https://doi.org/10.29309/TPMJ/2022.29.01.6399

The Professional Medical Journal
www.theprofesional.com
2022, Volume, 29 Issue, 01

ORIGINAL ARTICLE

Association of Non HDL-Cholesterol and other lipid parameters in patients with Acute Coronary Syndrome.

Syeda Sabahat Haider[1], Muhammad Shahid[2], Khalid Razaq[3], Shama Iqbal[4], Muhammad Tariq Ghafoor[5], Nabila Rauf[6]

Article Citation: Haider SS, Shahid M, Razaq K, Iqbal S, Ghafoor MT, Rauf N. Association of Non HDL-Cholesterol and other lipid parameters in patients with Acute Coronary Syndrome. Professional Med J 2022; 29(1):82-87. https://doi.org/10.29309/TPMJ/2022.29.01.6399

ABSTRACT… Objective: To determine the frequency of hypercholesterolemia in patients who are diagnosed with acute coronary syndrome and to also document the association of Non HDL-C with Acute coronary syndrome in these patients. **Study Design:** Observational Cross Sectional study. **Setting:** Department of Cardiology and Pathology of Sheikh Zayed Hospital, Rahim Yar Khan. **Period:** September 2019 to February 2020. **Material & Methods:** One hundred and thirty five patients with Acute coronary syndrome were included using non probability purposive sampling technique and equal number of patient who visited the outpatient department or admitted in indoor with complaints other than ACS were taken as control (n=135). Frequency and percentages were calculated and odd ratio was determined to see the association. Statistical significance was set at P-value<0.05. **Results:** Patient's mean age was 55.5±12.4 years and there were 98(73%) male and 37(27%) female. Higher Non HDL-C (>130mg/dl) was found in 120(88.9%) cases and in 38(28.1%) controls with odd ratio 20.4211 at 95 %CI and p value <0.001.Hypercholesterolemiawas seen in 49(36.3%) of the cases while in 21(15.6%) of control group (without ACS) with odd ratio of 3.3 and p-value <0.001. Odds ratio was maximum for Non HDL cholesterol, followed by LDL cholesterol, HDL cholesterol and Total cholesterol. **Conclusion:** Non-HDL cholesterol showed a good association in patients with ACS than with primary target LDL-C or total cholesterol.

Key words: Acute Coronary Syndrome (ACS), Association, Dyslipidemia, Hypercholesterolemia, Non HDL-C.

INTRODUCTION

Twentieth century has declared cardiovascular diseases as the major cause of worldwide disability as shown by epidemiological transition. Cardiovascular disease which encompass coronary heart disease, peripheral vascular disease and cerebrovascular disease will be the major cause of fatality among developed and developing countries by 2030.[1] South Asian region has high morbidity and mortality rates due to CVD as compare to the western part of globe. Being located in the Southern part, Pakistan also shares the same fate as the rest of the Southern countries regarding this debilitating disease manifesting quite at earlier age by 2020.[2] This is an alarming situation and appropriate strategies should be developed for the prevention of CVD.

A study showed that among the documented conventional risk factor, 91% individuals in Pakistan have at least one out of four risk factors. But the risk factor differ in respect of age group and gender of the study population.[4]

Large prospective study like The Framingham Heart Study and many other have documented the role of these major cardiovascular disease risk factor in the development of vascular events. However there is a considerable proportion of individuals who do not express any of the classical risk factor. So the search of new and novel biomarkers was initiated that can better predict and assess cardiovascular event. In recent years, many biomarkers have been recommended by researchers to anticipate about atherosclerosis and its thrombotic complications.[5] Disturbance in the lipid parameters like total cholesterol, LDL and triglycerides is the major causative factor

1. MBBS, FCPS, Associate Professor Pathology, Sheikh Zayed Hospital, Rahim Yar Khan.
2. MBBS, FCPS, Assistant Professor Cardiology, Sheikh Zayed Hospital, Rahim Yar Khan.
3. MBBS, FCPS, Assistant Professor Cardiology, Sheikh Zayed Hospital, Rahim Yar Khan.
4. MBBS, M.Phil, Associate Professor Physiology, Sheikh Zayed Hospital, Rahim Yar Khan.
5. MBBS, FCPS, Professor of Surgery, Sheikh Zayed Hospital, Rahim Yar Khan.
6. MBBS, M.Phil (Chemical Pathology), Assistant Professor Pathology, Sheikh Zayed Hospital, Rahim Yar Khan.

