

A STUDY OF ASSOCIATION OF TOTAL CHOLESTEROL, TRIGLYCERIDE TO HDL CHOLESTEROL RATIO WITH HEMORRHAGIC TRANSFORMATION OF ISCHEMIC STROKE

Neurology

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ABSTRACT

Background: Hemorrhagic transformation (HT) is a well-known complication after ischemic stroke, with its incidence being higher after thrombolysis. Various risk factors like older age, high blood pressure, and poor glycemic control are associated with HT. Recent studies showed associations of low level of Low-density lipoprotein (LDL) cholesterol with HT, however the association of total cholesterol, triglyceride to high density lipoprotein cholesterol (HDL-C) ratio with HT is less frequently studied. In this study, we analyzed the association of total cholesterol level, triglyceride to HDL-C ratio with HT of ischemic stroke. **Aims and objectives:** To study the association of total cholesterol level, triglyceride to HDL-C ratio with the HT of ischemic stroke. **Methodology:** Data from a total of 100 consecutive patients with ischemic stroke (from 15.05.2023 to 15.08.2023) were collected. Lipid profile including total cholesterol, triglycerides, HDL-C and MRI brain imaging details of HT were collected. All the patients were divided into 4 groups based on total cholesterol level (group 1 – total cholesterol $\leq$ 153 mg/dl, group 2 – 153 to 177 mg/dl, group 3 – 178 to 202 mg/dl, group 4 $>$ 202 mg/dl). HT and its association with lipid profile was assessed. **Results and conclusions:** Of 100 patients, 34 (34%) had HT. 16 out of 34 (47.1%) had HT in group 1. 8 out of 19 (42.1%) had HT in group 2. 4 out of 15 (26.7%) had HT in group 3. 6 out of 32 (18.8%) had HT in group 4. The triglyceride to HDL ratio was in the range of 2.1 to 6.1 among 31.5% of patients with HT. From our study we concluded that HT occurred more commonly in groups 1 and 2, however this association was not statistically significant. Triglyceride to HDL-C ratio had no significant association with HT.

KEYWORDS

Hemorrhagic transformation, Total cholesterol, Triglyceride to HDL-C ratio

INTRODUCTION:

Hemorrhagic transformation (HT) is one of the major complications after ischemic stroke. HT poses high mortality and morbidity (1). Mechanisms underlying HT include immune mediated inflammatory responses, dysfunction of Sodium- potassium ATPase pumps secondary to ischemia related local hypoxia, thereby leading to disruption of blood brain barrier, extravasation of blood, and cytotoxic edema (2,3). Various studies showed incidence of HT being 10 to 40%, with symptomatic HT incidence in the range of 0.6 to 20 (1,4). Various risk factors reported to be associated with HT after ischemic stroke include advanced age, atrial fibrillation, cardioembolic stroke, high systolic blood pressure, severe stroke (high NIHSS), massive stroke etc. (1,5) (6). Thrombolysis or reperfusion therapy itself poses a risk for occurrence of HT (1,7). Various studies reported low levels of low density lipoprotein cholesterol (LDL-C) as an independent risk factor for HT. Wang et al., in their study found that in patients with HT, there was low level of LDL-C, total cholesterol (8). Zhang et al., in their study reported high levels of high density lipoprotein cholesterol (HDL-C) in patients with HT after thrombolysis (9). However, few studies reported no significant association of total cholesterol, HDL-C levels with HT (10). There are very few studies which studied the association of Total cholesterol, Triglyceride to HDL-C ratio with HT. Thorough literature search revealed very limited Indian data. With this background, we did a study to assess the association of total cholesterol, Triglyceride to HDL-C ratio with HT.

METHODOLOGY:

This is a prospective observational study done on 100 consecutive ischemic stroke cases admitted in the wards of neurology in Madras medical college, Chennai. The study was conducted during the time from May 2023 to August 2023 after obtaining the Institute ethical committee clearance. All patients with acute ischemic stroke confirmed by history, neurological examination, imaging and willing to give written informed consent were included in the study. Patients who were already on antiplatelets, anticoagulants, who underwent thrombolysis, and CT brain showing hemorrhagic stroke were excluded from the study. The blood samples drawn for routine investigations were used for the purpose of the study thereby avoiding exclusive blood withdrawal. 2ml of blood sample was obtained from the antecubital vein of the patient and lipid profile (total cholesterol, triglyceride, HDL-C level) was assessed. All patients underwent Magnetic resonance imaging of the brain as part of routine stroke care. Data regarding hemorrhagic transformation (HT) was collected from

the imaging results. The data was analyzed.

