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Corelation Between Serum Triglycerides and Stroke at Navodaya Medical College, Raichur, Karnataka

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Abstract: ***Introduction**: The World Health Organization (WHO) definition of stroke is: "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin". Hypertriglyceridemia may lead to Ischemic stroCO-ke through its contribution to atherosclerosis and/or thrombogenicity. So, it becomes necessary to address prevention of dyslipidemia in today's scenario that will further prevent the incidence of cerebrovascular accidents and minimize the risk in future. So, the present study is planned in order to assess serum triglyceride levels in patients with stroke. **Material and Methods**: A hospital based descriptive observational study was conducted on 100 diagnosed cases of stroke admitted in Navodaya Medical College, Raichur. The inclusion criteria was diagnosed cases of Age group of individuals- 35-80 years, patients admitted in Navodaya Medical College Hospital and Research Centre with a first ever diagnosis of cerebrovascular disease and onset of the symptoms within the preceding three days on presentation to the hospital and those who are willing to participate in study after written consent. **Results**: Hypertension, smoking, diabetes mellitus and alcohol consumption were significantly ($p<0.05$) associated with ischemic stroke. On the other hand, ischemic stroke is associated significantly with a higher level of triglycerides. Proportion of hemorrhagic stroke patients with elevated TG levels were 12% as against 36% with normal TG levels. There was statistically significant difference in the proportion of ischemic stroke patients between two groups. So, there was significant association between type of stroke and TG levels in our study ($p<0.05$). Ischemic stroke was commonly seen in patients with elevated TG levels. **Conclusion**: Hypertension, smoking, diabetes mellitus and alcohol consumption were significantly ($p<0.05$) associated with ischemic stroke. On the other hand, ischemic stroke is associated significantly with a higher level of triglycerides. Therefore, this current study result confirms that hypertriglyceridemia may be a risk factor for ischemic stroke.*

Keywords: ischemic stroke, hypertriglyceridemia, serum triglycerides, cerebrovascular risk factors, dyslipidemia

1. Introduction

Ischemic stroke accounts for 50%-85% of all strokes worldwide.[5] Hemorrhagic stroke are due to subarachnoid hemorrhage or intracerebral hemorrhage; they account for 1%-7% and 7%-27% respectively of all cases of stroke worldwide.[5]

Hypertriglyceridemia may lead to IS through its contribution to atherosclerosis and/or thrombogenicity. Studies suggest that hypertriglyceridemia fosters the development of atherosclerosis via several mechanisms. Postprandial hypertriglyceridemia in diabetic patients was found to produce endothelial dysfunction, oxidative stress due to lipid derived free radicals, and impairment of endothelium dependent vasodilatation. [9] Triglyceride-rich lipoproteins, including very-low-density lipoprotein and intermediate density lipoprotein, in addition to LDL-C particles, become trapped in blood vessel walls and have been demonstrated in human atherosclerotic plaques. [10]
So, the present study is planned in order to assess serum triglyceride levels in patients with stroke.

Objectives
To identify if serum triglyceride levels on admission predict severity of stroke.

2. Review of Literature

2.1 Epidemiology of CVA (stroke):

The term "stroke" (syn: apoplexy) is applied to acute severe manifestations of cerebrovascular disease. It causes both physical and mental crippling. WHO defined stroke as "rapidly developed clinical signs of focal disturbance of cerebral function; lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin" The 24 hours threshold in the definition excludes transient ischemic attacks (TIA) and patients with stroke symptoms caused by subdural hemorrhage, tumours, poisoning or trauma are excluded [13]

The stroke includes a number of syndromes with differing etiologies, epidemiology, prognosis and treatment. These are listed as follows: [13]

a) Ischemic stroke:
- Lacunar infarcts
- Carotid circulation obstruction
- Vertebrobasilar obstruction

b) Haemorrhagic stroke:
- Spontaneous intracerebral haemorrhage
- Subarachnoid haemorrhage
- Intracranial aneurysm
- Arteriovenous malformations

2.2 Problem Statement

Indian scenario:
Although the prevalence of stroke appears to be comparatively less in In India than developed countries, it is likely to be increased proportionately with the increase in life expectancy. The proportion of stroke in young population is significantly more in India than in developed countries. Some of the more important causes for this are likely to be rheumatic heart diseases, ischemic strokes in peripartum period and arteriopathies as a sequelae of CNS infections like bacterial and tubercular meningitis.[18]

The prevalence rate of stroke in India is about 1.54 per thousand and death rate is about 0.6 per 1000. The dalys lost is about 597.6 per lac.[13]

The reasons for a rise in stroke burden in India include smoking, increasing longevity, and changes in lifestyle accompanying urbanization. In India, the average life expectancy rose from 41.2 years in 1951-1961 to 61.4 years in 1991-1996. Indians may also be genetically prone to stroke due to a high prevalence of the metabolic syndrome consisting of central obesity, high levels of triglycerides, and low levels of HDL cholesterol with or without glucose intolerance.[19]

Indian studies have shown that about 10% to 15% of strokes occur in people below the age of 40 years, which is high compared to other countries.[20, 21] Cerebral venous thrombosis and rheumatic heart disease are important causes of stroke in the young.[21] Subacute tubercular meningitis leading to arteritis or autoimmune angiitis are also important stroke risk factors.[22] Reported risk factors among the young include coagulopathy, elevated lipoprotein(a) and elevated anticardiolipin antibodies.[23, 24, 25] Some Indian studies have reported interesting causes of stroke, like viper envenomation and also suggested mechanisms like squatting whilst on the toilet as an important triggering factor for stroke in Indians, by raising the blood pressure.[26]

Limited study data available on stroke survival outcome in India. It suggests that recurrence may be higher in India due to poor compliance with treatment and control of risk factors. Of the stroke survivors, only about one third is fully independent in their daily activities of living while more than one-fourth cases are bed ridden. The poor outcome in functional recovery may be due to lack of rehabilitation and treatment facilities.[27]

2.3 Pathophysiology of ischemic stroke:

Most ischemic strokes are embolic in nature, with an embolus or blood clot (or even atheroma) forming either within the cerebral arteries themselves or elsewhere in the body and migrating to the brain. Onset is usually rapid.[28] Ischemic strokes also can be caused by perfusion failure, which arises as the result of plaque buildup within the cerebral vessels, typically within the carotid arteries or the basilar artery. [29] The onset of symptoms may range from minutes to days.

