Original Article

Nepalese Heart Journal 2022; Vol 19(1), 35-38

Apolipoprotein B and Lipid Profile among Patients Diagnosed with Acute Myocardial Infarction

Deependra Shrestha[1], Binod Kumar Yadav[1], Ratna Mani Gajurel[2], Vijay Kumar Sharma1, Mithlesh Raut[1], Aseem Bhattarai[1], Sweta Shrestha[1], Sapana Ghimire[1], Basu Shakya[1], Eans Tara Tuladhar[1]

[1] Department of Biochemistry, Maharajgunj Medical campus, Institute of Medicine, Kathmandu, Nepal.
[2] Department of Cardiology, Manmohan Cardiothoracic Vascular and Transplant Center (MCVTC), Institute of Medicine, TUTH, Kathmandu, Nepal

Corresponding author: Eans Tara Tuladhar
Department of Biochemistry, Maharajgunj Medical campus, Institute of Medicine, Kathmandu, Nepal.
Email: eanstara@gmail.com
ORCID ID NO: 0000-0001-5705-3953

Cite this article as: Shrestha D., Yadav B.K., Gajurel R.M., et al. Apolipoprotein B and Lipid Profile among Patients Diagnosed with Acute Myocardial Infarction. Nepalese Heart Journal 2022; Vol 19(1) : 35-38

Submission date: 3rd January 2022
Acceptance date: 26th April 2022

Abstract

Background and Aims: Acute myocardial infarction (AMI) is a leading cause of death among men and women globally and often a sequelae to atherosclerotic cardiovascular disease [ASCVD]. Atherosclerosis is linked with abundance of Apolipoprotein B [ApoB] and the lipid constituents they are carrying. There are limited data of ApoB status and its usage alongside conventional lipid profile parameters among AMI patients of Nepal. The study aimed to estimate the blood level of ApoB and determine its usefulness alongside analysis of total cholesterol[TC], triglycerides[TG], high density lipoprotein cholesterol[HDL-C], low density lipoprotein cholesterol[LDL-C],non-HDL cholesterol, LDL/HDL ratio in AMI patients .

Methods: This was a hospital based comparative cross-sectional study conducted in patients attending Manmohan Cardiothoracic Vascular and Transplant Centre [MCVTC] and Shahid Gangalal National Heart Centre[SGNHC] over a period of 1 year. Seventy three diagnosed AMI patients were enrolled using convenient sampling technique. Forty patients undergoing regular general health checkup in Tribhuvan University Teaching Hospital [TUTH] were recruited as controls. Laboratory analysis was carried by turbidimetric method for Apolipoprotein B and enzymatic methods for lipid profile parameters in department of Biochemistry, TUTH. Data was analyzed using SPSS version 18.0.

Results: AMI was seen in the mean age of 56±11 years with male predominance. Mean level and standard deviation of ApoB was 99.2±17.7mg/dl in AMI which was significantly higher than controls. ApoB showed moderate correlation with non-HDL cholesterol [r=0.378,p<0.001] and HDL-C[r= -0.490,p< 0.001].

Conclusion: Our study found a significantly higher level of ApoB in AMI with moderate correlation with non HDL-C and HDL-C, necessitating its usage as a complementary marker to conventional lipid profile.

Keywords: Apolipoprotein B, Atherosclerotic cardiovascular disease, Lipid profile

DOI: https://doi.org/10.3126/njh.v19i1.45292

Introduction

Cardiovascular disease is the most common cause of morbidity among non-communicable diseases and myocardial infarction is the fatal one.[1] Nepal lies in Southeast Asia Region which has among the highest burden of cardiovascular disease in the world.[2] A report showed that the incidence of CVD in Nepal was 569.5 per 100,000 population in males and 479.1 per 100,000 population in females in the year 2017.[3] AMI is mostly associated with coronary artery occlusion through plaque rupture/fissuring which is a consequence of atherosclerosis, also called atherosclerotic cardiovascular disease[ASCVD]. Atherosclerosis is carried out from the initiation to the end by inflammatory process within blood vessel wall by the retention of apoB lipoproteins.[4] ApoB containing particle is considered the basic unit of injury to vascular wall signifying the atherogenic particle population of lipoproteins. It represents and unifies all non-HDL lipids like triglycerides of chylomicrons and VLDL and cholesterol of LDL, IDL and chylomicron remanants.[5] The fluctuating level of lipid profile parameters have been witnessed in AMI by different studies emphasizing ApoB study. [6,7,8] ApoB level status study is emphasized alongside conventional lipid profile in Nepalese population of AMI.9,10 However, there is paucity of such studies in context to Nepal. We aim to estimate ApoB level in AMI patients and compare with the healthy controls, analyze how lipid parameters like TC,TG,LDL-C,HDL-C behave in the diagnosed cases of AMI of Nepalese population , prior to any therapeutic intervention and finally correlate lipid profile parameters with ApoB.

