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ASSOCIATION BETWEEN SERUM APOLIPOPROTEIN B AND ACUTE ISCHEMIC STROKE: EXPLORING A POTENTIAL BIOMARKER IN A TERTIARY CARE SETTING

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ABSTRACT **Introduction:** Acute ischemic stroke remains a major cause of mortality and morbidity worldwide. Identification of biomarkers that improve risk stratification beyond conventional lipid parameters remains clinically important. Apolipoprotein B, a major component of low-density lipoprotein (LDL), represents the total number of circulating atherogenic lipoprotein particles and is emerging as a more precise predictor of vascular risk. **Objective:** To evaluate the association between serum Apolipoprotein B levels and acute ischemic stroke. **Methods:** This was an observational case–control study conducted over 18 months in a tertiary care medical college hospital. 30 patients diagnosed with acute ischemic stroke were enrolled as cases, while 30 age- and sex-matched individuals served as controls. Fasting lipid profile parameters and Apolipoprotein B levels were measured and compared between the two groups. **Results:** The mean age of both stroke cases and controls in our study was found to be 62.83+12.42 years. Cases and controls, each group consisted of 70% males and 30% females. Stroke cases had significantly higher Total Cholesterol levels (192.5 ± 115.81 mg/dL) compared to controls (146.27 ± 36.53 mg/dL), elevated LDL-C levels (119.25 ± 41.53 mg/dL) compared to controls (92.93 ± 33.18 mg/dL) and significantly greater Apolipoprotein B levels (123.13 ± 74.58 mg/dL) compared to controls (78.23 ± 21.87 mg/dL), all being statistically significant. **Conclusion:** Elevated Apolipoprotein B levels have positive correlation with the occurrence of acute ischemic stroke. This suggests that ApoB could serve as a potential biomarker for early detection and risk assessment of acute ischemic stroke.

KEYWORDS : Acute Ischemic Stroke, Apolipoprotein B, LDL, Atherosclerosis.

INTRODUCTION

Stroke is defined as a sudden onset of neurological deficit caused by acute focal injury to the central nervous system of vascular origin and remains a major cause of morbidity and mortality worldwide. Ischemic stroke results from reduced cerebral blood flow due to vascular occlusion, leading to neuronal injury and infarction.[1]

Dyslipidemia and abnormal plasma lipoproteins are well-established risk factors for atherosclerosis and may contribute to ischemic stroke.[2] Apolipoproteins are structural proteins of lipoproteins that regulate lipid transport and metabolism. Apolipoprotein B (ApoB) is the principal component of LDL, very low-density lipoprotein (VLDL), and intermediate-density lipoprotein (IDL).[3]

Traditional lipid measurements such as LDL cholesterol estimate cholesterol content but do not reflect the number of circulating atherogenic particles. Whereas, ApoB is a direct measure of circulating atherogenic particle number because each cholesterol particle contains a single ApoB molecule.[4,5]

Previous studies have demonstrated a strong association between ApoB levels and coronary artery disease; and found it as a superior predictor of cardiovascular and cerebrovascular events compared to traditional LDL-C, particularly in patients with metabolic syndrome or diabetes where LDL particles are often small and dense.[6,7,8] However, the relationship between ApoB and acute ischemic stroke remains less clearly defined in the Indian population. Thus, there is a need for evaluating ApoB as a measurable biomarker for stroke risk which is aimed through this study.

METHODOLOGY

This observational case–control study was conducted in Kempegowda Institute of Medical Sciences, Bengaluru, India over a period of 18 months. 30 patients with acute ischemic stroke were enrolled as cases and 30 age- and sex-matched individuals, without a history of stroke or significant vascular disease, were included as controls. Acute ischemic stroke was diagnosed clinically and confirmed radiologically. Participants aged more than 18 years were included. Patients with rheumatic, congenital and valvular heart disease, atrial fibrillation, renal failure, hepatic insufficiency, malignancy, sepsis and those on lipid-lowering therapy were excluded.

The study protocol was reviewed and approved by the Institutional Ethics Committee of the institute. Written informed consent was obtained from all participants. Clinical history, demographic data, and laboratory investigations such as complete hemogram, renal and liver function tests, HbA1c, fasting blood sugar, and a full lipid profile were recorded. Serum ApoB levels were measured using commercially available kits. Statistical analysis was performed using SPSS 22.0 software. Quantitative variables were expressed as mean ± standard deviation. Independent t-test was used to compare groups. A p value <0.05 was considered statistically significant.