Aortic arch atherosclerosis has been implicated in brain infarction, particularly in stroke of unknown origin or cryptogenic stroke, which constitutes up to 30% of all stroke. [30,31] This condition is common in persons older than 60 years. Mural thrombi can develop and break away to travel to the brain or other organs; unstable ulcerated plaques may release atheromatous material that forms emboli as well.[32] Aortic arch plaques may also play a role in strokes that occur during coronary artery bypass graft surgery

Because the pcas are located at the terminal end of the vertebrobasilar artery system, they are often the target for thrombo-emboli from the heart, the aorta, and both extra- and intracranial vertebral arteries. [36] Imaging studies have shown that the most common cause of PCA infarcts is an intra-arterial embolism originating from atherosclerotic lesions of the vertebral and basilar arteries. [37]

Ischemic Damage: [39]

Ischemic damage is complex and time dependent and is the result of a number of interrelated events that occur as a consequence of CBF failure. The immediate ischemic core can be salvaged only if blood flow is restored before irreversible injury occurs, usually within 1 or 2 h of the event at normothermia. After that point, ionic imbalances perpetuate damage within the ischemic zone and reversal of ATP depletion is no longer possible. Calcium has been implicated in a number of destructive interactions, including lipolysis, proteolysis, and activation of endonucleases that degrade DNA, which may trigger apoptosis of neurons. Disruption of cellular Ca2+ homeostasis is believed to be one of the fundamental triggers in the neuronal death and dysfunction that results in clinical disability. Disruption of the BBB, a known consequence of ischemia, leads to brain edema, which is a major complication of stroke and a critical determinant of outcome. In the initial phase following ischemia, the BBB remains intact and, as the result of ionic gradient disruptions, brain cells swell, decreasing the extracellular space and causing cytotoxic edema. As time goes on, however, the BBB becomes permeable, allowing an influx of plasma constituents, which leads to expansion of extracellular spaces and gives rise to vasogenic edema. A compromised BBB also may allow an increase in the concentration of excitatory amino acids, which are believed to contribute to ischemic brain injury. Elevated extracellular levels of the excitatory neurotransmitter glutamate are believed to play an important role in ischemic injury. In the normal brain, cellular uptake of glutamate maintains extracellular levels below the neurotoxic threshold; under ischemic conditions, however, depletion of energy stores impedes this uptake.

Mechanisms of Ischemic Stroke:

Although the molecular mechanisms described may be common to all types of ischemic stroke, the importance of determining specific stroke pathogenesis (i.e., mechanism) in order to select appropriate treatment and secondary prevention cannot be overemphasized. Currently, the most widely used categorization of ischemic stroke was developed and validated in the context of an acute therapeutic trial,[40,41] It is "crisp" and different than that found in nature, and although simplified for daily diagnostic purposes, a more logical model was suggested recently that considers fuzzy logic of multiple concurrent mechanisms.[42, 43] As can be seen from Table 1, the patient's history and neurologic examination, along with a combination of brain imaging (usually by computed tomography), cerebrovascular imaging (usually by carotid ultrasound), and cardiac studies (electrocardiogram and usually echocardiography) will determine the pathogenesis. This latter may not be only one in condition, but multidimensional.

The relative frequencies of stroke subtypes are small vessel occlusion (20% to 30%), large artery intracranial or extracranial atherosclerosis (30% to 40%), or a cardiac source of embolism (20% to 30%). Coagulopathies and unknown mechanisms contribute, to a varying degree, to the total. Magnetic resonance imaging and magnetic resonance angiography, selective cerebral arteriography, transesophageal echocardiography, coagulation studies, and other newly developed noninvasive diagnostic tools can

provide critical information about stroke pathogenesis in all patients. In up to 5% to 10% of patients, such investigations may uncover other causes of stroke, such as dissection or vasculopathies such as Moyamoya disease (bilateral obliteration of the intracranial internal carotid arteries of unknown origin); hematological abnormalities, such as antiphospholipid antibodies; or occult cardiac sources of embolism, such as patent foramen ovale. Finally, the cause of stroke remains cryptogenic in up to 15% of patients.

Pathophysiology of atherosclerosis:[43]

Hypercholesterolaemia is considered one of the main triggers of atherosclerosis. The increase in plasma cholesterol levels results in changes of the arterial endothelial permeability that allow the migration of lipids, especially LDL-C particles, into the arterial wall. Circulating monocytes adhere to the endothelial cells that express adhesion molecules, such as vascular adhesion molecule-1 (VCAM-1) and selectins, and, consequently, migrate via diapedesis in the subendothelial space. Once in the subendothelial space, the monocytes acquire macrophage characteristics and convert into foamy macrophages. LDL particles in the subendothelial space are oxidised and become strong chemo attractants. These processes only enhance the accumulation of massive intracellular cholesterol through the expression of scavenger receptors (A, B1, CD36, CD68, for phosphatidylserine and oxidised LDL) by macrophages, which bind native and modified lipoproteins and anionic phospholipids. Clinical sequelae of atherosclerosis are vessel narrowing with symptoms (angina pectoris) and acute coronary syndromes due to plaque instability. The majority of coronary thrombi are caused by plaque rupture (55–65%), followed by erosions (30–35%), and least frequently from calcified nodules (2–7%). Rupture-prone plaques typically contain a large, soft, lipid-rich necrotic core with a thin (65 μm) and inflamed fibrous cap. Other common features include expansive remodelling, large plaque size (>30% of plaque area), plaque haemorrhage, neovascularisation, adventitial inflammation, and 'spotty' calcifications. Vulnerable plaques contain monocytes, macrophages, and T-cells. T-cells promote the vulnerability of plaques through their effects on macrophages. LDL-C, TG and HDL-C emerged as strong independent predictors of atherosclerotic disease after the analysis of the data from the Framingham study. While the role of other parameters is being investigated, TC, LDL-C and HDL-C remain to date the cornerstone in risk estimation for future atherosclerotic events.