Correspondence Address:
Dr. Syeda Sabahat Haider
Associate Professor Pathology
Sheikh Zayed Hospital, Rahim Yar Khan.
sabahatTariq@gmail.com

Article received on: 03/02/2021
Accepted for publication: 12/06/2021

for CVD affecting South Asian population.[6] This can be attributed by the excessive use of trans and saturated fats in routine cooking while deep frying along with lack of physical activity are one of emerging feature of Pakistani population, thus leading to derangement in the lipid profile. High consumption of carbohydrates and processed food with artificial sweetener also contributes among the reasons for unhealthy dietary habits.[2] The use of non high density lipoprotein as therapeutic target is not a novel concept. This concept was also used to randomize the study population in The Helsinki Heart Study.[7] All atherogenic lipoprotein (cholesterol content) which are responsible for CVD are represented in Non-HDL as compare to LDL-C alone. Therefore, in the management of dyslipidemia, physicians also focus on non-HDL levels than targeting LDL-C alone which has well documented role in the pathogenesis of CHD.[8] In many researches, it was found that Non-HDL cholesterol has a promising role in the prediction of CHD risk than LDL-C alone.[9,10] Researchers have also found the beneficial role of Apo-lipoprotein B and non HDL cholesterol on coronary risk assessment.[11] But inadequate data is available to establish the role of the non-conventional risk factor in acute coronary syndrome (ACS). Hence, this research was planned to find out the relationship of non HDL-C in patients with acute coronary syndrome and to compare the non-HDL cholesterol and other lipid parameters in patients and control.

MATERIAL & METHODS

It was an observational cross sectional study of six month duration i.e; From September 2019 to February 2020 in the Sheikh Zayed Hospital Rahim Yar khan. The study started after taking the ethical approval from the IRB department of SZMC, RYK (260/IRB/SZMC/SZH). Total 200 patients were selected on the basis of inclusion criteria based on American Heart Association[12] and informed consent was given to all of them. We lost 75 patient follow up details so 135 study subject (group-A) were finally included.

All those patients who were diagnosed with severe liver disease, malignancy, active infectious disease or using immunosuppressant or anticoagulants were excluded to reduce the bias. We collected the baseline laboratory data and detailed medical history of the study subjects. Whereas controls were the patients admitted in the same hospital during the same period with diagnosis other than acute coronary syndrome (Group B). The blood sample were drawn within 30 minutes of admission, sera was separated and kept frozen till analysis. Lipid profile of cases and control was run on the automated chemistry analyzer (Beckman Coulter AU 680). The record of all the conventional risk factors of the selected subjects was collected and confirmed by their past medical history. Dyslipidemia was labeled when serum cholesterol was found to be >200 mg/dl, serum triglycerides level >150 mg/dl, serum LDL –C level>130 mg/dl and low serum levels of HDL-C level <40 mg/dl. Non HDL-C was calculated by deducting the HDL-C from total cholesterol in both of cases and control.

The Data of qualitative variables was presented as frequency and percentage (%). While mean ± Standard Deviation (SD) presented the continuous variables. The resultant group difference was compared using Student's t-test or Mann Whitney test and, chi-square test or Fisher's exact test for continuous and categorical variables, respectively. A two tailed p-value of less than 0.05 was taken as statistically significant. SPSS 17.0 version was used to perform the data analysis.

RESULTS

The mean age was 55.5±12.4 year in the cases in group A and in group B (control) 38.5±11.7 year respectively. Out of 135 cases 98(72.6%) were male and 37 (27.4%) were female while in control group 66(49%) were male and 69(51%) were female. Total cholesterol, LDL-C and NHDL-C were found comparatively higher in group A (cases) than in Group B (control) while HDL-C was quite low in Group A than in Group B. Majority of patients (group B) with acute coronary syndrome (88.9%) have shown increased non HDL-C, followed by raised LDL (80%) and low HDL (76.3%) and hypercholesterolemia (36.3%) with odd ratio of 20.4; 8.5; 5.5 and 3.3 respectively.