Methods

This was hospital based comparative cross-sectional study. Ethical approval was taken from IRC of Institute of Medicine[Ref:305(6-11-E)2/074/075] and SGNHC (SGNHC/IRC no:25-2018).A total of 73 patients with AMI were recruited for the study . Diagnosed AMI patients were recruited from Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC) and Shahid Gangalal National Heart Centre (SGNHC) over a period

between November 2017 to December 2018 through convenient sampling after informed consent. The leftover blood samples used for diagnosis of AMI patients in the laboratories MCVTC and SGNHC were retained for our study. Such blood sample provided the scope to analyse the parameters prior to treatment. Forty patients undergoing regular checkup in general health clinic of Tribhuvan University Teaching Hospital (TUTH) were recruited for comparison. The laboratory reference range was also used for comparison for lipid profile and kit specific reference range for ApoB. The research component of laboratory analysis was carried in department of Biochemistry, Tribhuvan University Teaching Hospital. Apolipoprotein B was measured by turbidimetric method [SPINREACT, Spain] in ERBA XL-200 fully automated analyzer. Total serum cholesterol (TC), High density lipoprotein cholesterol (HDL-C), total serum triglycerides (TG) were measured by using standard enzymatic method [BIOLABO kits, France]. Serum Low density lipoprotein cholesterol [LDL-C] was directly measured by LDL-C Select FS kit [DiaSys, Germany]. TC, HDL-C, LDL-C and TG were all analyzed in fully automated spectrophotometry-based BT Analyzer 1500.Non HDL cholesterol was calculated using formula [total cholesterol -HDL cholesterol].LDL/HDL ratio was also calculated using the value of LDL-C and HDL-C. All the data were collected, summarized and analyzed by SPSSs software version 18.

Results

Demographic characteristics showed that AMI group had 48 (66%) males and 25 (34%) females with male to female ratio as 1.9:1. The age of patients suffering from MI ranged between 30 and 85 years with the mean age of 56±11 years and the median age was 60 years. The interquartile range was 47 to 62 years in males and 50 to 69 in females. Five out of 73 (6.8%) patients were under 40 years of age. There were total of 42 (57.5%) smokers in the AMI group whereas control group had total of 14 (35%) smokers. The mean ApoB level with its range is tabulated for AMI and the healthy control group in Table 1. Apo B level was found to be significantly higher in the AMI cases than the non AMI healthy controls ($p<0.001$). The risk ratio of AMI 1.6 [95%CI: 1.3,2.0] and odd ratio is 8.1[95%CI: 2.3,28.8] based on the reference value of the kit.

The comparison of mean level and the range of different lipid profile parameters [TC, TG, HDL, LDL, VLDL, non-HDL cholesterol, LDL/HDL] have been compared between AMI cases and controls and presented in Table 1.This study showed that triglycerides ,LDL-C and VLDL-C level were significantly higher in AMI than control ($p<0.05$) and HDL-C level was significantly lower in the cases than the control group($p<0.001$). The total cholesterol level did not show any significant difference between AMI and healthy controls. Based on guidelines ATP III of national cholesterol education program, the frequency of the cases and controls who have lipid profile parameters beyond the recommended cutoffs are presented in table 2 with the relative risk [RR] and odds ratio[OR].

Pearson correlation was carried out between the ApoB and other lipid parameters. ApoB showed fair correlation with LDL[r=0.296,p=0.001], positive moderate correlation with non HDL-C[r=0.378,p<0.001] and moderate negative correlation with HDL-C[r= -0.490,p< 0.001] .The correlation of ApoB with lipid profile parameters are tabulated in table 3.

