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A Study of Correlation between Serum Triglycerides and Severity of Cerebrovascular Accident

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Abstract

Stroke is the second leading cause of death worldwide; it is accounting for up to 20 percent of all central nervous system disorders in the urban sectors of India. Stroke defined as an abrupt neurologic deficit that is attributable to focal vascular etiology. Risk factors for stroke mainly are hypertension, diabetes, carotid stenosis, smoking, hyperlipidemia, atrial fibrillation, myocardial infarction, and atrial myxomas.

Nikolai Anichkov first proposed the relationship between cholesterol and atherosclerosis way back in 1912. Later on, observational studies have undoubtedly established hyperlipidemia as an independent risk factor for coronary artery disease. Law confirmed that low cholesterol concentrations are associated with an increased risk of death from ischaemic heart disease. Weir observed that low Triglyceride (TG), not low Total Cholesterol concentration, predicts poor outcomes after acute stroke. The probable mechanism responsible for the association between TG level and stroke severity is unknown. This study is undertaken to correlate serum triglyceride levels on admission with the severity of stroke as measured by the Scandinavian stroke scale.

Keywords: Triglycerides; Scandinavian stroke scale; Stroke; Hypertension; Diabetes; Ischaemic heart disease

Abbreviations: TG: Triglycerides; SSC: Scandinavian Stroke Scale; IHD: Ischemic Heart Disease.

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Introduction

Stroke is the second leading cause of death worldwide [1]; it is accounting for up to 20 percent of all central nervous system disorders in the urban sectors of India. Stroke defined as an abrupt neurologic deficit that is attributable to focal vascular etiology. Risk factors [2] for stroke mainly are hypertension, diabetes, carotid stenosis, smoking, hyperlipidemia [3], atrial fibrillation, myocardial infarction, and atrial myxomas.

Nikolai Anichkov first proposed the relationship between cholesterol and atherosclerosis way back in 1912. Later on, observational studies have undoubtedly established hyperlipidemia as an independent risk factor for coronary artery disease. Law confirmed that low cholesterol concentrations are associated with an increased risk of death from ischaemic heart disease. Weir observed that low Triglyceride (TG), not low Total Cholesterol concentration, predicts poor outcomes after acute stroke.

The probable mechanism responsible for the association between TG level and stroke severity is unknown. This study is undertaken to correlate serum triglyceride levels on admission with the severity of stroke as measured by the Scandinavian stroke scale.

Aim and objectives of study

The present study aims to study the significance of serum triglycerides levels in ischemic stroke severity.

Measurement of triglyceride

Enzymatic methods: The chemical methods used earlier have been now replaced by enzymatic assays employing lipase for the

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hydrolysis of the triglycerides coupled with enzymatic procedures for measuring the glycerol released. Currently [4], triglyceride measurement methods fall into two groups depending on whether glycerol measurement is based on glycerol dehydrogenase or glycerol kinase. Glycerol dehydrogenase acts on glycerol in the presence of NAD^+ to produce dihydroxyacetone and NADH. The reaction measured by the change in absorbance at 340 nm. The method criticised because of unfavourable equilibrium due to product inhibition, sensitivity to pH and lack of linearity.

Glycerol kinase, which used more frequently, acts on glycerol in the presence of ATP to produce glycerol-3-phosphate and ADP. Further enzymatic reactions may measure either of these products. In the presence of phosphoenolpyruvate and pyruvate kinase, ADP converted to ATP and pyruvate is generated. Pyruvate is then converted to lactate by lactate dehydrogenase with the equimolar conversion of NADH to NAD+. The reaction monitored by the change in absorbance at 340 nm. The disadvantage of this method is that serum components cause NADH consumption additional to that due to glycerol: ideally, a specimen blank should be run with lipase omitted from the reagent mixture. Methods that measure glycerol-3-phosphate produce by glycerol kinase are divided into those that use Glycerol Phosphate Dehydrogenase (GPDH) and those that use Glycerol-3-phosphate oxidase (GPO) for the next step.

GPDH converts Glycerol-3-phosphate to dihydroxyacetone phosphate with the equimolar reduction of NAD^+, which can be measured by the change in absorbance at 340 nm. A modification of this procedure was introduced by Megraw, who added diaphorase and INT (2-(p-iodophenyl)-3-(p-nitrophenyl)-5-phenyltetrazolium) to the reaction mixture. In the presence diaphorase, the NADH generated by the earlier reactions reduces the INT to formazan, which is measured calorimetrically at 500-550 nm.

