

Study of Lipid Profile in Non-diabetic Ischemic heart Disease Patients in Jalalabad, Afghanistan

Associate professor Dr. M. Azim Azimee

Assistant professor Dr. Abdul Ghafar Sherzad

Lecturers of Biochemistry Department, Nangarhar Medical Faculty.

Abstract

Coronary artery disease is leading cause of morbidity and mortality in both developing and developed countries. This cross sectional analytic study was conducted in Nangarhar university Teaching hospital in 2017 June to 2018 July , was undertaken to study dyslipidemia among the patients admitted to hospital with coronary artery disease. 111 subsequent cases diagnosed as coronary artery disease 49 were male (44.1%) and 62(55.9%) female age range 38-80 years. Age, sex, Blood pressure, History of smoking and Body Mass Index were recorded in each subject in standard questioner. Blood samples for investigations of lipid profile i.e. serum cholesterol (CHO), Triglyceride (TG), High Density Lipoprotein-cholesterol (HDL-C) and Low Density Lipoprotein-cholesterol (LDL-C) were collected from Patients. In study 87(78.37% were Have hypertension and 84(75.7 %) had family history of hypertension. It was found that LDL (Mean \pm SD) (92.47 \pm 17.50), HDL (40.44 \pm 6.90) and TG high level (193.46 \pm 40.83) and total cholesterol (175.55 \pm 31.43). 62(55.9%) has positive family history of Diabetes mellitus, 87(78.37%) History of Hypertension, and it was found that High prevalence of Dyslipidemia (hypercholesterolemia, Hypertriglyceridemia and Low HDL) were significantly in all age groups. 13.46% normal weight, 76.57% were overweight and 23.42% are obese.

Key words: Lipid profile, Cronary heart disease, Dyslipidemia.

Introduction

Atherosclerosis is a progressive inflammatory disorder of the arterial wall that is characterized by focal lipid-rich deposits of atheroma. Atherosclerosis begins early in life. Abnormalities of arterial function have been detected among high-risk children and adolescents, such as cigarette smokers and those with familial hyperlipidemia or hypertension.¹

In the recent past there has been an addition of several molecular markers to the well-established risk factors of smoking, family history, hypertension, diabetes and high levels of LDL cholesterol². In current strategies of coronary risk assessment, lipid testing in the blood routinely recommended³ Because of critical importance of LDL-C in atherogenesis, LDL-C is the focus for the determination of the risk of coronary disease⁴.

Coronary artery disease (CAD) is a condition that develops due to the accumulation of atherosclerotic plaque in the pericardial coronary arteries leading to myocardial ischemia. It is a common multifactorial public health crisis today and a leading cause of morbidity and mortality in both developing and developed countries.⁵ It is projected that CAD will be the leading cause of death in developing countries by the year 2020.^{6,7} According to WHO

statistics⁸ the age-standardized mortality rates from CAD are one of the highest worldwide. One possible explanation is the high prevalence rate of CAD risk factors. Unfortunately, systematically documented data on CAD prevalence, incidence and rate of cardiovascular risk factors in developing countries are scanty.^{9, 10} there is geographic and genetic variability in the prevalence of CV risk factors and in their contribution to the development of CAD.^{11, 12} When investigating the relationship between CAD and lipid disturbances it is necessary to use regional data on blood lipid profile in each region. The prevalence, type of lipid abnormalities and its association with CAD were not reported among Afghans. Knowledge about the determinants of disease in persons within populations and of lipid profile in this group of relatively high-risk patients could be used to make recommendations on lipid management. Prevention programs will give priority to the most common risk factors and possibly the predominant type of dyslipidemia.