Statistical Analysis:

Data entered Microsoft excel sheet and analyzed using SPSS software version 21.0 (IBM-SPSS Science Inc., Chicago, IL). Quantitative data was given as mean and standard deviation, whereas qualitative data was given as percentage and frequency. Categorical variables were compared using Pearson Chi-square test. Significance was defined as P value less than 0.05 using a two-tailed test.

RESULTS:

Of the 100-study population, 67 (67%) were males, 33 (33%) were females. Mean age was 54 $\pm$ 11.7 years. Diabetes mellitus was present in 49 (49%) individuals. Hypertension was present in 50 (50%) individuals. Coronary artery disease (CAD) was present in 11 out of 100 individuals. The arterial territory involved was the anterior cerebral artery (ACA), Middle cerebral artery (MCA), Posterior cerebral artery (PCA) in 2%, 78%, 20% individuals respectively. 13 out of 100 (13%) individuals had massive stroke. General characteristics of study population are given in table 1.

Table 1: General characteristics of the study population

		Number of study population	%
Age group	<30	3	3.0%
	31-40	12	12.0%
	41-50	25	25.0%
	51-60	35	35.0%
	61-70	16	16.0%
	>71	9	9.0%
Gender	Male	67	67.0%
	Female	33	33.0%
DIABETES	No	51	51.0%
	Yes	49	49.0%
HYPERTENSION	No	50	50.0%
	Yes	50	50.0%
CAD	No	89	89.0%
	Yes	11	11.0%
Territory involved	ACA	2	2.0%
	MCA	78	78.0%
	PCA	20	20.0%

Massive infarct	No	87	87.0%
	Yes	13	13.0%

Haemorrhagic transformation (HT) was present in 34 out of 100 (34%) cases. 34 out of 100 (34%) had total cholesterol <154 mg/dl (group 1), 19 out of 100 (19%) had total cholesterol from 154 to 177mg/dl (group 2), 15 out of 100 (15%) had total cholesterol from 178 to 202 mg/dl (group 3), and 32 out of 100 (32%) had total cholesterol above 202mg/dl (group 4). 16 out of 34 (47.1%), 8 out of 19 (42.1%), 4 out of 15 (26.7%), 6 out of 32 (18.8%) had haemorrhagic transformation in group 1, 2, 3, 4 respectively (p value 0.078). Figure 1 shows the association of total cholesterol level with HT.

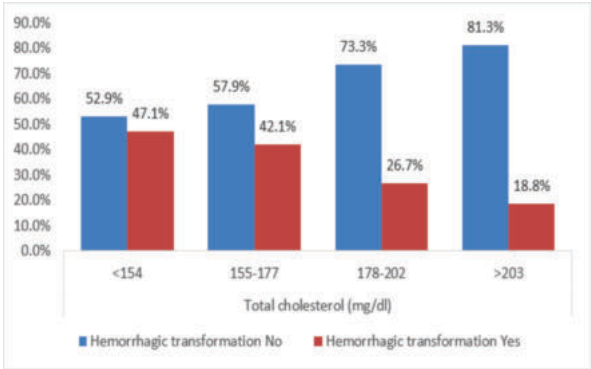


Figure1: Total cholesterol and hemorrhagic transformation (P 0.078)

Triglyceride to HDL-C ratio was <2.1 in 11 out of 100, 2.1 to 6 in 73 out of 100, > 6 in 16 out of 100 individuals. 4 out of 11 (36.4%) individuals with triglyceride to HDL-C ratio of <2.1 had HT, 23 out of 73 (31.5%) individuals with triglyceride to HDL-C ratio of 2.1 to 6 had HT, and 7 out of 16 (43.8%) individuals with triglyceride to HDL-C ratio of >6 had HT (P value 0.635). Table 2 shows association of Triglyceride to HDL-C ratio with HT. Of the 34 individuals with HT, 2 had massive stroke, whereas 32 had no massive stroke.