Table 1: ApoB and lipid profile parameters among cases and controls

Parameters	AMI Mean ±SD [range]	Healthy controls Mean±SD [range]	p value
TC (mmol/L)	4.97±1.03 [3.1 to 7.2 mmoles/l]	4.84±0.29 [4.3to 5.5mmoles/l]	0.438
Triglycerides	3.18±1.90 [0.13 to 6.75mmoles/l]	2.50±1.29 [0.11to 5.16mmoles/]	<0.05**
HDL (mmol/L)	1.05±0.12 [0.8 to 1.4 mmoles/l]	1.62±0.25 [1.1 to 2.3 mmoles/l]	<0.001*
LDL (mmol/L)	2.47±0.72 [1.2 to 4.4 mmoles/l]	2.08±0.49 [1.1 to 3.0 mmoles/l]	<0.05**
VLDL (mmol/L) (calculated)	1.44±0.86 [0.06 to 3.07 mmoles/l]	1.13±0.58 [0.05 to 2.34 mmoles/l]	<0.05**
Non HDL Cholesterol	3.92±0.92 [2.28 to 5.85 mmoles/l]	3.21±0.38 [2.46 to 4.14 mmoles/l]	<0.001*
LDL/HDL	2.33±0.59 [1.25 to 3.24]	1.30±0.37 [0.77 to 2.01]	<0.001*
ApoB (mg/dl)	99.25±17.70 [28 to130 mg/ dl]	70.73±16.74 [35.5 to117mg/dl]	<0.001*

**Significant at 0.001 level.*
***Significant at 0.05 level.*

Table 2: Frequencies of cases and controls with lipid profile parameters beyond the desirable range

Parameters	Desired range [ATP III guidelines, NCEP]17	No of Cases [lipid parameters outside the desired range]	No of Controls [lipid parameters outside the desired range]	Odds ratio [95% CI]	Risk ratio [95% CI]
Total cholesterol	Less than 5.17 mmoles/l [<200mg/dl]	33	6	4.67 [1.75, 12.49]	1.565 [1.22, 2.01]
LDL cholesterol	Less than 2.6 mmoles/l [<100mg/dl]	33	8	3.3 [1.34, 8.13]	1.449 [1.122, 1.871]
HDL cholesterol	More than 1.04 mmoles/l [>40mg/dl]	34	1	34 [4.43, 260.80]	1.943 [1.545, 2.443]

triglycerides	Less than 1.69 mmoles/l [<150mg/dl]	53	35	0.37 [0.13, 1.10]	0.7528 [0.58, 0.97]
Non HDL cholesterol	Less than 3.3 mmoles/l [≤130mg/dl]	54	12	6.632 [2.82, 15.5]	2.024 [1.4, 2.9]
VLDL	Less than 0.79mmoles/l [≤30mg/dl]	53	27	1.276 [0.55, 2.95]	1.093 [0.7966, 1.5]

Table 3: Pearson correlation of ApoB with lipid profile parameters[p value in brackets]

	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides	Non HDL cholesterol
ApoB	r=0.18, p=0.052	r=0.296, p=0.001	r=-0.490, p< 0.001	r=0.148, p=0.119	r=0.378, p<0.001

Discussion

We found that AMI was prevalent almost twice in males than females which was also depicted in other similar studies conducted in Nepal.[9,11,12] Currently, many studies in Nepal are focused on younger age group AMI and the incidence of AMI has been seen below 40 years of age with the onset as young as 20 years.[9,12, 13] In this study, the minimum age of onset of AMI recorded was 35 years in males and 30 years in females. Deranged lipoprotein metabolism has been linked to as one of the risk factors for AMI through ASCVD. Assay of biochemical parameters like TC,TG,LDL-C,HDL-C to non HDL-C and LDL/HDL ratio have been looked into to encompass the role of this deranged lipoprotein metabolism and its association with cardiovascular disease especially ASCVD.[4-15] Due to its representation as a particle, ApoB has been preferred for assessment of cardiovascular risk.[5,16] In our study, twenty nine AMI cases had ApoB value above 105mg/dl which accounts for 40% of total cases .This is based on the ApoB reference range[60-105mg/dl as per the kit (SPINREACT, Spain: Apolipoprotein B, turbidimetry principle)]. Only three non- MI control group had ApoB level above 105mg/dl. The odds of manifestation of AMI was found to be 8.1[95%CI:2.3.28.8]. According to 2018 guidelines on management of blood cholesterol, ApoB level >130mg/dl is considered risk enhancing factor for ASCVD.[15] On this basis, our ApoB values in both AMI and healthy controls are within the low risk range. When we compared the ApoB level between MI and control group, there was a significant difference [p<0.001, table1]. Marston et al study showed ApoB can capture the risk of MI than other lipid parameters.[16] There is strong association between between ApoB and Cardiovascular risk.[17] So, this may indicate that baseline ApoB need to be recorded in each individual and can be monitored for risk stratification for ASCVD. Dahal et.al and Tamang et.al have also shown higher ApoB level in AMI than healthy controls in Nepalese population.[9,10] However, ApoB may not be a good predictor of cardiovascular risk in patients already on lipid lowering drug therapy.[14] The drug history of lipid lowering therapy prior to AMI is the limitation of this study.