2.4 Risk Factors for stroke:

Careful understanding of risk factors can help in avoiding the onset of stroke. Age, gender, race, ethnicity, hereditary are non-modifiable risk factors. Systemic Hypertension, smoking, chronic alcoholism, dyslipidemia, obesity, sedentary life style, atrial fibrillation, previous heart disease, transient ischemic attack are potentially treatable/modifiable factors in the incidence of stroke. The epidemiological studies on stroke are much least in developing countries. The prevalence of stroke is 40-270 in rural populations which is lower compared to western countries.[44] The reason for variation may be due to socioeconomic factors, ethnicity & cultural habits.

Lipids in human blood: [100]

Cholesterol:

Cholesterol is probably the best-known steroid because of its association with atherosclerosis. However, it is also important, being the precursor of a large number of equally important steroids which include bile acids, vitamin D and sex hormones Cholesterol is present in tissues and in plasma lipoprotein as free cholesterol or combined with long-chain fatty acid as cholesterol ester. It is synthesized in many tissues from acyl–COA and is eliminated from the body in the bile as cholesterol or bile salts.

Triglycerides:

Triglycerides are the ideal means of energy storage in fat cells, where they also act as ―cushions‖ and provide a layer of insulation.

Fatty Acids:

Fatty acids are released by the effect of the enzyme lipoprotein lipase from glycerol to which they are bound in the stored triglycerides. Released free fatty acids (FFA) bind to serum albumin and are used as sources of energy for muscle activity. Then they are taken up by the liver or re-synthesized back in to triglycerides.

Lipoproteins:[100]

Lipoproteins are complexes of lipids and proteins that are essential for transport of cholesterol, triglycerides, and fat-soluble vitamins. Lipoproteins are large macromolecular complexes composed of lipids and proteins that transport poorly soluble lipids (primarily triglycerides, cholesterol, and fat-soluble vitamins) through body fluids (plasma, interstitial fluid, and lymph) to and from tissues. Lipoproteins play an essential role in the absorption of dietary cholesterol, long chain fatty acids, and fat-soluble vitamins; the transport of triglycerides, cholesterol, and fat-soluble vitamins from the liver to peripheral tissues; and the transport of cholesterol from peripheral tissues to the liver and intestine. Lipoproteins contain a core of hydrophobic lipids (triglycerides and cholesteryl esters) surrounded by a shell of hydrophilic lipids (phospholipids, unesterified cholesterol) and proteins (called apolipoproteins) that interact with body fluids. The plasma lipoproteins are divided into five major classes based on their relative density: 1. Chylomicrons, 2. Very-low-density lipoproteins (vldls), 3. Intermediate-density lipoproteins (idls), 4. Low density lipoproteins (ldls), and 5. High-density lipoproteins (hdls). Chylomicrons are the most lipid-rich and least dense lipoprotein particles, whereas hdls have the least lipid and are the densest lipoproteins. In addition to their density, lipoprotein particles can be classified according to their size, determined either by non-denaturing gel electrophoresis or by nuclear magnetic resonance profiling. There is a strong inverse relationship between density and size, with the largest particles being the most buoyant (chylomicrons) and the smallest particles being the densest. (HDL) The proteins associated with lipoproteins, called *apolipoproteins*, are required for the assembly, structure, function, and metabolism of lipoproteins. Apolipoproteins activate enzymes important in lipoprotein metabolism and act as ligands for cell surface receptors. Apob is a very large protein and is the major structural protein of chylomicrons, vldls, idls, and ldls; one molecule of apob, either apob-48

(chylomicron) or apob-100 (VLDL, IDL or LDL), is present on each lipoprotein particle.

2.5 Similar studies conducted in the past

Shyampada Dan et al[107] in 2017 observational cross-sectional study evaluated 100 stroke patients in 40-90 years age group. A thorough history and clinical evaluation was done in each patient as also necessary investigations were conducted meticulously among patients admitted in Medicine ward of a peripheral state medical hospital. Lipid profile was assessed in all participants along with neuroimaging to classify the stroke. Out of 100 patients, 26 patients had dyslipidemia (7 in hemorrhagic & 19 in ischemic stroke patients).

Weiping Sun et al[108] in 2017 conducted the study with the objective to compare the risk factors and lipid profile pattern in ischemic and hemorrhagic strokes. This was a descriptive retrospective cross-sectional study carried on new onset acute stroke patients admitted to Osmania General Hospital, Telangana State. 100 patients (n=50 ischemic stroke (isch), n=50 hemorrhagic stroke (haem) was studied over a period of one year from May 2014-April 2015. Present study concludes hypertension in 62 %, low HDL (< 40 mg/dl) in 60 %, smoking in 41% are the risk factors for both ischemic and haemorrhagic strokes which are modifiable risk factors. Low HDL cholesterol is more significant with a p=0.0124 which can be improved by exercise.

Mahesh kumar et al[109] in 2019 conducted the study with the objective to determine the prevalence of abnormal lipid profile including extended lipid profile in patients with stroke. A total of 200 patients with stroke were studied. Among the studied patients 112 (56%) were males and 88 (44%) were females. Mean age of the study population was 56.98yrs (SD = 13.8). Out of 200, 108 (54%) were having total cholesterol value <200mg>> 200 mg/dl. 86(43%) subjects were having Triglyceride level above 150 mg/dl, whereas 114 (57%) were having less than 150 mg/dl. 129 (64.5%) were having HDL value less than 40mg/dl whereas 71 (35.5%) were having HDL > 40 mg/dl. 106 (53%) were having VLDL value < 30mg>>30 mg/dl. 159 (79.5%) were having LDL values above 100 mg/dl and 41 (20.5%) were having LDL value less than 100mg/dl. 74 (37%) were having Apolipoprotein–A1 value less than 120 mg/dl and 126 (63%) were having value > 120 mg/dl. 126 (63%) were having Apolipoprotein–B value <130>> 130 mg/dl. There was no statistically significant difference among males and females in the study subjects. There was statistically significant positive correlation between Total cholesterol & LDL with Apolipoprotein–B (p < 0>

Conclusion: In the present study dyslipidemia, low Apolipoprotein-A1 and high Apolipoprotein B have been found to be associated with stroke.

