

Variability in Lipid Profile in Patients with Acute Myocardial Infarction from two tertiary care hospitals in Pakistan

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Introduction

Disorders in lipid metabolism (dyslipidemia) can result in premature atherosclerosis¹, leading to the development of cardiovascular disease (CVD).¹ It has recently been pointed out that there is an epidemic of CVD in urban South Asians.² Pakistanis being part of this ethnic group have very high rates of coronary artery disease (CAD).³ According to official estimates CVD results in more than 100,000 deaths every year⁴, however, the actual figure may even be much higher than that. Several large scale clinical trials have shown that lipid lowering interventions are associated with reduced coronary events and mortality.⁵ This shows the significance of determining the lipid status of CAD patients in order to reduce any further coronary events in them.

With the exception of a couple of reports, there is hardly any published data on variability of lipid profile in Pakistani patients with acute myocardial infarction (AMI).⁶ The present study was undertaken to investigate changes in lipid profile in Pakistani patients with AMI due to age, gender, body mass index (BMI), diabetes mellitus, hypertension and smoking, and also find out the prevalence of hypertriglyceridemia, low-HDL-cholesterol (both of these constitute an important component of metabolic syndrome), hypercholesterolemia and "isolated low-HDL cholesterol" in a population from two tertiary care hospitals.

Patients and Methods

A total of four hundred and fifty one consecutive patients with AMI (age 30-75 years) admitted to the National Institute of Cardiovascular Diseases (NICVD), Karachi from January 2001 to June 2001 (n=250) and the Armed Forces Institute of Cardiology, Rawalpindi from August 2003 to

September 2003 (n=201) were included in this study. All of them had first acute attack of myocardial infarction.

They had the confirmed diagnosis of AMI on the basis of WHO criteria of clinical history suggestive of myocardial ischaemia, ECG changes of myocardial damage and elevation of biochemical markers (creatinine kinase and creatine kinase MB). All the patients were assessed for risk factors such as, diabetes mellitus, hypertension, BMI, smoking etc. using the criteria given below. All those patients who were pregnant, having malabsorption syndrome, suffering from tuberculosis, liver disease, uremia, cancer or using vitamin B-complex supplements during the past 6 months were not included in this study. The study was approved by the Ethical Review Committee of the Aga Khan University.

Criteria for diabetes were set as an abnormal fasting blood sugar level >125 mg/dl at admission, or having taken hypoglycemic agents for already established diabetes. All those with systolic blood pressure greater than 140 mmHg and/or diastolic blood pressure of 90 mmHg or those on regular anti-hypertensive medications were classified as hypertensive. Those who were smoking cigarettes or "beeri" regularly (one or more per day) were classified as smokers. A body mass index of greater than 25 was classified as overweight/obese.

Hypercholesterolemia: Serum cholesterol level >200 mg/dl.

Hypertriglyceridemia: Serum triglyceride level >200 mg/dl.

Low HDL-cholesterol: Serum HDL-cholesterol level <35 mg/dl.

Isolated low HDL-cholesterol: Serum HDL-cholesterol level < 40 mg/dl and serum triglyceride level <150 mg/dl.

Five ml venous blood was collected from patients within 24 hours of AMI and immediately transferred

to plain tubes. After clotting, the serum was separated by centrifugation and stored frozen at -60°C until analysis. Total cholesterol, high density lipoprotein (HDL)-cholesterol and triglycerides were analyzed using calorimetric kit methods (RANDOX, UK). The concentration of low density lipoprotein (LDL)-cholesterol was calculated using the Friedwald formula.