According to ATP III national cholesterol education program guidelines, we found dyslipidemia in both MI and healthy controls. Studies show that dyslipidemia contribute to AMI as well as dyslipidemia may be diagnosed at the onset of AMI.[11,12] This indicate that there is future risk of developing ASCVD even in non-MI healthy controls. The protective effect in healthy controls seem to be HDL cholesterol which is in the desired range in around 99%. Apo B containing lipoproteins singularly play a more sensitive role in risk stratification of AMI than total cholesterol, VLDL-C, LDL-C and triglycerides separately. HDL-C [RR 1.9;95% CI:1.5,2.4] is almost parallel with non- HDL cholesterol[RR2.02; 95% CI:1.4,2.9] in risk stratification of AMI. So, non- HDLC and HDL-C need to be assayed together for cardiovascular risk. Apo B showed fair correlation with LDL , positive moderate correlation with non HDL correlation and moderate negative correlation with HDL. We can suggest that Apo B assay should be a primary marker of cardiovascular risk and or may complement the lipid profile assay as has been suggested by other researchers too.[19,20] The outcome of AMI patients in different levels of Apo B and lipid profile is our another limitations which would have contributed to the severity of disease .

Conclusion

Our study depicted a significantly higher level of ApoB in AMI than the normal healthy controls. ApoB also showed moderate correlation with non HDL-C and HDL-C. Thus, we recommend ApoB analysis as a complementary marker to conventional lipid profile for cardiovascular risk assessment in AMI.

References

1. WHO. Noncommunicable diseases [Internet]. [cited 2022 Feb 1]. Available from: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

2. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. Journal of the American College of Cardiology [Internet]. 2017 Jul 4 [cited 2022 Feb 28];70(1):1. Available from: /pmc/articles/PMC5491406/

3. Bhattarai, S., Aryal, A., Pyakurel, M., Bajracharya, S., Baral, P., Citrin, D., Cox, H., Dhimal, M., Fitzpatrick, A., Jha, A. K., Jha, N., Karmacharya, B. M., Koju, R., Maharjan, R., Oli, N., Pyakurel, P., Sapkota, B. P., Shrestha, R., Shrestha, S., Spiegelman, D., … Shrestha, A. (2020). Cardiovascular disease trends in Nepal - An analysis of global burden of disease data 2017. International journal of cardiology. Heart & vasculature, 30, 100602. https://doi.org/10.1016/j.ijcha.2020.100602

4. Linton MRF, Yancey PG, Davies SS, et al. The Role of Lipids and Lipoproteins in Atherosclerosis. [Updated 2019 Jan 3]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK343489/

5. Sniderman AD, Thanassoulis G, Glavinovic T, et al. Apolipoprotein B Particles and Cardiovascular Disease: A Narrative Review. JAMA Cardiol. 2019;4(12):1287-1295. doi:10.1001/jamacardio.2019.3780

6. Karthikeyan G, Teo KK, Islam S, McQueen MJ, Pais P, Wang X, Sato H, Lang CC, Sitthi-Amorn C, Pandey MR, Kazmi K, Sanderson JE, Yusuf S. Lipid profile, plasma apolipoproteins, and risk of a first myocardial infarction among Asians: an analysis from the INTERHEART Study. J Am Coll Cardiol. 2009 Jan 20;53(3):244-53. doi: 10.1016/j.jacc.2008.09.041. PMID: 19147041.

7. Khan HA, Alhomida AS, Sobki SH. Lipid profile of patients with acute myocardial infarction and its correlation with systemic inflammation. Biomark Insights. 2013;8:1-7. doi:10.4137/BMI.S11015

8. Pitt B, Loscalzo J, Yčas J, Raichlen JS. Lipid Levels After Acute Coronary Syndromes. J Am Coll Cardiol [Internet]. 2008;51(15):1440–5. Available from: https://www.sciencedirect.com/science/article/pii/S0735109708003914

9. Kashyap Dahal, Prahlad Karki, Robin Maskey et al. Risk factors of acute myocardial infarction in young adults of Nepalese population. International Journal of Medicine in Developing Countries. 2018;2(3):80–85. doi: 10.24911/IJMDC.51-1529054592