RESULTS

The study population consisted of 60 individuals, with 21 males (70%) and 9 females (30%) in both cases and controls. The mean age of participants was 62.83+12.42 years. Among the participants, 6.7% of the cases and 3.3% of the controls, consumed alcohol only. In both the groups, 10% were, only smokers. Additionally, 10% of the cases and 23.3% of the controls were both smokers and alcoholics. Among comorbidities, Diabetes mellitus was noted in 53.3% of the cases and 50% of the controls. Hypertension was found in 50% of the cases and 16.6% of the controls.

Table 1: Prevalence of Comorbidities and Habits in Cases and Controls

Parameter	Cases (N=30)	Controls (N=30)
Hypertension	15 (50%)	5 (16.6%)
Diabetes mellitus	16 (53.3%)	15 (50.0%)
Smoking (only)	3 (10.0%)	3 (10.0%)
Alcohol consumption (only)	2 (6.7%)	1 (3.3%)
Smoking and Alcohol consumption	3 (10.0%)	7 (23.3%)

The lipid profiles revealed that the mean triglyceride levels were 323.53 ± 906.11 mg/dL for cases and 105.33 ± 41.86 mg/dL for controls. The mean total cholesterol levels were significantly higher in cases at 192.50 ± 115.81 mg/dL compared to 146.27 ± 36.53 mg/dL in controls. The mean LDL-C levels were also higher in cases at 119.25 ± 41.53 mg/dL compared to 92.93 ± 33.18 mg/dL in controls. The HDL-C levels were similar between cases (34.63 ± 9.75 mg/dL) and controls (33.83 ± 8.97 mg/dL). The mean VLDL levels were 21.99 ± 14.25 mg/dL for cases and 19.07 ± 12.86 mg/dL for controls. The mean non-HDL-C levels were higher in cases at 157.87 ± 120.01 mg/dL compared to 112.43 ± 33.49 mg/dL in controls. These results indicate significant increase in total cholesterol, LDL-C, and non-HDL-C levels among the cases.

Table 2: Comparison of Mean Lipid Profile Parameters and Apolipoprotein B levels in cases and controls

Parameter (mg/dL)	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value

Triglycerides (TG)	323.53 ± 906.11	105.33 ± 41.86	0.193
Total Cholesterol (TC)	192.5 ± 115.81	146.27 ± 36.53	0.041
HDL-C	34.63 ± 9.75	33.83 ± 8.97	0.742
LDL-C	119.25 ± 41.53	92.93 ± 33.18	0.01
VLDL-C	21.99 ± 14.25	19.07 ± 12.86	0.416
Non-HDL-C	157.87 ± 120.01	112.43 ± 33.49	0.05
Apolipoprotein B	123.13 ± 74.58	78.23 ± 21.87	0.02

The mean TC/HDL ratio was higher in cases at 7.05 ± 9.79 compared to 4.44 ± 1.23 in controls. The mean LDL/HDL ratio was also higher in cases at 3.49 ± 1.81 compared to 2.78 ± 1.01 in controls. The mean ApoB levels were significantly higher in cases at 123.13 ± 74.58 mg/dL compared to 78.23 ± 21.87 mg/dL in controls, with a p-value of 0.02. This indicates a statistically significant difference, suggesting the diagnostic utility of higher levels of ApoB in acute ischemic stroke cases.

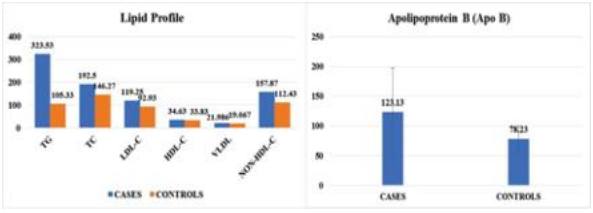

Figure 1: Bar Graphs Comparing Mean Lipid Profile Parameters and ApoB Levels in Cases and Controls

DISCUSSION

The current study was designed to evaluate the association between serum Apolipoprotein B levels and the occurrence of acute ischemic stroke in a tertiary care setting. The results demonstrated significantly higher ApoB levels among stroke patients compared to controls. Additionally, cases also exhibited statistically significant elevations in total cholesterol, LDL-C, and Non-HDL-C levels. Meanwhile, HDL-C and triglycerides, though elevated in cases, did not show statistically significant differences.