The present study has two objectives. First: to define the lipid profile in Afghans patients with CAD who are not on lipid-lowering therapy. Second: to examine the effects of age, gender, type of CAD and the presence of hypertension on changes in lipid profile. By 2020, the disease is predicted to be the major cause of morbidity and mortality in most developing-countries.^{13, 14}

Opinion is divided on the changes that occur in serum lipids and lipoproteins following myocardial Ischemia (MI). Most workers have reported a reduction in total cholesterol^{15,19}, HDL-cholesterol¹⁸ and LDLcholesterol^{17,18} after acute MI. Others have, however, reported no change in serum total cholesterol²⁰ and HDL-cholesterol^{17, 20}

Similar variations have also been noted in serum triglycerides levels^{16, 20, 21}. From these reports it is clear that phasic changes do occur in patients following MI and therefore there is a recommendation for detection of hyperlipidemia in patients with acute MI that the serum lipids should be assessed either within 24 hours after infarction or after 2-3 months of acute MI^{19, 22, 23}. While the recommendation may hold true for absolute levels there is no consensus on when ratios of various fractions of lipids should be assessed. Further, the magnitude, pattern and mechanism of these phasic changes in lipids are also not clearly outlined for our Afghan subjects. The present study was, therefore, undertaken to examine the changes in serum lipids and lipoproteins in our subjects with acute myocardial infarction.

Definitions:

High blood pressure (BP) was diagnosed based on at least Two separate clinic visit (average of the last two of the three measurements during each visits) if mean SBP was ≥ 140 mmHg or if patients were receiving treatment for hypertension.

Chronic stable angina: Classic history of typical anginal pain with evidence of myocardial ischemia on stress testing or an abnormal coronary angiogram.

Myocardial infarction: History and results of hospital records (ECG changes and elevated cardiac enzymes) or history and ECG changes showing pathologic Q waves. Only patients with remote MI (at least 3 months) were included in the study.

Body Mass Index (BMI): Normal weight 18.5-24.99, Overweight was defined as BMI between 25–29.9 kg/m². Obesity, defined as ≥ 30 kg/m².

Dyslipidemia: Three different Cutpionts were used to analyze the prevalence of High LDL-C and low HDL-C based on the different existing consensus recommendations. The selected Cutpionts for high LDL-C were 100,130 and 160 mg/dl and for low HDL were 35, 40 and 50 mg/dl. Cutpionts used to analyze prevalence of hypertriglyceridemia was (>150mg/dl). A total plasma cholesterol level ≥ 200 mg/dl was considered abnormal .Diabetes mellitus was diagnosed if Fasting plasma glucose was ≥ 126 mg/dl on two laboratory results of if the patient was on hypoglycemic therapy.

The following data were entered into a computer program with: SPSS version 16.0 statistical package for detailed statistical analysis.

- Demographic characteristics: age, Gender& socioeconomic status.
- Lipid profile: total cholesterol (TC), LDL-C, HDL-C Triglycerides and TC/HDL-C ratio.
- Hypertension state.
- Mean values were reported for continuous variables. Prevalence and frequencies are expressed in terms of percentage.

Exclusion criteria: The person having evidence of diseases which may adversely affect the outcome was not included in study group. They were

- Patients with Liver & Renal diseases.
- With hypothyroid / hyperthyroid disease.
- With cerebrovascular disease and anemia.
- Chronic obstructive lung disease.
- Patients with Diabetes mellitus.
- Patients under lipid lowering therapy.

Table 1: Cut off level for different Biochemical parameters used in our study.

Biochemical parameters	Cut of level
Cholesterol	>200mg/dl
Triacylglycerol	>150mg/dl
High density lipoprotein (HDL-C)	<40mg/dl
Low Density lipoprotein(LDL-C)	>130mg/dl

Data was recorded using standard forms on sex, age, gender, Blood pressure, previous history of attacks of myocardial infarction. Blood samples were collected from all the subjects after taking proper consent. Lipid profile investigations that included serum cholesterol, triglyceride, HDL –cholesterol and LDL-cholesterol were all carried out on a semi-automated analyzer using standard kits. The SPSS version.16.0 statistical package was used for analysis. P value < 0.05 was considered as significant.

Material and Methods:

The study design was a prospective consecutive sampling of all patients with CAD who satisfied the inclusion criteria. And was carried out in 111 patients 49 male (44.1%)

and 62 (55.9%) female) aged between 38 to 80 years, admitted to our intensive coronary care unit with ischemic heart disease. The diagnosis of MI was established by clinical, ECG and serum cardiac enzymes examination.

The patients data were collected from specialized cardiac clinic records during the 2017 June to 2018 July. Included in the study were patients with complete records showing detailed lipid profiles on 12 h fasting plasma samples who had a diagnosis of chronic stable angina or remote (at least 3 months) myocardial infarction and were not receiving statins or lipid lowering drugs on their initial clinic visit.

