (Mareirosyan et. al.2007). It is a class of diseases that involve the heart or blood vessels (arteries, capillaries and veins) (Manton 1993), which refers to any disease that affects the cardiovascular system, principally cardiac disease, vascular diseases of the brain and kidney, and peripheral arterial disease (Bridget et.al.2010). The causes of CVD are divers but atherosclerosis and / or hypertension are the most common, though over the last two decades, cardiovascular mortality rates have declined in many high-income countries. At the same time cardiovascular deaths and the disease have increased at an astonishing fast rate in low-and middle-income countries (Mendis et.al.2011).

 One of the major risk factor for the development of CVD is dyslipidemia, which may be primary associated with hypertension, diabetes mellitus and obesity. Dyslipidemia usually involve elevated plasma levels of Triglycerides (TG), Total Cholesterol (TCh), Low Density Lipoprotein cholesterol (LDL-C), Very Low Density Lipoprotein cholesterol (VLDL-C) and a low level of High Density Lipoprotein cholesterol (HDL-C) (Shen 2007).

Lipid profile consists of a group of biochemical testes often used in predicting , diagnosing and treating lipid-related disorder i.e. atherosclerosis. Generally, the hyperlipidemias are of interest to the physician in the context of risk factors for Ischemic heart disease (IHD) and peripheral vascular disease. The first step in diagnosis of hyper-and hypolipoproteinaemias is to define the lipoprotein pattern by chemical analysis of the plasma lipid and lipoproteins (Nwagha et.al.2010). Accumulated evidences relating the concentrations of lipids (TCh and TG) and their associated blood transporting lipoproteins (HDL-C, LDL-C,VLDL-C) with the occurrence of atherosclerosis in general and Cardiovascular artery Diseases(CAD) in particular(Cumming 2003) .

 Epidemiological studies have shown that an elevated concentration of TCh in the blood is a powerful risk factor of coronary disease (Ademuyiwa et.al. 2005).Increased plasma level of LDL-C and VLDL–C is often found in hypertension and diabetes mellitus as a risk factor for CVD. Decreases in plasma LDL –C have been considered to reduce risk of CHD , also high plasma TG level is both an independent and synergistic risk factor for CVD , and is often associated with hypertension, abnormal lipoprotein metabolism ,obesity ,insulin resistance and diabetes mellitus(McBride 2007).On the other hand dyslipidemia has been found to be associated with Coronary Heart Disease CHD(Veerendra et.al.2011).

Increases in plasma HDL–C have been considered to reduce risk in CHD(Rang et.al. 2005) High HDL exerts a protective effect by enhancing reverse cholesterol transport by scavenging excess cholesterol from peripheral tissue, which it esterifies with the aid of lecithin cholesterol acyltransferase (LCAT) and delivers to the liver and steroidogenic organs for subsequent syntheses of bile acids and steroid hormones , and eventual elimination from the body(Ademuyiwa et.al. 2005), and inhibiting the oxidation of LDL-C as well as the atherogenic effects of

oxidized LDL-C by virtue of its antioxidant(Brunzellet.al. 2008) and anti-inflammatory properties(Ademuyiwa et.al. 2005).

The strong association between the risk of CAD, high levels of LDL-C and low levels of HDL-C has been well established (Igweh et.al. 2005). However enormous contributions of TG to CVD have been underestimated (Nwagha & Igweh 2005). Indeed high levels of TG have been associated with an increased incidence of CAD (Hokanson & Austin 1996), and an increased population of small dense LDL-C particles (Guerin et.al. 2001). A lot of work has been done on the relationship between TG and HDL-C which proved that the ratio of TG to HDL-C is a strong predictor of Myocardial Infarction (MI) (Gaziano et.al. 1997).

The total cholesterol(TC)/HDL-C and the LDL-C /HDL-C molar ratios have a good predictive value for future cardiovascular events .Dobiasova and Frohlich (2001) proposed a term "Atherogenic Index of Plasma " (AIP) ,which was defined as a log(TG/HDL-c) , which indicated that plasma atherogenecity was also a significant independent predicator of CAD An abnormal ratio of TG/HDL-C indicates an atherogenic lipid profile and a risk for the development of MI(Veerendra et.al.2011).

Our object was primarily to evaluate the serum lipid profile and to estimate the atherogenic indices: Cardio Risk Ratio (CRR), Atherogenic Coefficient (AC) and Atherogenic Index of Plasma (AIP) in Myocardial Infarction (MI), Ischemic Heart Disease (IHD) and to compare these indices with that for healthy subjects, to predict their efficiency in the development of (MI) and (IHD).

Sampling (Subjects)
In a plain tube (no anti coagulant), 5 mL of venous blood placed, which was taken from the groups, left for (15 min) at room temperature, then centrifuged (at 2500 rpm for 10min) to get the serum, which was divided into small portions and stored at (-20°C) unless used some of them immediately .