The mean age in the study, was found to be 62.83 years. This aligns with Fahmy EM et al. and Kalani R, et al., who reported that advancing age is a significant non-modifiable risk factor for ischemic stroke and its subtypes.[9,10] Specifically, Park JH, et al. noted that older individuals tend to exhibit higher ApoB levels, which further heightens their cerebrovascular risk profile.[11]

The gender distribution in our study, mirrors the findings of Park JH, et al., suggesting that gender may not significantly impact lipid profile differences in stroke.[11] Meanwhile studies by Chou YC, et al. and Fahmy EM et al. elucidated impact of gender and other factors such as lifestyle and genetic predispositions arising from gender differences on incidence of stroke.[12,9]

The findings revealing elevated ApoB levels in ischemic stroke cases (p=0.02), supports the hypothesis that ApoB, as a biomarker of total atherogenic particle burden, is closely linked to the pathophysiology of stroke and it aligns with international studies by Shilpasree, et al., Islam MS, et al., and Mahesh Kumar et al.[8,13,2,14] This substantiates that ApoB is a more robust marker than traditional lipid profile parameters, as it accounts for the atherogenic risk associated not just with LDL, but also with VLDL and IDL remnants, which are often overlooked.[15,16] Additionally, the observation of high ApoB levels in a cohort where 53.3% had diabetes mellitus resonates with Hermans MP et al., who emphasized the importance of ApoB in diabetic dyslipidemia, where LDL-C may be deceptively normal despite high atherogenic particle counts.[17]

The significantly higher Total Cholesterol and LDL-C levels in the stroke cohort (p=0.041) are consistent with findings by Shilpasree et al., Islam MS et al., and Mahesh Kumar CH et al. and underscores the role of dyslipidemia in ischemic stroke.[13,2,14] Although the findings pertaining to Triglyceride levels were not statistically significant, the trend toward higher levels in cases is supported by other research, such as Malek R, et al., and Jie Lin et al. though their significance varied.[18,19] The fact that, HDL-C and triglyceride levels did not differ significantly between groups reveals that atherogenic particle number rather than cholesterol content alone may be more relevant in development of stroke.[20]

The atherogenicity of ApoB-containing lipoproteins stems from their ability to enter the arterial wall, where they become trapped in the sub-endothelial space and undergo oxidation, triggering foam cell formation, plaque development, endothelial dysfunction and eventually arterial occlusion, which predisposes to ischemic stroke.[21] Unlike traditional LDL-C measurements, which quantify the mass of cholesterol, ApoB provides a direct molecule-for-molecule count of all potentially atherogenic particles (small and dense LDL, VLDL, and IDL) thereby provides a comprehensive assessment of the total "atherogenic pressure" on the arterial wall. This highlights that the number of particles, rather than just the lipid content in cholesterol particles, is a primary driver of the atherosclerotic process leading to ischemia.[22]

The strengths of this study include case-control design, matched controls and measurement of ApoB using standardized methods. However, several limitations must be considered. The sample size was relatively small. The study was conducted at a single center. Potential confounding variables were not fully adjusted. And lastly, the observational design prevents causal inference.

Despite these drawbacks, given the high burden of stroke in India, the conclusions drawn from the study, have immediate practical implications for stroke prevention. Identifying "at-risk" individuals solely through LDL-C or Total Cholesterol may lead to the under-treatment of patients who have high numbers of small, dense LDL particles but a low total cholesterol mass. Routine screening for ApoB can refine risk stratification and guide more aggressive primary and secondary prevention strategies, such as lipid-lowering therapy, even in patients with apparently "normal" traditional lipid profiles.

Future research should prioritize longitudinal, multi-center studies with larger cohorts to validate these findings across different ethnic and demographic groups. Additionally, integrating genetic markers for dyslipidemia with ApoB levels could offer a more personalized approach to cerebrovascular risk assessment. Prospective studies observing the impact of ApoB-targeted treatments on stroke recurrence would be particularly valuable, establishing definitive clinical thresholds for ApoB in stroke prevention and enhance its clinical utility as a biomarker of acute ischemic stroke.

CONCLUSION

This study confirms a strong association between elevated serum Apolipoprotein B levels and acute ischemic stroke and establishes ApoB as a comprehensive and reliable biomarker of atherogenic risk. Furthermore, ApoB offers a more precise tool for risk assessment than traditional lipid markers, especially in high-risk metabolic populations. Its adoption as a standard clinical metric could revolutionize stroke risk assessment, significantly improve the prevention and management of ischemic stroke, and help mitigate the global burden of cerebrovascular disease.