Variable	Case (n=135)	Control (n=135)	P-Value
Total Cholesterol (mg/dl)	215±14.2	169±12.1	<0.001
HDL-C (mg/dl)	33.4±4.8	47.6±10.1	<0.001
LDL-C (mg/dl)	122.7±33.6	89.9±29.8	<0.001
NHDL-C (mg/dl)	155.9±34.6	124.9±29.8	<0.001
TC/HDL ratio	5.5 ±2.1	3.5 ± 1.6	< 0.001

Table-I. Comparison of serum lipid parametersb/w cases and control.

Lipid Profile	Group A (n=135)	Group B (n=135)	Odds Ratio (95% CI)
Total Cholesterol (mg/dl) >200 < 200	49 (36.3%) 86 (63.7%)	21 (15.6%) 114 (84.4%)	3.3 (11.73-3.9)
HDL-C (mg/dl) < 40 >40	103 (76.3%) 32 (23.7%)	50 (37%) 85 (63%)	5.5 (3.2-9.3)
LDL-C (mg/dl) > 100 < 100	108 (80%) 27 (20%)	43 (31.9%) 92 (68.1%)	8.5 (4.9-14.7)
NHDL-C (mg/dl) > 130 < 130	120 (88.9%) 15 (11.1%)	38 (28.1%) 97 (71.9%)	20.4 (10.5-38.5)

Table-II. Association of Non HDL-C and other lipid parameters.

DISCUSSION

Dyslipidaemia, risk factor of CVD, is generally defined as total cholesterol, LDL and Triglycerides levels above 90th percentile of general population and HDL below 10th percentile of general population. Dyslipidaemia especially increase in LDL decrease in HDL and increased in Total cholesterol and total triglycerides are more common and important modifiable risk factors. The evidence from multiple randomized clinical trials has been collected that lowering levels of TC and LDL-C are beneficial in reducing risk of atherosclerotic diseases.[13-15]

In this study total cholesterol was significantly higher in group A (215.8 ± 14.2) as compared to control group (169.3 ± 12.2) with P value < 0.001 and odds ratio 3.3. 63.7 % of patients had total cholesterol < 200 mg/dlwhile 36.3 % of individuals had cholesterol > 200mg/dl. Total cholesterol was found to be high in 15.6%.

HDL-C was significantly lower in diseased patients (36.4 ± 6.8) as compared to control group (42.8 ± 12.3) with P value < 0.001 and odds ratio 5.5. This is in accordance to study done by Alberto Cordero et. al.[16] that found patient with ACS has lower plasma concentration of HDL-C. Low HDL-C level is associated with rapid progression of asymptomatic atherosclerotic process to symptomatic functional clinical phenomenon. This process would be mediated by abnormal endothelial function, enhanced LDL-C oxidation, diminished cholesterol transport andinflammatory process in vessel wall. 76.3% of cases had HDL-C < 40 and 23.7 % of cases had HDL-C> 40 mg/dl in control group 37% of individuals had< 40 mg/dl HDL-C.LDL-C was significantly higher in group A (122.7 ± 33.6) as compared to group B (89.9 ± 29.8) with P value < 0.001 and odds ratio 8.5. 80 % of the cases had LDL > 100 mg/dl as compared to control group in which 31.9 % of individuals had> 100 mg/dl. These results are in accordance with the studies done byNayaket.al[17], Nigam et al.[18] and Reddy and Bittner[19] who reported similar results in acute coronary syndrome as compared to control.

NHDL-C was found to be significantly higher in group A (cases with ACS), (155.9 ± 34.6) as compared to control group (124.9 ± 29.8) with P value < 0.001 and odds ratio 20.4. 88.9 % of cases had NHDL-C > 130 mg/dl as compared to only 28.1 % of the control.