Onkar Nath Rai et al[110] in 2017 involved 100 patients of stroke who were admitted to B.R.D. medical college, Gorakhpur. The patients were classified as having ischemic or hemorrhagic stroke definitive on the basis of CT scan of head (plain and contrast). Lipid profile estimation was done. Out of 100 patients 46 had hemorrhagic stroke and 54 had Ischemic stroke. Abnormal lipid values were found in 54 patients. Total cholesterol was abnormal in 83% of ischemic stroke and 17% of hemorrhagic stroke. LDL cholesterol was abnormal in 86% of ischemic stroke and 14% of hemorrhagic stroke. So they concluded regular monitor of lipid profile among stroke patients may decrease the risk of atherosclerosis and cardiovascular disease among the stroke patients. Abnormal lipid values were found in 54 patients. Out of which increased non-HDL cholesterol was found in 53% patients. Increased LDL cholesterol was found in 35% patients followed by increased triglycerides in 34% patients. Increased total cholesterol was present in 30 patients.

De Groot R et al[111] in 2018 conducted a systematic review and meta-analysis with reference to urban-rural differences in the association between blood lipids and characteristics of the built environment. Pub Med, EMBASE and Web of Science were searched for peer-reviewed papers on population-based studies up to 9 October 2017. We included studies that reported on built-environment characteristics and blood lipid levels in adult populations (≥18 years). Two reviewers independently screened titles/abstracts and full-texts of papers and appraised the risk of bias of included studies using an adapted version of the Quality Assessment Tool for Quantitative Studies. We performed meta-analyses when five or more studies had sufficient homogeneity in determinant and outcome. After screening 6902 titles/abstracts and 141 potentially relevant full-text articles, we included 50 studies. Forty-seven studies explored associations between urban versus rural areas with blood lipid levels. Meta-analyses on urban versus rural areas included 133 966 subjects from 36 studies in total. Total cholesterol levels were significantly and consistently higher in urban areas as compared with rural areas (mean difference 0.37mmol/L, 95% CI 0.27 to 0.48). Urban/rural differences in high-density lipoprotein cholesterol were inconsistent across studies and the pooled estimate showed no difference (0.00mmol/L 95% CI-0.03 to 0.04). Low-density lipoprotein (LDL) cholesterol and triglyceride levels were higher in urban than in rural areas (mean difference 0.28, 95% CI 0.17 to 0.39 and 0.09, 95% CI 0.03 to 0.14, respectively). So the conclusion was total and LDL cholesterol levels and triglycerides were consistently higher in residents of urban areas than those of rural areas. These results indicate that residents of urban areas generally have less favourable lipid profiles as compared with residents of rural areas.

Zaozianlungliu Gonmei et al[113] in 2018 conducted study with an objective to assess the prevalence of dyslipidemia among the elderly in slums of West Delhi. A cross-sectional study was carried out in slums of West Delhi covering a total of 234 elderly aged 60 and above. 5 ml blood was collected from 103 elderly and was analyzed for serum total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol by enzymatic method using fully automatic analyzer (Roche Hitachi-902). Dyslipidemia was defined using the National Cholesterol Education Program, ATP-III guidelines. The overall prevalence of high cholesterol (≥200 mg/dl), high triglyceride (≥150 mg/dl), low HDL cholesterol (male - <40 mg/dl; female - <50 mg/dl), and high LDL cholesterol (≥130 mg/dl) was 20.39%, 45.63%, 64.08%, and 17.31%, respectively. Low HDL cholesterol and high triglyceride were

the most form of dyslipidemia among the elderly. Awareness on dietary and lifestyle modification for management of dyslipidemia needs to be imparted.

Deshpande JJ et al[114] in 2018 from Maharashtra conducted a study on lipid profile in patients with Ischemic Stroke in Rural coastal region of Maharashtra. It was a cross-sectional study carried out in the patents with Ischemic Stroke at Rural area Konkan during the one-year period i.e. Sep 2017 to Aug 2018. In the one-year period there were 201 patients enrolled into the study, all details of the patients like age, sex, lipid profile etc. Investigations were carried out, similarly the age matched patients without stroke were also enrolled into study selected from the ward. The average age of Patients of Stroke was 60 ± 4.56 Yrs. And patients without stroke was 61±3.76 Yrs. Which was comparable with each other (t=1.23, df=399, p>0.05). The male and Female ratio In both the group was comparable with each other 1.25 and 1.35 which was also comparable with each other (X2=0.129, df=1, p>0.05). The values were significantly higher in Patients of Stroke like Cholesterol 230± 7.12 and 205 ±5.64 (t=38.96,df=399,p<0.001); TG - 169 ± 4.5 and 154± 3.45 (t=42.92,df=399,p<0.0001); LDL- 152 ± 5.76 and 132 ± 4.12 (t=47.45,df=399,p<0.001) and HDL was significantly lower in Patients of Stroke i.e. 43± 3.54 and 58 ± 5.78 (t=29.82,df=399,p<0.001) as compared to patients without stroke respectively. They concluded from that majority of the patients were old and significantly the patients with stroke were having higher values of Cholesterol, LDL, TG and lower values of HDL as compared to the patients without stroke.