REFERENCES

1. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJB, Culebras A, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013;44:2064–89.
2. Islam MS, Uddin MJ, Bhattacharjee M, Farzana MN, Talukder RK, Rahman MA, et al. Association between Serum Apolipoprotein-B and Acute Ischemic Stroke. Mymensingh Med J 2018;27:229–36.
3. Bayly GR. Lipids and disorders of lipoprotein metabolism. Clinical Biochemistry: Metabolic and Clinical Aspects. Elsevier; 2014, 702–36.
4. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993;24:35–41.
5. Ceci FM, Ceccanti M, Petrella C, et al. Alcohol drinking, apolipoprotein polymorphisms and the risk of cardiovascular diseases. Curr Neurovasc Res. 2021;18(1):150–61.
6. Zhou Y, Little PJ, Ta HT, Xu S, Kamato D. Lysophosphatidic acid and its receptors: pharmacology and therapeutic potential in atherosclerosis and vascular disease. Pharmacol Ther. 2019;204:107404.
7. Hua R, Li Y, Li W, Wei Z, Yuan Z, Zhou J. Apolipoprotein B/A1 ratio is associated with severity of coronary artery stenosis in CAD patients but not in non-CAD patients undergoing percutaneous coronary intervention. Dis Markers. 2021;2021:8959019.
8. Morita SY. Metabolism and modification of apolipoprotein B-containing lipoproteins involved in dyslipidemia and atherosclerosis. Biol Pharm Bull. 2016;39(1):1-24.
9. Fahmy EM, El Awady MAE, Sharaf SA, Selim NM, Abdo HES, Mohammed SS. Apolipoproteins A1 and B and their ratio in acute ischemic stroke patients with intracranial and extracranial arterial stenosis: an Egyptian study. Egypt J Neurol Psychiatr Neurosurg. 2020;56(1):115.
10. Kalani R, Krishnamoorthy S, Deepa D, Gopala S, Prabhakaran D, Tirschwell D, Sylaja PN. Apolipoproteins B and A1 in ischemic stroke subtypes. J Stroke Cerebrovasc Dis. 2020;29(4):104670.
11. Park JH, Hong KS, Lee EJ, Lee J, Kim DE. High levels of apolipoprotein B/A1 ratio are associated with intracranial atherosclerotic stenosis. Stroke. 2011;42(11):3040-3046.
12. Chou YC, Chan PC, Yang T, You SL, Bai CH, Sun CA. Apolipoprotein B level and the apolipoprotein B/apolipoprotein A-I ratio as a harbinger of ischemic stroke: a prospective observation in Taiwan. Cerebrovasc Dis. 2020;49(5):487-494.
13. Shilpasree AS, Sahukar S, Murthy J, Kumar K. A study of serum apolipoprotein A1,

apolipoprotein B and lipid profile in stroke. J Clin Diagn Res. 2013;7(7):1303-1306.
14. Mahesh Kumar CH, Gayatri M, Maski A. Study of lipid profile in patients with stroke. Indian J Pathol Oncol. 2019;6(2):242-247.
15. Benn M, Nordestgaard BG, Jensen GB, Tybjaerg-Hansen A. Improving prediction of ischemic cardiovascular disease in the general population using apolipoprotein B: The Copenhagen City Heart Study. Arterioscler Thromb Vasc Biol. 2007;27:661–670.
16. Cao J, Steffen BT, Guan W, et al. A comparison of three apolipoprotein B methods and their associations with incident coronary heart disease risk: The Multi-Ethnic Study of Atherosclerosis. J Clin Lipidol. 2018;12:300-304.
17. Hermans MP, Sacks FM, Ahn SA, Rousseau MF. Non-HDL-cholesterol as valid surrogate to apolipoprotein B100 measurement in diabetes: Discriminant Ratio and unbiased equivalence. Cardio Diabetol. 2011;10:20.
18. Malek R, Hoque M, Shaha PR, Hossain MS, Ahmed A, Akhter M. Association of Apo B, Apo A1 and lipid profile with early onset stroke. J Bangladesh Soc Physiol. 2015;10(2):51-55.
19. Lin J, Si Z, Wang A. Predictive value of ApoB/ApoA-I for recurrence within 1 year after first incident stroke. Front Neurol. 2024;14:1308442.
20. Walldius G, Jungner I, Holme I, Aastveit AH, Kolar W, Steiner E. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. Lancet. 2001;358(9298):2026-2033.
21. Tabas I, Williams KJ, Borén J. Subendothelial retention of apolipoprotein B-containing lipoproteins in early atherosclerosis: the response-to-retention hypothesis. Circulation. 2007;116(16):1832-1844.
22. Cantey EP, Wilkins JT. Discordance between lipoprotein particle number and cholesterol content: An update. Curr Opin Endocrinol Diabetes Obes. 2018;25: 130–136.