Collection of blood
Patients samples were collected in Ibn-Alnafees Teaching Hospital, from January to April 2013 (at the time of diagnosis), while the control were collected from some voluntaries.
They have been classified into three groups as follow:
1. Control group: include (25) healthy individual (15 male, 10 female) with no previous diseases which may interfere with the parameters analyzed in this study.
2. Myocardial Infarction (MI) patients group: include (25) patients (15 male, 10 female).
3. Ischemic Heart Disease (IHD) patients group: include (25) patients (15 male, 10 female).

Laboratory work.
A -Lipid Profile
Enzymaticaly with commercial test kits from Randox Company, the following fractions of lipids were assayed:
 -Plasma Total cholesterol (TCh), (Richmond, 1973).

-Plasma HDL-Cholesterol (HDL-C), (Yaung & Pestancer, 1975).

-Plasma Triglycerides (TG) (Fossati & Principle, 1982).

-Plasma Low Density Lipoprotein cholesterol (LDL-C) and Very Low Density Lipoprotein (VLDL-C) was calculated using the Friedwald equation (Friedwald, et.al, 1972), as follow:

$$LDL\text{-}C = TCh - HDL\text{-}C - TG / 2.2$$
$$VLDL = TG / 2.2$$

B-The atherogenic indices was calculated as follow:

- Cardio Risk Ratio (CRR) = TCh / HDL-C (Martriosyan, et al., 2007).
- Atherogenic Coefficient (AC) = (TCh – HDL-C)/ HDL-C (Brehm, et al., 2004).
-Atherogenic Index of Plasma (AIP) = log (TG / HDL-C) (Dobiasova, 2001).

  (AIP   was calculated by using the Czech online calculator of atherogenic risk.)

Statistical analysis
Data presented were the means ± and standard deviations; student-t-test was used to compare the significance of the difference in the mean values of any two groups. (P≤0.05) was considered statistically significant (Bailey,

1974). The overall predictive values for the results in all studied groups were performed according to program of Office Excel 2007.

Results

Table (1) showed the levels of TCh and TG in serum of MI, IHD patients and control.
It showed no significant difference in TCh and TG levels in both MI and IHD groups compared to control.
Table (2) showed the levels of lipoproteins HDL-C, LDL-C and VLDL-C in serum of MI, IHD patients and control. In this table HDL-C showed no significant changes in both MI and IHD, but LDL-C showed significant increases in MI group and in IHD group, while VLDL-C showed highly significant decrease in MI group and significant IHD group compared to control.
Table (3) shows the values of atherogenic indices (CRR, AC and AIP) for MI, IHD patients and control. In this table CRR, AC and AIP values showed significant increases in MI group compared to control, while non-significant increases appeared in IHD group compared to control.

Discussion

High plasma concentrations of total cholesterol (TCh) is well-established and recognized as a risk factor for developing atherosclerosis and other CVD, therefore follows that a reduction in plasma TCh level will reduce the risk of CVD. An increased level of triglyceride (TG) is both independent and synergistic risk factor for CVD (McBride 2007). High plasma levels of LDL – C and VLDL-C is a risk factor for CVD (Lichtennstien et. al. 2006). Decreases in plasma LDL-C have been considered to reduce risk of coronary heart disease (Rang 2005). Clinical studies showed that increasing plasma HDL-C concentration decreases cardiovascular risk, and vice versa (Shen 2007). High HDL-C exerts a protective effect by decreasing the rate of entry of cholesterol into the cell via LDL-C and increasing the rate of cholesterol release from the cell by enhancing reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues, and inhibiting the oxidation of LDL-C as well as the atherogenic effects of oxidized LDL-C by virtue of its antioxidant (Brunzell 2008) and anti-inflammatory property (McBride 2007).
A number of lipid related parameters have been used to predict the risk of CAD. According to Grover et.al. (1999), either the ratio of LDL-C /HDL-C or TG/HDL-C is the best related predictor of future cardiovascular events. Later, TG/HDL-C was shown to be a more accurate predictor to CHD. The logarithamatically transformed ratio of plasma TG /HDL-C correlated closely with the LDL-C particle size and could serve as an indicator of the atherogenic lipoprotein phenotype (Priya et. al. 2011).
The Atherogenic Index of Plasma (AIP) defined as long (TG/HDL-C), has recently been proposed as a marker of plasma atherogenicity because it is increased in people at high risk for CHD and its inversely correlated with LDL-C particles (Meng et.al. 2004). AIP indicates a balance between the actual concentration of plasma TG and HDL-C, which predetermine the direction of the cholesterol transport in an intravascular pool i.e. the flux of newly produced cholystreyl esters by lecithin cholesterol acyl transferase (LCAT) towards atherogenic LDLs or beneficial HDLs (Dobiasova & Frohlich 1998). Studies also showed that AIP predicts cardiovascular risk and that it is an easily available cardiovascular risk marker and a useful measure of the response to treatment (Frohlich & Dobiasova 2003).
Indeed HDL-C/LDL-C ratio has been great value in the assessment of cardiovascular risk, especially when the absolute values of the individual lipoprotein seem normal. Thus, the use of other indices which has been minimally applied should be encouraged. Isolated elevation in triglyceride increases CHD risk more in women than men, but its effect can be contracted by the levels of HDL-C (Stensvold et. 1993). The atherogenic index of plasma which is a mathematical relationship between TG and HDL-C has been successfully used as an additional index when assessing cardiovascular risk factors (Meng et. al. 2004).
It has been demonstrated that the development of CAD is a function of the particle size of LDL-C and HDL-C, with the small particle size exhibiting great atherogenic potential (Drexel et.al. 1992). Indeed, cholesterol etherification rate in HDL-C plasma (FERHDL) has a strong relationship between lipoprotein particle sizes and thus can be considered as a functional risk marker for CAD (Dobiasova &Frohlich 1998). Researchers have shown that the log arithmetically transformed ratio TG/HDL-C is the best determinant for FERHDL and thus a better predictor of cardiovascular risk than other previously used lipid parameters (Dobiasova et. al. 2005).Furthermore, in situations where other atherogenic risk parameters appear normal, AIP may be the diagnostic alternative.
Atherogenic indices are powerful indicators of the risk of heart disease the higher the value, the higher the risk of developing CVD and vice versa (Usoro et. al.2006). (An abnormal ratio of TG to HDL-C indicates an atherogenic lipid profile and a risk for the development of MI (Suman et. al. 2012).