Majority of patients (88.9%) have shown increased non HDL-C, followed by raised LDL (80%) and low HDL (76.3%). These results showed resemblance to Zaman Q et al[20] that also found raised LDL in patients with acute coronary syndrome. Arun Bahulikar et al[21], also documented similar results that Coronary artery disease events can be best predicted and measured by non HDL-C. But some other study suggested that non HDL –C was not a predictive marker of acute coronary syndrome.[22] As it is known that Non-HDL-C

includes all potential atherogenic lipoproteins, including LDL, VLDL, lipoprotein (a), IDL and chylomicron remnants. Therefore, this calculated parameter can be regarded as better indicator of atherogenic potential of lipid particles than LDL-C. As Non-HDL-C can be calculated from simply from already advised and measured lipid profile (non-HDL-C = total cholesterol minus HDL-C), and thus it causes no additional cost or discomfort to the patient. Moreover fasting sample is required for the measurement of LDL-C while it's not the case with NON-HDL. This is very helpful for the risk assessment of admitted patients which mostly are not in fasting state. Other important atherogenic lipoprotein like Apo B and LDL remnant particle measurement assay are costly and mostly not standardized. That is why measuring these particles has not been included in the general guidelines of national cholesterol treatment plan. Whereas non-HDL-C is a calculated parameter so adds no further cost, uses a standard (fasting or no fasting) lipid panel for calculation, and is endorsed by current guidelines. Focusing on non-HDL-C will avert the peculiar attention upon expansive test measuring total Apo B concentration, LDL particle number or its phenotyping (type A or B). Some studies have explored the risk factors of atherosclerosis and tried to find relationships between them and compared their role in progression of ischemic heart lesion especially between LDL-C or Non-high density lipoprotein. The Health Professionals Follow-up Study[23] suggested that the risk of coronary heart disease was more strongly related with non HDL -C. Similarly, the observation of Framingham Heart Study[24] was that for every non-HDL-C level, the risk for coronary heart disease was not linked with LDL-C concentration. On the other hand, at every LDL-C level, non HDL showed direct and graded correlation with risk of coronary heart disease. Liu et al.[25] study supported the results in favor of non HDL- C even in patients with diabetes mellitus concluding that Non-HDL-C was better predictor of ischemic heart events than LDL-C.

LIMITATION

Although we attempted to choose a control group that was matched with the cases with respect to most of the conventional cardiovascular risk factors, but smoking, and BMI could not be matched. Hence, they may act as confounding factors. This research was conducted in a single tertiary care hospital and represents only a small population. Patients may have other cardiovascular risk factors like chronic inflammatory diseases, raised high sensitivity C-reactive protein, raised fibrinogen etc. which were not studied.

CONCLUSION

Non-HDL cholesterol showed a good association in patients with ACS than with primary target LDL-C or total cholesterol. The results showed correlation between Non-HDL and ACS. Measurement of Non- HDL cholesterol is simple, cost-effective and convenient because it does not require 12-hour fasting and no additional cost, clinicians may choose Non-HDL as a routine measure in everyday practice.

REFERENCES

1. Sasaki J, Yokoyama M, Matsuzaki M, Saito Y, Origasa H, Ishikawa Y, et al. **Relationship between coronary artery disease and non-HDL-C, and effect of highly purified EPA on the risk of coronary artery disease in hypercholesterolemic patients treated with statins: Sub-analysis of the Japan EPA Lipid Intervention Study (JELIS).** J AtherosclerThromb. 2012; 19(2):194-204.

2. Nishtar S, Wierzbicki AS, Lumb PJ, Lambert-Hammill M, Turner CN, Crook MA, et al. **Waist-hip ratio and low HDL predict the risk of coronary artery disease in Pakistanis.** Curr Med Res Opin. 2004; 20(1):55–62.

3. Butt Z, Shahbaz U, Hashmi AT, Naseem T, Khan MM, Bukhari MH. **Frequency of conventional risk factors in patients with acute coronary syndrome in males and females. Annals of King Edward Medical University.** 2010; 16(1):56.

4. Jayachandra S, Agnihotram G, Rao RP, Murthy CV. **Risk factor profile for coronary artery disease among young and elderly patients in Andhra Pradesh.** Heart India. 2014; 2(1):11.

5. Berry JD, Dyer A, Cai X, Garside DB, Ning H, Thomas A, Greenland P, et al. **Lifetime risks of cardiovascular disease.** N Engl J Med. 2012; 366:321- 329.

6. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. **Executive summary: Heart disease and stroke statistics.2010 update: A report from the American Heart Association.** Circulation 2010; 121:948-54.

7. Frick MH, Elo O, Haapa K, Heinonen OP, Heinsalmi P, Helo P, et al. **Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease.** N Engl J Med 1987; 317(20):1237–45

8. Heart Protection Study Collaborative Group. **MRC/BHF HeartProtection Study of cholesterol lowering with simvastatin in high-risk individuals: A randomized placebo-controlled trial.** Lancet 2002; 360:7-22.

9. Blaha MJ, Blumenthal RS, Brinton EA, Jacobson TA. **The importance of non-HDL cholesterol reporting in lipid management.** J ClinLipidol. 2008 Aug; 2(4):267-73.

10. **Acute Coronary Syndrome [Internet].** Heart.org. 2017 [cited 11 February 2017]. Available from: http://www.heart.org/HEARTORG/Conditions/HeartAttack/AboutHeartAttacks/Acute-Coronary Syndrome_UCM_428752_Article.jsp#.WJ-lYzt97IU.

11. Lu W, Resnick HE, Jablonski KA, Jones KL, Jain AK, Howard WJ, Robbins DC, Howard BV. **Non-HDL cholesterol as a predictor of cardiovascular disease in type 2 diabetes: The strong heart study.** Diabetes Care. 2003 Jan; 26(1):16-23.

12. Ramjee V, Sperling LS, Jacobson TA. **Non-high-density lipoprotein cholesterol versus Apo lipoprotein B in cardiovascular risk stratification: do the math.** J Am CollCardiol. 2011 Jul 26; 58(5):457-63.

13. Collins R, Armitage J, Parish S, Sleigh P, Peto R; **Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: A randomized placebo-controlled trial.** Lancet.2003; 361(9374):2005-16.

14. Wilkins JT, Ning H, Stone NJ, Criqui MH, Zhao L, Greenland P, Lloyd-Jones DM. **Coronary heart disease risks associated with high levels of HDL cholesterol.** J Am Heart Assoc. 2014 Mar 13; 3(2).

15.. Milani RV, Lavie CJ. **Another step forward in refining risk stratification: Moving past low-density lipoprotein cholesterol.** J Am CollCardiol. 2011 Jul 26; 58(5):464-6.

16. Cordero A, Moreno-Arribas J, Bertomeu-González V, Agudo P, Miralles B, Masiá MD et al. **Low levels of high-density lipoproteins cholesterol are independently associated with acute coronary heart disease in patients hospitalized for chest pain.** Rev EspCardiol (Engl Ed). 2012 Apr; 65(4):319-25.

17. Nayak SB, Pinto Pereira LM, Boodoo S, Kimberlyali A, Baptiste C, Maraj S et al. **Association of troponin T and altered lipid profile in patients admitted with acute myocardial infarction Arch PhysiolBiochem.** 2010 Feb; 116(1):21-7.

18. Nigam PK, Narain VS, Hasan M. **Serum lipid profile in patients with acute myocardial infarction.** Indian J ClinBiochem. 2004 Jan; 19(1):67-70.

19. Reddy G, Bittner V. **LDL lowering after acute coronary syndrome: Is lower better?** Curr Treat Options Cardiovasc Med. 2013 Feb; 15(1):33-40.

20. Zaman Q, Arif MB, Fazal I, Mirza SA, Ali A, Satti L. **Frequency of dyslipidemia in young patients with acute myocardial infarction.** Pak Armed Forces Med J. 2012; 3- 10.