10. Tamang, H. K., Timilsina, U., Singh, K. P., Shrestha, S., Raman, R. K., Panta, P., Karna, P., Khadka, L., & Dahal, C. (2014). Apo B/Apo A-I Ratio is Statistically A Better Predictor of Cardiovascular Disease (CVD) than Conventional Lipid Profile: A Study from Kathmandu Valley, Nepal. Journal of clinical and diagnostic research : JCDR, 8(2), 34–36. https://doi.org/10.7860/JCDR/2014/7588.4000

11. Sahi R, Shah R, Gajurel RM, Khanal RR, Poudel CM, et al. (2020) Cardiovascular risk factors and clinical pattern in young Nepalese population with acute coronary syndrome presenting to a tertiary care center of Nepal. J Cardiovasc Med Cardiol 7(3): 235-241. DOI: 10.17352/2455-2976.000145

12. Adhikari CM, Acharya KP, Manandhar R, et al. Shahid Gangalal National Heart Centre-ST-elevation Myocardial Infarction Registry (SGNHC-STEMI-Registry), Nepal. Nepalese Heart Journal 2020; Vol 17 (1), 7-16

13. Kafle RC, Jha GS, Sharma D, et al. Prevalence of Myocardial Infarction with Non-Obstructive Coronary Arteries in Western Nepal. Nepalese Heart Journal 2020; Vol 17 (2), 39-42

14. 14.Boekholdt SM, Arsenault BJ, Mora S, Pedersen TR, LaRosa JC, Nestel PJ, Simes RJ, Durrington P, Hitman GA, Welch KM, DeMicco DA, Zwinderman AH, Clearfield MB, Downs JR, Tonkin AM, Colhoun HM, Gotto AM Jr, Ridker PM, Kastelein JJ. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. JAMA. 2012 Mar 28;307(12):1302-9. doi: 10.1001/jama.2012.366.

15. Grundy, S. M., Stone, N. J., Bailey, A. L., Beam, C., Birtcher, K. K., Blumenthal, R. S., Braun, L. T., de Ferranti, S., Faiella-Tommasino, J., Forman, D. E., Goldberg, R., Heidenreich, P. A., Hlatky, M. A., Jones, D. W., Lloyd-Jones, D., Lopez-Pajares, N., Ndumele, C. E., Orringer, C. E., Peralta, C. A., Saseen, J. J., … Yeboah, J. (2019). 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation, 139(25), e1082–e1143. https://doi.org/10.1161/CIR.0000000000000625

16. Marston NA, Giugliano RP, Melloni GEM, Park JG, Morrill V, Blazing MA, Ference B, Stein E, Stroes ES, Braunwald E, Ellinor PT, Lubitz SA, Ruff CT, Sabatine MS. Association of Apolipoprotein B-Containing Lipoproteins and Risk of Myocardial Infarction in Individuals With and Without Atherosclerosis: Distinguishing Between Particle Concentration, Type, and Content. JAMA Cardiol. 2022 Mar 1;7(3):250-256. doi: 10.1001/jamacardio.2021.5083. PMID: 34773460; PMCID: PMC8590731.

17. Sniderman AD, Williams K, Contois JH, Monroe HM, McQueen MJ, de Graaf J, Furberg CD. A meta-analysis of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B as markers of cardiovascular risk. Circ Cardiovasc Qual Outcomes. 2011 May;4(3):337-45. doi: 10.1161/CIRCOUTCOMES.110.959247. Epub 2011 Apr 12. PMID: 21487090.

18. McKenney, J.M. (2003), Update on the National Cholesterol Education Program Adult Treatment Panel III Guidelines: Getting to Goal. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 23: 26S-33S. https://doi.org/10.1592/phco.23.11.26S.32710

19. Sniderman AD, Navar AM, Thanassoulis G. Apolipoprotein B vs Low-Density Lipoprotein Cholesterol and Non–High-Density Lipoprotein Cholesterol as the Primary Measure of Apolipoprotein B Lipoprotein-Related Risk: The Debate Is Over. JAMA Cardiol. 2022;7(3):257–258. doi:10.1001/jamacardio.2021.5080

20. Sniderman AD, St-Pierre AC, Cantin B, Dagenais GR, Després JP, Lamarche B. Concordance/discordance between plasma apolipoprotein B levels and the cholesterol indexes of atherosclerotic risk. Am J Cardiol. 2003 May 15;91(10):1173-7. doi: 10.1016/s0002-9149(03)00262-5. PMID: 12745098.