Myocardial infarction   MI patients have higher positive values of AIP than IHD patients as compared to healthy subjects. AIP has been reported to range from negative to positive with a zero value corresponding to LDL-C particle diameter of 25.5nm(Dobiasova &Frohlich 2001).

Atherogenic Index of Plasma AIP which can easily be calculated from standard lipid profile can act as an adjunct that significantly adds predictive value beyond that of the individual lipids, and / or TC /HDL-C, LDL-C / HDL-C ratios(Nwagha et. al. 2010).

Conclusion

The risk factor according to AIP for MI is more in developing CVD than IHD.

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Table (1)

The levels of TCh and TG in serum of MI, IHD patients and control

Group distribution	NO.&Sex	Age Range years	TCh mean±SD mmol/L	TG mean±SD mmol/L	P	P*
control	25(15m,10f)	30-65	4.01±0 .25	1.69±0 .13		
Myocardial infarction (MI)	25(15m,10f)	30-70	5.15±1.20	2.23±0.89	NS	NS
Ischemic heart disease (IHD)	25(15m,10f)	32-70	4.58±0 .96	2.34±0.94	NS	NS

P represents the correlation between MI group and control for TCh.
P* represent the correlation between IHD group and control for TG.
S = considered significant $P \leq 0.05$
NS = considered non-significant $P \geq 0.05$

Table (2)

The levels of lipoproteins HDL-C, LDL-C and VLDL-C in serum of MI, IHD patients and control

Group distribution	NO.& Sex	Age Range years	HDL-C mean±SD mmol/L	LDL-C mean±SD mmol/L	VLDL-C mean±SD mmol/L	P	P*	P**
Control	25(15m,10f)	30-65	1.36±0.04	2.02±0.12	0.77±0.03			
Myocardial infarction (MI)	25(15m,10f)	30-70	1.18±0.47	3.52±1.22	0.45±0.18	NS	S	S
Ischemic heart disease (IHD)	25(15m,10f)	32-70	1.35±0.44	3.03±0.96	0.42±0.21	NS	S	S

P represents the correlation between MI, IHD group and control for HDL-C
P* represent the correlation between MI, IHD group and control for LDL-C.
P*** represents the correlation between MI, IHD and control for VLDL-C.

Table (3)

The mean values of atherogenic indices (CRR, AC and AIP) for MI, IHD patients and control

Group distribution	NO.& Sex	Age Range years	CRR mean±SD	AC mean±SD	AIP mean±SD	P	P*	P**
Control	25(15m,10f)	30-65	3.55±0.21	2.55±0.21	0.1 ±0.03			
Myocardial infarction (MI)	25(15m,10f)	30-70	5.02±2.14	4.00±2.12	0.27±0.11	S	S	S
Ischemic heart disease (IHD)	25(15m,10f)	32-70	4.0±2.1	2.73±1.64	0.15±0.08	NS	NS	NS

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P represents the correlation between MI, IHD group and control for CRR.

P* represent the correlation between MI, IHD group and control for AC.

P*** represents the correlation between MI, IHD and control for AIP.

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