Khandelwal R et al[115] in 2018 conducted community based cross-sectional study during 2015 - 2016 in District Nainital, Uttarakhand. A list of all villages with their population in the district was developed. From this list, thirty villages were identified using population proportionate to size sampling method. From each village 30 geriatric subjects were selected. A total of 1003 geriatric subjects aged 60 years and above were included in the study. The data was collected on socio demographic profile and lipid profile from all the enrolled subjects. The prevalence of dyslipidemia was assessed using National Cholesterol Education Programme (NCEP) criteria. The mean age of subjects was 69.5 ± 7.4 years (males) and 67.7 ± 7.2 years (females). The overall prevalence of dyslipidemia was 50.6%. 26.3% participants had hypercholesterolemia, 34.2% had hypertriglyceridemia and 23.5% had high LDL levels. Derangement of lipid profile was noted for triglyceride (34.2%) followed by total cholesterol (26.3%) and low-density lipoprotein (23.5%). The prevalence of dyslipidemia was higher in women compared to men. High prevalence of dyslipidemia was found amongst geriatric rural population.

Vakilian A et al[116] in 2019 conducted the study with the objective to compare the serum lipid profile of patients with ischemic stroke (IS) and hemorrhagic stroke (HS). A total of 201 patients with IS and HS, who were admitted to the neurology ward of Ali-Ibn Abi-Talib Hospital and had not used any lipid-reducing drugs, were evaluated on the first day of admission. The serum lipid profile, including triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), and high-density lipoprotein-cholesterol (HDL-C), was measured in these patients. The participants were 48.8% male and 51.2% female. The serum TG level was significantly higher in IS patients in comparison with HS patients. The findings showed a significant association between the type of stroke and serum level of HDL-C. The results indicated a significant association between the lipid profile and type of stroke.

3. Results

Table 1: Distribution according to triglyceride level

		Frequency	Percent
TG	Normal	25	25.0
	Elevated	75	75.0
	Total	100	100.0

Prevalence of hypertriglyceridemia in our study was 75%

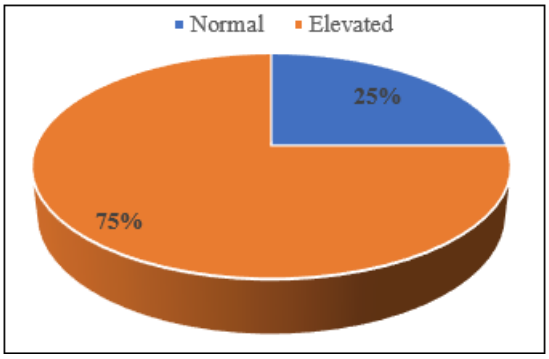

Figure 1: Distribution according to triglyceride level

Table 2: Association of triglyceride level with age group

		Normal		Elevated		Total	P
		Frequency	Percent	Frequency	Percent		
Age group in years	< 40	0	0.0	1	1.3	1	0.55 Not significant
	41-50	3	12.0	5	6.7	8	
	51-60	3	12.0	12	16.0	15	
	61-70	5	20.0	25	33.3	30	
	> 70	14	56.0	32	42.7	46	
	Total	25	100.0	75	100.0	100	

Out of 75 cases with elevated TG levels, majority were from above 70 years i.e. 32(42.7%) followed by 25 (33.3%) from 61-70 years, 12(16%) from 51-60 years, 5(6.7%) from 41-50 years and 1.3% from below 40 years age group. Out of 25 cases with normal TG levels, majority were from above 70 years i.e. 14(56%) followed by 5(20%) from 51-60 years and 3(12%) each from 41-50 and 51-60 years age group. We observed no significant association between age and TG level in our study (p>0.05)

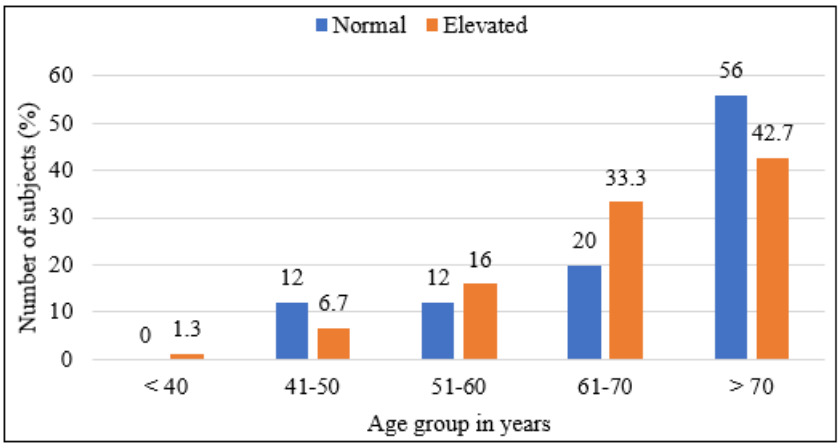

Figure 13: Association of triglyceride level with age group

Table 14: Association of triglyceride level with gender

		Normal		Elevated		Total	P
		Frequency	Percent	Frequency	Percent		
Gender	Male	16	64.0	48	64.0	64	1.00 Not significant
	Female	9	36.0	27	36.0	36	
	Total	25	100.0	75	100.0	100	

Proportion of males with elevated TG levels were 64% as against 64% of males with normal TG. Proportion of females with elevated TG levels were 36% as against 36% of females with normal TG. We observed no significant association between gender and TG level in our study (p>0.05)

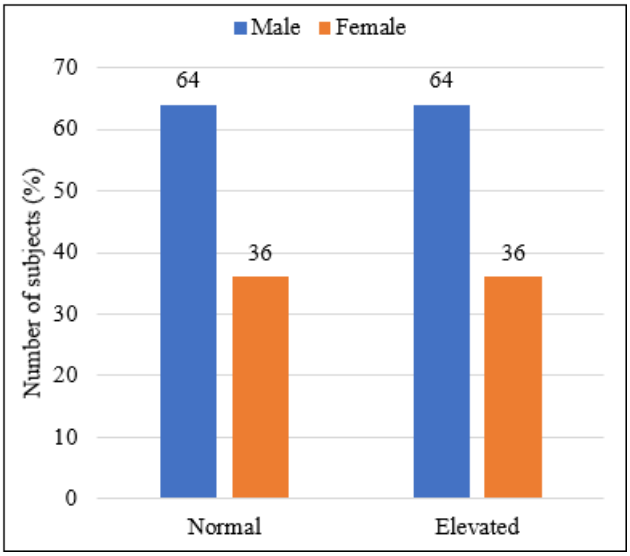

Figure 14: Association of triglyceride level with gender

Table 15: Association of triglyceride level with type of stroke

		Normal		Elevated		Total	P
		Frequency	Percent	Frequency	Percent		
Type of stroke	Ischemic	16	64.0	66	88.0	82	0.048 Significant
	Haemorrhagic	9	36.0	9	12.0	18	
	Total	25	100.0	75	100.0	100	