Mean values have been presented as means ±

Table 1. Demographic and clinical characteristics (n=451)

Variable	Value (mean ± SD)	Frequency (%)
Age (years)	54.3 ± 10.7	
Gender		
Male		341 (75.6)
Female		110 (24.4)
BMI (Kg/m ²)	25.0 ± 4.1	
>25		189 (43.8)
Hypertensive yes		243 (57.4)
No		180 (43.6)
Diabetic Yes		153 (34.6)
No		289 (65.4)
Glucose (mg/dl)	137 ± 76	
Cholesterol (mg/dl)	181 ± 50	
Triglycerides (mg/dl)	177 ± 127	
HDL-cholesterol (mg/dl)	34.7 ± 11.3	
LDL-cholesterol (mg/dl)	110 ± 47	

standard deviation (SD). Univariate and multivariable analyses were carried out using the SPSS® (statistical package for social sciences) Software Version 10 for Windows® to study the effect of various factors on lipid levels. Independent sample t-test, chi-square test and simple linear regression were used to test the significance at the univariate level. Multiple linear regression was used to test the significance at multivariable level. All variables with p-value <0.2 were considered for multivariable analysis. For comparison of lipid levels in younger and

older groups, the patients were divided into those above 50 years and those below 50 years. This cut off age of 50 years was chosen to exclude the effect of female sex hormones on lipid levels in older females, because the usual age of menopause in female population is considered to be about 49 years. A p-value of <0.05 was considered significant.

Results

Table 1 shows the demographic and clinical characteristics of patients. There were 341 males and 110

Table 2. Effect of age, gender, BMI, diabetes mellitus, hypertension and smoking on serum levels of lipids in AMI patients (mean ±SD).

Variable	Value	Value	Value	Value	Value
Age (years)	<50	171	187±52	35.6±10.8	111±51
	>50	279	177±48	35.7±11.68	110±44
			(p value 0.055)	(p value 0.911)	(p value 0.942)
Gender	Male	341	179±48	35.3±11.2	109±45
	Female	110	187±54	36.8±11.8	114±54
			(p value 0.113)	(p value 0.253)	(p value 0.324)
BMI (kg/m ²)	<25	243	177±48	35.5±11.7	106±44
	>25	189	185±51	36.2±11.0	114±50
			(p value 0.077)	(p value 0.514)	(p value 0.082)
Diabetes	Yes	153	186±51	34.2±9.8	116±49
	No	289	177±49	36.3±12.2	106±45
			(p value 0.082)	(p value 0.089)	(p value 0.050)*
Hypertension	Yes	243	179±47	35.2±11.7	109±47
	No	180	181±52	36.3±11.2	108±46
			(p value 0.695)	(p value 0.385)	(p value 0.748)
Smoking	Yes	123	184±53	34.2±11.2	111±49
	No	203	181±48	35.0±10.3	113±46
			(p value 0.639)	(p value 0.51)	(p value 0.723)

*Significant at p<0.05

a = Discrepancy in total number for certain factors (being less than 451) is due to some missing information.

b = Those who had quitted smoking or were occasional smokers were not included.

females. Mean age of the group was 54.3 ± 10.7 years with range 30-75 years. Mean BMI was 25 ± 4.1 kg/m². Mean value of fasting serum glucose was 137 ± 76 mg/dl. Thirty five percent of patients were diabetic, 57% were hypertensive, while 43.8% were overweight/obese (BMI >25). Mean values of serum total cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol were 181 ± 50 mg/dl, 177 ± 127 mg/dl, 35.7 ± 11.3 mg/dl, and 110 ± 47 mg/dl, respectively.

Table 3. Prevalence of hypercholesterolemia, hypertriglyceridemia, low HDL-cholesterol and isolated low HDL-cholesterol in AMI patients

Variable	Frequency (%)		Total (n=451)	P-value*
	Males (n=341)	Females (n=110)		
Hypercholesterolemia (>200mg/dl)	98 (28.7)	40 (36.4)	138 (30.6)	0.13
Hypertriglyceridemia (>200 mg/dl)	99 (29)	37 (33.6)	136 (30.1)	0.36
Low HDL-cholesterol	174 (51)	45 (40.1)	219 (48.6)	0.04
Isolated low-HDL- cholesterol(HDL<40 mg/dl and TG <150 mg/dl)	121 (35.5)	33 (30)	154 (34.1)	0.29

*P-value compares percentages in male and female groups and is based on test of association using chi square.