Table 2: Triglyceride to HDL ratio with Haemorrhagic transformation

		Hemorrhagic transformation				P value
		No		Yes		
		Number of study population	%	Number of study population	%	
Triglyceride to HDL ratio	<2	7	63.6%	4	36.4%	0.635
	2.1-6	50	68.5%	23	31.5%	
	>6.1	9	56.3%	7	43.8%	

DISCUSSION:

In our study, the mean age of study population was 54+/-11.7 years, which was comparable to previous studies. HT occurred in 34% of study population. Zhang et al., in their review article reported the incidence of HT ranging from 13% to 43% (4). Of the 100-study population, 34%, 32% had fallen into groups 1, 4 (according to total cholesterol level) respectively. Majority were in groups 1 and 4. HT occurred in 47.1% in group 1, 18.8% in group 4. There was less occurrence of HT in patients with high total cholesterol. In our study, we found no statistically significant association between total cholesterol level and HT (P 0.078). Nardi et al, in their systemic review found no association of total cholesterol, HDL-C with HT (10). Of the total 34 patients with HT, 4 (11.7%) had triglyceride to HDL-C ratio <2.1 and 23 (67.6%) had Triglyceride to HDL-C ratio of 2.1 to 6% . Lower the triglyceride to HDL-C ratio, higher the risk of HT in large artery atherosclerosis. Molecular basis for increased HT with low lipid levels remain unclear. Qi-Wen Deng et al., in their study found statistically significant association of low triglyceride to HDL-C ratio with HT (11). However, in our study, there was no statistically significant association between low triglyceride to HDL-C ratio with HT. This could be because of low numbers in the study group.

CONCLUSION:

HT occurred more frequently in patients with low total cholesterol level. There was no significant association of total cholesterol, triglyceride to HDL-C level with HT. Further studies with large sample size and follow up are required to ascertain these findings.

Conflict Of Interest

The authors declared that there are no conflicts of interest.

REFERENCES:

1. Thomas SE, Plumber N, Venkatapathappa P, Gorantla V. A Review of Risk Factors and Predictors for Hemorrhagic Transformation in Patients with Acute Ischemic Stroke. *Int J Vasc Med.* 2021 Dec 6;2021:e4244267.
2. Spronk E, Sykes G, Falcione S, Munsterman D, Joy T, Kamtchum-Tatuene J, et al. Hemorrhagic Transformation in Ischemic Stroke and the Role of Inflammation. *Front Neurol [Internet].* 2021 [cited 2023 Oct 9];12. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2021.661955>
3. Sussman E, Connolly Jr. E. Hemorrhagic Transformation: A Review of the Rate of Hemorrhage in the Major Clinical Trials of Acute Ischemic Stroke. *Front Neurol [Internet].* 2013 [cited 2023 Oct 9];4. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2013.00069>
4. Zhang J, Yang Y, Sun H, Xing Y. Hemorrhagic transformation after cerebral infarction: current concepts and challenges. *Ann Transl Med.* 2014 Aug;2(8):81–81.
5. Pande SD, Win MM, Khine AA, Zaw EM, Manoharraj N, Lolong L, et al. Haemorrhagic transformation following ischaemic stroke: A retrospective study. *Sci Rep.* 2020 Mar 24;10(1):5319.
6. Paciaroni M, Agnelli G, Corea F, Ageno W, Alberti A, Lanari A, et al. Early Hemorrhagic Transformation of Brain Infarction: Rate, Predictive Factors, and Influence on Clinical Outcome. *Stroke.* 2008 Aug;39(8):2249–56.
7. Bernardo-Castro S, Sousa JA, Brás A, Cecilia C, Rodrigues B, Almendra L, et al. Pathophysiology of Blood–Brain Barrier Permeability Throughout the Different Stages of Ischemic Stroke and Its Implication on Hemorrhagic Transformation and Recovery. *Front Neurol [Internet].* 2020 [cited 2023 Oct 9];11. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2020.594672>
8. Wang Y, Wei C, Song Q, Liu J, Cheng Y, Li Y, et al. Reduction in the Ratio of Low-density Lipoprotein Cholesterol to High-density Lipoprotein Cholesterol is Associated with Increased Risks of Hemorrhagic Transformation in Patients with Acute Ischemic Stroke. *Curr Neurovasc Res.* 16(3):266–72.
9. Zhang W, Li W, Tian R, Cao L. High-density lipoprotein level is associated with hemorrhage transformation after ischemic stroke treatment with intravenous thrombolysis: A systematic review and meta-analysis. *J Clin Neurosci.* 2022 Dec 1;106:122–7.
10. Nardi K, Leys D, Eusebi P, Cordonnier C, Gautier S, Hénon H, et al. Influence of lipid profiles on the risk of hemorrhagic transformation after ischemic stroke: systematic review. *Cerebrovasc Dis Extra.* 2011;1(1):130–41.
11. Deng QW, Liu YK, Zhang YQ, Chen XL, Jiang T, Hou JK, et al. Low triglyceride to high-density lipoprotein cholesterol ratio predicts hemorrhagic transformation in large atherosclerotic infarction of acute ischemic stroke. *Aging.* 2019 Mar 10;11(5):1589–601.