Proportion of ischemic stroke patients with elevated TG levels were 88% as against 64% with normal TG levels. Proportion of hemorrhagic stroke patients with elevated TG levels were 12% as against 36% with normal TG levels. There was statistically significant difference in the proportion of ischemic stroke patients between two groups. So, there was significant association between type of stroke and TG levels in our study (p<0.05). Ischemic stroke was commonly seen in patients with elevated TG levels.

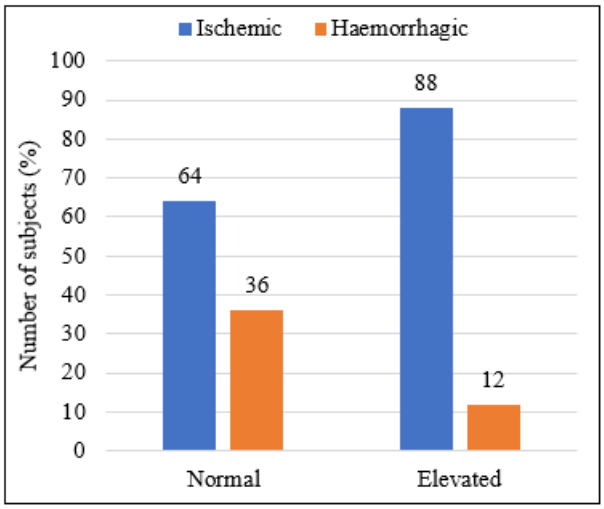

Figure 15: Association of triglyceride level with type of stroke

Table 20: Association of triglyceride level with diabetes

		Normal		Elevated		Total	P
		Frequency	Percent	Frequency	Percent		
DM	Yes	16	64.0	63	84.0	79	0.033 significant
	No	9	36.0	12	16.0	21	
	Total	25	100.0	75	100.0	100	

Proportion of diabetic stroke patients with elevated TG levels were 84% as against 64% with normal TG levels. There was statistically significant difference in the proportion of stroke patients between two groups with respect to diabetes. So, there was significant association between diabetes and TG levels in our study ($p<0.05$).

Table 21: Association of triglyceride level with hypertension

		Normal		Elevated		Total	P
		Frequency	Percent	Frequency	Percent		
HTN	Yes	22	88.0	68	90.7	85	0.028 Significant
	No	3	12.0	7	9.3	15	
	Total	25	100.0	75	100.0	100	

Proportion of hypertensive stroke patients with elevated TG levels were 90.7% as against 88% with normal TG levels. There was statistically significant difference in the proportion of stroke patients between two groups with respect to hypertension. So, there was significant association between hypertension and TG levels in our study ($p<0.05$).

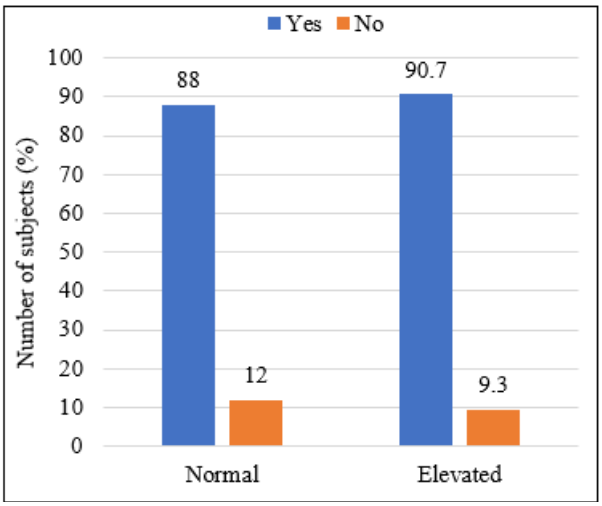

Figure 21: Association of triglyceride level with hypertension

4. Discussion

In diabetes, many factors affect blood lipid levels, because of the relationship between carbohydrates and lipid metabolism. The disorder in carbohydrate metabolism leads to disorder in lipid metabolism and vice versa. Insulin resistance is the primary defect in patients with type 2 diabetes mellitus. Insulin has an effect on the apolipoprotein production by liver and also regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport proteins, which causes dyslipidemia in patients of diabetes mellitus, which are shown in some studies. Insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase. Individuals with diabetes have hypertriglyceridemia with decreased HDL cholesterol which is a prominent feature. The cluster of lipid abnormalities associated with type 2 diabetes is defined by a high concentration of Triglycerides and small dense LDL and a low concentration of HDL cholesterol.

Hypertriglyceridemia is the product of increased hepatic secretion of VLDL and delay in clearance of triglyceride rich lipoproteins, which is due to increased levels of free fatty acids and glucose required for triglyceride production.[121]

Demographic information

We included total 100 patients of stroke in our study. Out of 100 cases, majority were from above 70 years age group, followed by 30% from 61-70 years, 15% from 51-60 years, 8% from 41-50 years and 1% from below 40 years age group. Mean age of the study population was 69.62±12.05 years 64% were males and 36% were females. Males were predominant in our study with male to female ratio of 1.77:1

Hakim Mohammad Shafi[125] conducted study in Department of Radiodiagnosis, SMHS hospital, Jammu and Kashmir, India. A total of 100 subjects (59 males and 41 females) were registered for the study. The mean age of the subjects was 57.41±12.4 years with a male: female ratio of 1.44:1.