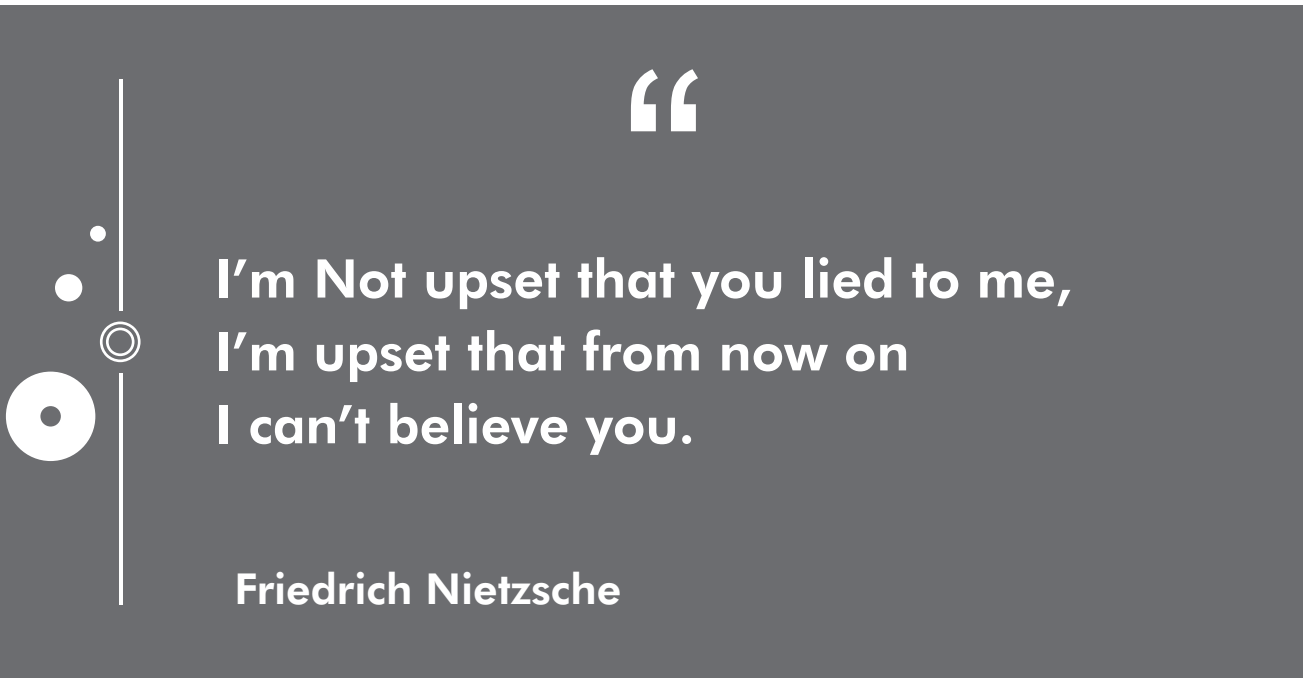
21. Bahulikar A, Tickoo V, Phalgune D. **Association of Non-HDL cholesterol, homocysteine and Vitamin D in acute coronary syndrome assoc physicians Ind.** 2018;66(8):22-5.

22. Koncsos P, Fülöp P, Juhász I, Bíró K, Márk L, Simonyi G et al. **Changes in triglyceride, HDL-C, and non-HDL-C levels in patients with acute coronary syndrome.** 2016; 128(23-24):858-63.

23. Chen M, Li Y, Sun Q, Pan A, Manson JE, Rexrode KM, et al. **Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults.** Am J ClinNutr. 2016; 104(5):1209-17.

24. Wongcharoen W, Sutthiwutthichai S, Gunaparn S, Phrommintikul A. **Is non-HDL-cholesterol a better predictor of long-term outcome in patients after acute myocardial infarction compared to LDL-cholesterol? a retrospective study.** BMC CardiovascDisord. 2017; 17(1):10.

25. Liu J, Sempos C, Donahue RP, Dorn J, Trevisan M, Grundy SM. **Joint distribution of non-HDL and LDL cholesterol and coronary heart disease risk prediction among individuals with and without diabetes.** Diabetes Care. 2005 Aug; 28(8):1916-21.



AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Syeda Sabahat Haider	Main concept, study design and literature review.	
2	Muhammad Shahid	Acquisition of data, or analysis & interpretation of data.	
3	Khalid Razaq	Acquisition of data, or analysis & interpretation of data.	
4	Shama Iqbal	Discussion and review of literature.	
5	Muhammad Tariq Ghafoor	Final approval of the version, babilography.	
6	Nabila Rauf	Data collection and analysis.	