Plasma concentrations of total cholesterol and Triglycerides were determined by enzymatic methods (Boehringer–Mannheim). HDL cholesterol was measured after precipitations of VLDL and LDL by the phosphotungstate method (Boehringer–Mannheim). LDL was estimated using the Friedwald formula when TG levels did not exceed 300 mg/dl and otherwise using direct quantitative homogenous enzymatic assays.²⁴

Inter-assay coefficients of variation for total lipids, total cholesterol, HDL cholesterol and triglycerides were 1.08%, 1.01%, 6.28% and 1.52% respectively.

Total cholesterol=HDL-c+VLDL+LDL-c

VLDL-c= TG/5 ^{mg}, LDL=Total cholesterol-HDL-c-TG/5 mg/dl

Findings:

Mean lipid levels in the total Patients were: cholesterol 175.55±31.43mg/dL, triglycerides 193.46±40.83mg/dL, HDL-cholesterol 40.45±6.1mg/dL, LDL 92.47±17.42mg/dl. (Mean±SD) cholesterol /high density lipoprotein male/female (women 1.08±0.107/women 4.43±0.77), LDL-c/HDL-c (women 2.28±0.4/men 2.33±0.45).

Hypertensive patients had higher cholesterol and triglyceride levels compared with normotensive patients (180.80±31.7 vs 174.60±27.48mg/dL) (201.79±41.23 vs 190.98±35.21) respectively. Women and men HDL-c level are equal (40.15±4.7mg /dL vs 40.70±7.02mg/dL).

The total cholesterol levels (Mean±SD values) ranged between 175.55±31.43 in different age groups of patients and these values were significantly high compared to the CHO normal levels in corresponding age groups, except in the age groups of < 40 years. Except in the age groups of < 40 years the triglyceride levels were significantly high in all the other age groups of patients compared to normal level. The HDL cholesterol levels were significantly low in all age groups of patients except in <40 years age group compared to the normal level.

The mean LDL cholesterol levels were not significantly different in any of the age groups compared to the normal levels. Accordingly the numbers of patients with raised LDL cholesterol levels in all the age groups were also not significantly high. Mean and SD levels of four biochemical parameters except LDL were statistically significant.

Table 3: Analysis of Different biochemical parameters.

Biochemical parameters	Mean±SD values	range	p-value	Cut off level
Cholesterol (mg/dl)	175.55±31.43	110-290	0.006	>200mg/dl
Triglyceride(mg/dl)	193.46± 40.83	100-290	0.007	>150mg/dl

HDL cholesterol(mg/dl)	40.44±6.9	27-59	0.0011	<40mg/dl
LDL cholesterol(mg/dl)	92.47± 17.5	46-130	0.318	>130mg/dl

In this study 86(77.5%) married, 22(19.8%) widows and 3(2.7%) are unmarried, 66(59.5%) Litratres,45(40.5%) were ilitratres,62(55.9%)patients have positive family history of Diabetes mellitus,49(44.11%) patients are Didn't have Family history of D.M, and 84(75.7%) have Family history of hypertension($P<0.000$), 45(40.5%) have smoking history and 66(59.5%) are not smokers. 87(78.37%) have hypertension ($p<0.06$). 11.71% were normal weight , 76.57% over weight and 23.42% are obese .

Table 4: Biochemical Parameters according to normotensive and hypertensive patients.

Normotensive Patients n =24	Cholesterol(mg/dl) (Mean±SD)	Triglyceride(mg/dl) (Mean±SD)	HDL-c(mg/dl) (Mean±SD)	LDL-c(mg/dl) (Mean±SD)
	174.60±27.48	190.98±35.21	39.38±5.4	89.38±18.5
Hypertensive patients n=87	180.80±31.7	201.79±41.23	40.15±4.7	93.33±17.12

Mean cholesterol, Triglyceride and LDL-c level are high in Hypertensive patients than Normotensive but HDL –c level is high in hypertensive patients than normotensive.

Table 5: Analysis of different biochemical parameters according to sex.