Deshpande JJ et al[114] from Maharashtra conducted a study on lipid profile in patients with Ischemic Stroke in Rural coastal region of Maharashtra. Average age of Patients of Stroke was 60 ± 4.56 Yrs. The male and Female ratio in both the group was comparable with each other 1.25.

Onkar Nath Rai et al[110] from Gorakhpur conducted study in 100 stroke patients. He reported that males were (59.0%) more commonly affected with stroke as compared to females (41.0%). Maximum incidence of stroke was observed in those aged above 60 years (29%).

Our study findings are consistent with the findings of above-mentioned authors.

Age is an important risk factor for stroke. The mean age of stroke onset in India (i.e. 63 years).[106]

Karim ME et al[104] reported that males were predominant in both groups which was 80.0% in case group and 84.0% in control group and male to female ratio was almost 4:1 in both groups. The difference was not statistically significant ($p>0.05$) between two groups

Prevalence of hypertriglyceridemia in stroke

Prevalence of hypertriglyceridemia in our study was 75%.

Our findings are almost comparable with the findings of the other authors as stated below:

A population-based study of 4737 people aged 45-69 years in Shahroud, Iran, reported that the prevalence of dyslipidemia was 63.4% (CI 95%: 62.0-64.9%).[127]

In the surfncd-2007 study, the prevalence of hypertriglyceridemia >=150 mg/dl and hypercholesterolemia >=240 mg/dl was 36.4 (34.1-38.9) and 14.1 (12.6-15.9), respectively. [128]

Similar prevalence (34%) of hypercholesteremia was also reported by **Sreenivasulu et al**[106] **Qizilbash et al**[127] concluded that there was a significant association between serum lipid profile and prevalence of stroke.

Tanveer et al[128] proved that hyperlipidaemia was present in 16% patients of stroke.

In a study by **Siddeswari et al**[108] dyslipidemia in stroke patients was 14%.

Gonmei Z et al[129] in his study from Delhi reported overall prevalence of high cholesterol (≥200 mg/dl), high triglyceride (≥150 mg/dl), low HDL cholesterol (male - <40 mg/dl; female - <50 mg/dl), and high LDL cholesterol (≥130 mg/dl) was 20.39%, 45.63%, 64.08%, and 17.31%, respectively.

Study carried out among adults in Tamil Nadu, Maharashtra, Jharkhand, and Chandigarh also reported the prevalence of low HDL cholesterol (72.3%) as the most common dyslipidemia compared to hypercholesterolemia (13.9%), hypertriglyceridemia (29.5%), and high LDL cholesterol (11.8%).[128] In our study, we found low HDL in 70.1% which is consistent with the studies from Maharashtra, Tamil Nadu and Chandigarh.

Onkar Nath Rai et al[110] reported abnormal lipid values in 54 patients. Out of which increased non-HDL cholesterol was found in 53% patients. Increased LDL cholesterol was found in 35% patients followed by increased triglycerides in 34% patients. Increased total cholesterol was present in 30 patients.

Gupta R et al[130] reported prevalence of dyslipidemia in rural area was 15-20%

Association of triglyceridemic and type of stroke

In our study, proportion of ischemic stroke patients with elevated TG levels were 88% as against 64% with normal TG levels. Proportion of hemorrhagic stroke patients with elevated TG levels were 12% as against 36% with normal TG levels. There was statistically significant difference in the proportion of ischemic stroke patients between two groups. So, there was significant association between type of stroke and TG levels in our study ($p<0.05$). Ischemic stroke was commonly seen in patients with elevated TG levels.

Dyslipidemia is a primary major risk factor for coronary artery disease (CAD) and ischemic stroke. It causes insulin resistance which results in increased levels of plasma triglycerides and low-density lipoprotein cholesterol (LDL-C) and a decreased concentration of HDL-C, as an important risk factor for peripheral vascular disease, stroke, and CAD.[131,132]

Although there are no studies that evaluated trends in hypercholesterolemia in rural populations, review of previous studies shows increasing trends in these populations also. The prevalence of total cholesterol >200 mg/dl in early 1990s was 16% and has increased to 25–35% in more recent Andhra Pradesh Rural Health Initiative and India Migration Study.[133]

Across the studies, there was high prevalence of overweight, hypertension, and lipid abnormalities. Age- and sex adjusted trends showed significant increases in mean body mass index, fasting glucose, total cholesterol, HDL cholesterol and triglycerides (quadratic and log-linear regression, $p<0.001$). Categorical trends showed increase in overweight and obesity ($p<0.05$) while insignificant changes were observed in truncal obesity, hypertension, hypercholesterolaemia and diabetes. On the other hand, the prevalence of hypertriglyceridemia increased. [134,135]

Vakilian A et al[116] in their study published that there was significant association between the serum levels of TG and type of stroke. The serum TG level was significantly higher in the IS group (ischemic), compared to the ICH group.

Our finding is in line with the results of a study by **Saadatnia et al**[136]

In another study by Bonaventure et al., it was reported that the increased level of TG was associated with the increased risk of ischemic events. [137]

Additionally, **Freiberg et al**[138] revealed a direct relationship between the serum level of TG and IS. However, in a study by **Willey et al**[139] there was no significant association between IS and the serum levels of TG.

Moreover, **Uddin et al**[140] noted that elevation of serum TC and LDL-C levels is an alarming risk factor for IS, while the serum level of TG has no effects on IS; in our study, no such finding was reported.

Karim ME et al[104] reported that the mean TG was found to be 179.9±62.8 mg/dl in cases and 148.0±51.9 mg/dl in controls ($p<0.05$). **Karim ME et al**[104] also observed in this current study that normal triglyceride was found 52.0% in cases and 72.0% in control. The mean TG was found 179.9±62.8 mg/ dl in cases and 148.0±51.9 mg/dl in controls, which was significantly ($p<0.05$) higher in case group.

Austin MA et al[10] found that the mean average of TG was 169.71 mg/dl in patients and 148.68 mg/dl in controls.

Tanne et al[11] showed the mean TG 178±108 mg/dl in Ischemic Stroke/ TIA and 164±102 mg/dl in No CVD.