Table 2 shows the effect of age, gender, BMI, diabetes mellitus, hypertension and smoking on serum levels of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides in AMI patients. Mean concentrations of total cholesterol and HDL-cholesterol were not significantly affected by age, gender, BMI, diabetes mellitus, hypertension and smoking. Mean LDL-cholesterol level, however, was found to be significantly increased in diabetes mellitus ($p=0.047$), while age, gender, BMI, hypertension and smoking had little effect on the level of this lipoprotein. Mean levels of triglycerides were significantly decreased in older patients (>50 years) compared to younger (<50 years) ones ($p=0.019$). Gender, BMI, diabetes, hypertension and smoking had no significant effect on triglyceride levels in these patients. Multivariable analysis of the data to see the combined effect of these factors revealed no significant association between any of these factors and the lipid levels in AMI patients. Prevalence of hypercholesterolemia, hypertriglyceridemia, "low HDL-cholesterol" and "isolated low HDL-cholesterol" is shown in Table 3. The frequencies of hypercholesterolemia, hypertriglyceridemia, "low HDL-cholesterol" and "isolated low HDL-cholesterol" were found to be 30.6%, 30.1%, 48.6% and 34.1%, respectively. A comparison of percentages in the male and female groups using chi square revealed statistically significant difference only in the low HDL-cholesterol ($p=0.04$) group.

Discussion

Pakistanis belong to an ethnic group which has the highest rates of CAD.³ According to a recent estimate based on scientific studies, nearly 100,000 individuals suffered an AMI in Pakistan in the calendar year 2002.⁷ Lehto et al. have demonstrated direct correlations between the incidence of AMI and plasma lipid abnormalities.⁸ There are only few reports on lipid profile of Pakistani AMI patients. A small study ($n=31$) carried out by Salahuddin et al. revealed significantly high levels of triglycerides and significantly low levels of HDL-cholesterol in AMI patients compared to normal controls.⁶ This was suggestive of an important role played by lipid abnormalities in the development of atherosclerosis in our population. Our results compare well with the baseline levels of lipids reported in two other studies.^{5,6} The high levels of triglycerides in coronary heart disease (CHD) have also been reported among

Indians by Gupta et al.⁹ and among Egyptians by Metwalli et al.¹⁰ The increased levels of triglycerides in Pakistani, Indian and Egyptian AMI patients could be due to their genetic makeup and nutritional habits involving high consumption of saturated fats.^{11,12} Our results show that hypertension has no effect on lipid levels in our patients (Table 2). This is suggestive that the factors leading to hypertension have little effect on the lipid profile in AMI patients. Similarly, diabetes mellitus also appears to have no significant effect on levels of total cholesterol, HDL-cholesterol and triglycerides in AMI patients. There was, however, an increase in LDL-cholesterol. Although, smoking is known to affect serum lipid levels, especially a decrease in the HDL-cholesterol^{13,14}, yet in the present study it did not appear to have any significant impact on lipid profile in AMI patients. This lack of association observed by us could have been due to the absence of information regarding the frequency and duration (number of years) of smoking by the patients. Thirty-one percent of our patients had hypercholesterolemia (Table 3). This frequency compares well with 37% reported by Ishaq et al. in a recent study.¹⁵ It is noteworthy that the baseline mean HDL-cholesterol levels in our patient population are well below the normal levels (40 mg/dl) recommended by the National Cholesterol Education Program¹⁶, indicating that low levels of HDL-cholesterol in our AMI patients may have contributed to their accelerated coronary atherosclerosis resulting into AMI. In fact, the prevalence of "low HDL-cholesterol" (<35 mg/dl) in our population of patients (48.6%) was among the highest in the world (Table 3) as compared to other studies done internationally.^{9,17-19} Similarly, the prevalence of "isolated low-HDL-cholesterol" (HDL <40 mg/dl and triglycerides <150 mg/dl) in our AMI patients was found to be 34.1% (Table 3) which is very high compared to its frequency in other populations.¹⁷ Hypertriglyceridemia appears to be a prominent feature in CHD. In our study, its prevalence in AMI patients was found to be 30% which is higher as compared to a study in a Caucasian population of CAD patients in Boston.¹⁹ In conclusion, our data confirms the previous observations that high levels of triglycerides and low levels of HDL-cholesterol are the most prominent lipid abnormalities in Pakistani AMI patients. These two lipid abnormalities constitute an important component of "metabolic syndrome" known as "atherogenic dyslipidemia".²⁰ This syndrome, which in addition to atherogenic dyslipidemia, also includes