Sex	Cholesterol(mg/dl) (Mean±SD)	Triglyceride(mg/dl) (Mean±SD)	HDL-c(mg/dl) (Mean±SD)	LDL-c(mg/dl) (Mean±SD)
Male No=49	175.4±31.8	189.29±39.47	40.15±4.7	93.05±18.44
Range	110-290	100-290	28-49	46-130
Female No=62	175.73±31.44	196.78±41.90	40.70±7.02	92.10±16.75
Range	110-230	110-286	27-59	54-120

Mean cholesterol, LDL-c and LDL-c level are equal in male and female patients, but Triglyceride is higher in female than male.

Table 6: analysis according to the family history of Disease, education, smoking, economic status of patients.

Parameters	Status	Numbers	Percentage (%)	p-value
Family history of hypertension	Yes	84	75.7	$P<0.000$
	No	72	24.3	
Family history of Diabetes mellitus	Yes	62	55.9	$p>0.217$
	No	49	44.1	
Occupation	Yes	38	34.2	$P<0.01$
	No	73	65.8	
Education	Yes	66	59.5	$P<0.405$
	No	45	40.5	
Economic	Good	16	14.4	$P<0.000$
	Middle	57	51.4	
	Bad	38	34.2	
Smoking	Yes	45	40.5	$P<0.046$

	No	66	59.5	
Patient Hypertension	Yes	87	78.4	P<0.000
	No	24	21.6	

In table no 6 explained, that 84(75.5%) has family history of hypertension ($P<0.000$), 62(55.9%) has Family history of Diabetes mellitus ($p>0.217$), 73(65.8%) patients doesn't have job ($P<0.01$), 66(59.5%) patients are educated ($P<0.405$), patient hypertension, smoking and economic are significant.

Discussion:

This is the first report of plasma lipid profile among afghan patients with CAD. It is one of the few studies in a developing country involving a large number of CAD patients over a wide age range. The effects of type of CAD, MI vs. AP, age, gender, high BP and body weight are described. This study was designed in a Nangarhar university Teaching Hospital of Jalalabad.

In atherosclerosis, fatty streaks tend to occur at sites of altered arterial shear stress such as bifurcations and are associated with abnormal endothelial function. They develop when inflammatory cells, predominantly monocytes, bind to receptors expressed by endothelial cells, migrate into the intima, take up oxidized low density lipoprotein (LDL) from the plasma and become lipid laden foam cells or macrophages. Extra-cellular lipid pools appear in the intimal space when these foam cells die and release their contents. Smooth muscle cells then migrate from the media of the arterial wall into the intima, in response to cytokines and growth factors produced by the activated macrophages, change from a contractile to a repair phenotype in an attempt to stabilize the atherosclerotic lesion. If they are successful, the lipid core will be covered by smooth muscle cells and matrix, producing a stable atherosclerotic plaque that will remain asymptomatic until it becomes large enough to obstruct arterial flow¹. Jellovesk (1997) has categorically proposed hypercholesterolemia and hyperlipidemia as risk factors for vascular disease²⁵.

The results were compared to population of normotensive and hypertensive Egyptians without CAD in the same age groups. The commonest isolated lipid abnormality was a reduced HDL-C in men (21.4%) and increased plasma TG (>150 mg/dl) in women (15.2%). A completely normal plasma lipid profile was present in 20.2% of Male and 29.9% of Female patients. Epidemiological studies have identified a number of important risk factors for CAD. Previous studies from India have reported importance of smoking, hypertension, diabetes mellitus and abnormal lipids in pathogenesis of CAD.²⁶

Almost all studies on risk factors for ischemic heart disease in Indians or abroad except one²⁷ have been cross sectional surveys.

Epidemiologically the strongest way to demonstrate a cause and effect relationship between a risk factor and disease would be a cohort study but is expensive in terms of money and time. So we believe that case-control design provides a reasonable alternative between a cross sectional and cohort study.