Bowman et al[140] (2003) obtained that the mean average of TG was 192.3±155.9 mg/dl in patients and 157.0±93.0 mg/dl in controls.

Hypertension and type of stroke

In our study, proportion of hypertensive stroke patients with elevated TG levels were 90.7% as against 88% with normal TG levels. There was statistically significant difference in the proportion of stroke patients between two groups with respect to hypertension. So, there was significant association between hypertension and TG levels in our study ($p<0.05$).

Hypertension is the most important modifiable risk factor for both ischemic stroke and ICH. However, hypertension appears to be a stronger risk factor for ICH than for ischemic stroke reported by **Qureshi et al**[141], **Lewington et al**[142] The risk of stroke increases exponentially with increasing diastolic blood pressure (DBP) mentioned by **macmahon et al**[143] However, hypertension is a highly preventable risk factor; a systematic review of 17 randomized clinical trials showed that lowering DBP by 5– 6 mmhg and systolic blood pressure (SBP) by 10–12 mmhg resulted in a 38% reduction in strokes. [141,142,143] Hypertension alone may also increase the risk of rupture related to degenerative changes of small arterioles documented by **Qureshi et al**[141]

Diabetes and type of stroke

In our study, proportion of diabetic stroke patients with elevated TG levels were 84% as against 64% with normal TG levels. There was statistically significant difference in the proportion of stroke patients between two groups with respect to diabetes. So, there was significant association between diabetes and TG levels in our study ($p<0.05$).

Karim ME et al[104] observed that 28.0% patients had diabetes mellitus in case group and 7.0% in control groups. Al most one third (32.0%) patients had hypertension in case group and 19.0% in control group. Alost one fourth (24.0%) patients had stroke in case group and 9.0% in control group. Only 4.0% and 19.0% had obesity in cases and controls respectively. Eight (8.0%) patients had dyslipidemia in cases and 18.0% in controls. Diabetes mellitus, hypertension and stroke were significantly ($p<0.05$) higher in case group; however, obesity and dyslipidemia were significantly ($p<0.05$) higher in control group.

Bowman et al[141] found diabetes 12.8% and 3.4% in case and control respectively.

5. Summary and Conclusion

5.1 Summary

The present descriptive observational study was carried out at Medicine OPD and IPD at Navodaya Medical College and Hospital Raichur involving 100 patients of stroke with the objective to identify if serum triglyceride levels on admission predict severity of stroke.

The results of our study are summarized as follows:

- We included total 100 patients of stroke in our study. Out of 100 cases, majority were from above 70 years age group, followed by 30% from 61-70 years, 15% from 51-60 years, 8% from 41-50 years and 1% from below 40 years age group. Mean age of the study population was 69.62±12.05 years
- Majority of the patients in our study had ischemic stroke i.e. 82% and remaining 18% had hemorrhagic stroke.
- Prevalence of diabetes in our study was 79%
- Prevalence of hypertension in our study was 85%
- Prevalence of overweight in our study was 27%
- Prevalence of hypertriglyceridemia in our study was 75%
- Out of 75 cases with elevated TG levels, majority were from above 70 years i.e. 32(42.7%) followed by 25 (33.3%) from 61-70 years, 12(16%) from 51-60 years, 5(6.7%) from 41-50 years and 1.3% from below 40 years age group. Out of 25 cases with normal TG levels, majority were from above 70 years i.e. 14(56%) followed by 5(20%) from 51-60 years and 3(12%) each from 41-50 and 51-60 years age group. We observed no significant association between age and TG level in our study ($p>0.05$)
- Proportion of males with elevated TG levels were 64% as against 64% of males with normal TG. Proportion of females with elevated TG levels were 36% as against 36% of females with normal TG. We observed no significant association between gender and TG level in our study ($p>0.05$)
- Proportion of ischemic stroke patients with elevated TG levels were 88% as against 64% with normal TG levels.

Proportion of hemorrhagic stroke patients with elevated TG levels were 12% as against 36% with normal TG levels. There was statistically significant difference in the proportion of ischemic stroke patients between two groups. So, there was significant association between type of stroke and TG levels in our study ($p<0.05$). Ischemic stroke was commonly seen in patients with elevated TG levels.

- Proportion of diabetic stroke patients with elevated TG levels were 84% as against 64% with normal TG levels. There was statistically significant difference in the proportion of stroke patients between two groups with respect to diabetes. So, there was significant association between diabetes and TG levels in our study ($p<0.05$).
- Proportion of hypertensive stroke patients with elevated TG levels were 90.7% as against 88% with normal TG levels. There was statistically significant difference in the proportion of stroke patients between two groups with respect to hypertension. So, there was significant association between hypertension and TG levels in our study ($p<0.05$).
- Proportion of overweight stroke patients with elevated TG levels were 24% as against 36% with normal TG levels. There was no statistically significant difference in the proportion of stroke patients between two groups with respect to BMI. So, there was no significant association between BMI and TG levels in our study ($p>0.05$).
- Mean TG level in stroke patients below 40 years was 270±0, 41-50 years was 202.88±79.01, 51-60 years was 230.67±92.07, 61-70 years was 201.6±68.15 and above 70 years was 193.07±68.87. When we compared the mean TG level in different age group, the difference was found to be statistically not significant in our study ($p>0.05$)
- Mean TG level in male stroke patients was 207.03± 76.85 and in female stroke patients was 195.33±66.73. When we compared the mean TG level between male and female patients, the difference was found to be statistically not significant in our study ($p>0.05$)

5.2 Conclusion

- This study was undertaken to evaluate the association of hypertriglyceridemia with ischemic stroke.
- Ischemic Stroke was more common in 6th and 7th decade and male predominant.
- Hypertension, smoking, diabetes mellitus and alcohol consumption were significantly ($p<0.05$) associated with ischemic stroke. On the other hand, ischemic stroke is associated significantly with a higher level of triglycerides. Therefore, this current study result confirms that hypertriglyceridemia may be a risk factor for ischemic stroke.

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