abdominal obesity, elevated blood pressure, insulin resistance, a proinflammatory state and a prothrombotic state poses a significant health risk to individuals and is a growing health crisis for our country.

Our dietary habits could have contributed to this atherogenic dyslipidemia in AMI patients. Decreased serum HDL-cholesterol is considered to be one of the most common lipid disorders in AMI patients.⁸ The mechanisms responsible for this change may reside in the decreased synthesis and secretion of HDL-cholesterol from liver and/or accelerated elimination from the blood stream by extravasation. Increased permeability of the capillary membranes during the acute inflammation after AMI has been shown to cause extravasation of HDL-cholesterol.²¹ A focus on the strategies to decrease triglyceride levels and increase HDL-cholesterol levels in CAD patients, such as cessation of smoking¹³ and use of low-fat diet which is high in polyunsaturated fatty acids^{22,23} decreased consumption of ghee (which has high proportion of saturated fats and trans fatty acids)²⁴, will greatly help in reducing future coronary events in them.

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Abstract

Objective: To investigate changes in total cholesterol, high density lipoprotein (HDL)-cholesterol, low density lipoprotein (LDL)-cholesterol and triglycerides in serum of Pakistani patients with AMI due to age, gender, body mass index (BMI), diabetes, hypertension, and smoking, and also find out the prevalence of hypercholesterolemia, hypertriglyceridemia, "low HDL-cholesterol" and "isolated low-HDL cholesterol" in them.

Patients and Methods: Serum samples from 451 consecutive AMI patients (250 from National Institute of Cardiovascular Diseases, Karachi and 201 from Armed Forces Institute of Cardiology, Rawalpindi) were analyzed for total cholesterol, HDL-cholesterol and triglycerides using kit methods. LDL-cholesterol was determined using the Friedewald formula.

Results: Mean serum concentrations of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides in AMI patients were found to be 181 ± 50 mg/dl, 35.7 ± 11.3 mg/dl, 110 ± 47 mg/dl and 177 ± 127 mg/dl, respectively. Mean levels of total cholesterol and HDL-cholesterol were not significantly affected by age, gender, BMI, diabetes mellitus, hypertension and smoking. Mean LDL-cholesterol concentration, however, was found to be significantly increased in diabetes mellitus ($p=0.047$), while age, gender, BMI, hypertension and smoking had no significant effect on the levels of this lipoprotein. Mean levels of triglycerides were significantly decreased in older patients (>50 years) compared to younger (<50 years) ones ($p=0.019$). Gender, BMI, diabetes mellitus, hypertension and smoking, however, had no effect on triglyceride levels. The frequencies of hypercholesterolemia, hypertriglyceridemia, "low HDL-

cholesterol" and "isolated low-HDL-cholesterol" were found to be 30.6%, 30.1%, 48.6% and 34.1%, respectively.

Conclusion: High prevalence of hypertriglyceridemia and low HDL-cholesterol (which constitute a component of metabolic syndrome) in Pakistani AMI patients is suggestive that these two lipid abnormalities could be playing a major role in the development of atherosclerosis in Pakistani population (JPMA 54:544;2004).