Enas et al. have shown that Indian emigrants to western states have a high prevalence of dyslipidemia and insulin resistance, thereby increasing the risk for CAD.^{28, 29}

Chodorowski et al.³⁰ found in patients with acute MI a decline in LDL-C until the age of 68, HDL-C levels did not change with age. Even though total cholesterol concentration represents a significant risk factor in the elderly, there is evidence that this relationship weakens progressively with advancing age to the point where TC levels do not appear to contribute to the risk of CAD or overall mortality beyond the age of 70 years.^{31, 32}

In our study demonstrates that with increasing age the cholesterol level and Coronary heart disease prevalence is increased, in the same patients high level of Triacylglycerol(>150mg/dl) is higher in female than male, cholesterol and HDL-c mean level are same in both sex, Low Density lipoprotein cholesterol level are same in both sex. But cholesterol, Triglyceride and LDL-c level are higher in hypertensive patient than Normotensive, but HDL-c level is equal in both hypertensive and Normotensive patients.

Conclusion:

This prospective Descriptive study shows that high serum cholesterol, LDL-c and Triglyceride and low HDL cholesterol are clinically significant in all the age groups above 40 years. In our study is associated with increased risk of coronary artery disease with LDL levels. The importance of this study lies in the fact that it reveals a distinct association of dyslipidemia with CAD and highlights patients with dyslipidemia as potential targets for early intervention. Hence early detection of abnormal lipid profile and its suitable management by life-style changes³³ and by drugs, if needed may play a key role in preventing the progress of the atherosclerotic plaque formation in coronary artery disease.

Suggestions:

- To decrease the prevalence of plasma lipid abnormalities in our society patients emphasizes the need for nationwide public awareness campaigns encourage healthy diet and physical activity.
- Routine screening in high risk groups for dyslipidemia and
- Other risk factors like: to stop smoking, control blood pressure, reduced weight in obese patients.

References

1. Newby DE, Grubb NR, Bradbury A. Cardio Vascular Disease. NR College, BR Walker, SHR Alston (Eds). (2010), Davidson's Principles & Practice of Medicine; 21st edition, Churchill Livingstone Elsevier Limited New Delhi, Pp. 577-579.
2. Brown DA, Breit SN. (06/06/2002); CRP and Vascular Risk. Syd path; Available from:[http://www.syddpath.stvincent.com.au/ tests/ CRP Risk. Html](http://www.syddpath.stvincent.com.au/tests/CRP_Risk.Html)
3. Ridker PM, Glynn RJ, Hennekens CH. C-Reactive Protein Adds to the Predictive Value of Total and HDL Cholesterol in Determining Risk of First Myocardial Infarction. *Circulation* 1998; 97: 2007- 2011.
4. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C - reactive protein and Low Density Lipoprotein Cholesterol Levels in the Prediction of First Cardiovascular Events. *N Eng J Med* 2002; 347: 1557-1565.
5. Lopez AD, Murray CC. The global burden of disease, 1990-2020. *Nat Med* 1998; 4:1241-3.
6. Murray CJL, Lopez AD. The global burden of disease: a comprehensive assessment of mortality and disability from disease, injuries and risk factors in 1990 and projected to 2020. Boston (Mass): Harvard School of Health; 1996.
7. The World Health Report 1999: The double burden: Emerging epidemics and persistent problems. WHO 1999. Available at: <<http://www.who.org>>.
8. World Health Statistics 2008: WHO. Available at: <[http:// www.who.int/whosis/whostat/EN_WHS08_TOCintro.pdf](http://www.who.int/whosis/whostat/EN_WHS08_TOCintro.pdf)>.
9. Beaglehole R. International trends in coronary heart disease mortality and incidence rates. *J Cardiovascular Risk* 1999; 6:63–8.
10. Okrainec K, Banerjee DK, Einsenberg MJ. Coronary artery disease in the developing world. *Am Heart J* 2004; 148:7–15.
11. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. INTERHEART study investigators. Effects of potentially modifiable risk factors associated with myocardial infarction in 52 countries (The INTERHEART Study) case-control study. *Lancet* 2004; 364:937–42.
12. Johnson CL, Rifkind BM, Semplos CT, Carroll MD, Bachorik PS, Briefel RR, et al. declining serum total cholesterol levels among US adults. The National Health and Nutrition Examination Surveys. *JAMA*. 1993; 269(23):3002–8.
13. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation* 1998; 97:596-601.
14. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. *Indian J Med Res* 2007; 125:217-30.
15. Biorch, G., Blomquist, G. and Sievers, J. (1957) Cholesterol values in patients with myocardial infarction and normal control group. *Acta. Med. Scand.* 156,493-497.
16. Tibblin, G. and Cramer, K. (1963) Serum lipids during the course of acute myocardial infarction and one year afterwards *Acta Med. Scand.* 174,451-455.
17. Avogaro, A., Bittilin Bon, G., Cazzalato, C. Quinci, G.B., Sanson, A., Sparla, H. and Zagatti, G.C. (1978). Variations in Apo lipoproteins B and A during the course of myocardial infarction. *Eur. J. Clin. Invest.* 8,121-129.
18. Ryder, R.E.J., Hayes, T.M., Mulligan, I.P., Kingwood, J.C., Williams, S. and Owens, D.R.(1984) How soon after myocardial infarction should plasma lipid values be assessed ? *Br.Med. J.* 289, 1651-1653..

19. Jackson, R., Scragg, R., Marshall, R., White, O'Brien, K. and Small, C. (1987) Changes in serum lipid concentrations during first 24 hours after myocardial infarction. *Br. Med. J.* 294, 1588-1589.
20. Heldenburg, D., Rubenstein, A., Levkov, O., Berns, L., Werbin, B. and Tamir, L. (1980) Serum lipids and lipoprotein concentrations during the acute phase of myocardial infarction. *Atherosclerosis* 35,433-437.
21. Swedarsen, M., Vythilingum, S., Jalal, I. and Nadar, R. (1988). Plasma lipids can be reliably assessed within 24 hours after acute myocardial infarction. *Postgrad. Med. J.* 64, 352-356.
22. Buckley, B.M. and Bold, A.M. (1982) Managing hyperlipidaemias, *Br. Med. J.* 285, 1293-1294.
23. Schlant, R.C. and Digirolamo, M. (1978) Modification of risk factor in the prevention and management of coronary atherosclerotic heart disease: *The Heart*, 4th Ed., Hurst J.W., Logue R.B., Schlant R.C., Wenger N.K., New York: McGraw Hill Book Co., p 1311-1344.
24. Friedwald, W.T., Levy, R.I. and Fredrickson, D.S.,(1972) Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin. Chem.* 18, 499-502.
25. Jelovesk FR. Cholesterol and Lipid Disorders. *Women's Diagnostic Cyber*; 1997; Available from: <http://www.wedxcyber.com/ngen15.htm>, 6 July 2004.
26. Jain P, Bhandari S, Siddhu A. A case control study of risk factors for coronary heart disease in urban Indian middle aged males. *Indian Heart J* 2008; 60:233-40.
27. Enas EA, Garg A, Davidson MA, Nair VM, Huet BA, Yusuf S. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. *Indian Heart J* 1996; 48:343-53.
28. Enas EA, Yusuf S, Sharma S. Coronary artery disease in South Asians. Second meeting of the International Working Group. 16 March 1997, Anaheim, California. *Indian Heart J* 1998; 50:105-13.
29. Maitra A, Shanker J, Dash D, John S, Sannappa PR, Rao VS, et al. Polymorphisms in the IL6 gene in Asian Indian families with premature coronary artery disease – The Indian Atherosclerosis Research Study. *Thromb Haemost* 2008; 99:944-50.
30. Chodorowski Z, Anand JS, Foerster J, Gruchaa M, Chlebus Differences in lipid profile in patients with first myocardial infarction occurring at different ages. *Borgis – New Medicine* 2004; 2:48–51.
31. Kronmal RA, Cain KC, Ye Z, Omenn GS. Total serum cholesterol levels and mortality risk as a function of age. A report based on the Framingham data. *Arch Intern Med* 1993; 153:1065–73.
32. Krumholz HM, Seeman TE, Merrill SS, Mendes de Leon CF, Vaccarino V, Silverman DI, et al. Lack of association between cholesterol and coronary heart disease mortality and morbidity and all-cause mortality in persons older than 70 years. *JAMA* 1994; 272(17):1335-40.
33. Thompson PD, Buchner D, Pina IL, Balady GJ, Williams MA, Marcus BH, et al. *Circulation* 2003;107:3109-16.