In GPO methods, glycerol-3-phosphate is converted in the presence of oxygen to dihydroxyacetone and hydrogen peroxide. In turn, the hydrogen peroxide is acted on by peroxidase in the presence of a suitable chromogen which is oxidized to a coloured product.

Fossati and Prencipe used 4-aminophenazone,3,5-dichloro-2-hydroxy- sulphonic benzene acid, and potassium ferrocyanide as the chromogenic mixture from which the colored product is quinine monoamine, which gives maximum absorbance at 510 nm. This method is known as the GPO-PAP method.

In all the above methods, free glycerol present in the specimens will be measured as triglycerides unless modifications to the methods are introduced. In healthy subjects, the concentration of free glycerol in serum is low, and it is common to practice to reduce triglycerides results by 0.11 mmol/L to allow for it. Free glycerol may be determined in a separate assay using the reagents employed in the triglyceride assay but omitting the lipase. Sulivan modified the GPO-PAP method in which the specimen is pre-incubated with GPO and peroxidase to destroy the free glycerol. Lipase and the chromogenic substrate are then added to measure triglyceride. Automated methods using any of the enzyme systems described above are now in use.

Standards, reference preparations and reference ranges: Triglycerides should be measured when the patient is in a metabolic steady-state, in fasting samples. Blood samples should be obtained after a 9 to 12 hour period of fasting by venipuncture in the sitting position, and the patient should sit quietly for at least 5 min before sampling. If necessary, the patient can take water and prescribed medications during this period. Prolonged venous occlusion should be avoided. The tourniquet should be removed within 1 min of the application [5,6].

Triglycerides can be measured in either serum or plasma. Serum or serum-equivalent values should be reported. To convert measurements made in EDTA plasma to serum-equivalent values, multiply the plasma value by 1.03. Triglyceride measurements made in heparin plasma are equivalent to serum values.

If the analysis is delayed, the specimen can be stored for up to several weeks at -20°C in a non-self-defrosting freezer in clean sealed containers to prevent evaporation. Considering the physiological variability of triglycerides, triglycerides should be measured in at least two serial samples.

Laboratories should use procedures that allow the measurement of triglycerides with a total error of ≤ 15%.

Interpretation: The normal range for triglycerides may be taken as 0.11 to 1.60 mmoL/L up to the age of 30, with an increase at the upper end with increasing age to 1.83 mmoL/L at 50, and 2.17 mmoL/L at 60 years [4]. The normal range for endogenous glycerol is 0.05 to 0.18 mmoL/L [4].

Serum triglyceride values are decreased following large doses of ascorbic acid and during the administration of halofenate, heparin, oral hypoglycaemic drugs like metformin and phenformin and oxandrolone or oxymetholone.

Increased levels of triglyceride are seen commonly in secondary disorders of lipoprotein metabolism like Diabetes mellitus, obesity, alcoholism, nephritic syndrome, and hypothyroidism.

Primary hyperlipoproteinemias

Hypertriglyceridemia is also a part of a variety of genetic conditions. Frederickson and Levy classified hyperlipoproteinemias according to the type of lipoprotein particles that accumulate in the blood. In this classification, except for type IIa hyperlipoproteinemia, all of the hyperlipidemias are characterized by elevated triglycerides.

A triglyceride level of >1000 mg/dL increases the risk of acute pancreatitis. Because triglycerides are so labile, levels above 500 mg/dL become the primary concern of therapy before turning to LDL-lowering therapy **(Table 1).**

The U.S. National Cholesterol Education Program (NCEP), Adult Treatment Panel (ATP III), a division of the National Institutes of Health (NIH), recommends the following on who should be treated for elevated triglyceride levels.

Treatment of hypertriglyceridemia takes priority over LDL treatment, if triglycerides are 500 or above, to prevent pancreatitis. In every patient of hypertriglyceridemia, secondary causes should be controlled **(Table 2).**

Table 1 Frederickson classification of Hyperlipoproteinemias.

Phenotype	I	IIa	IIb	IIII	IV	V
Lipoprotein, elevate	Chylomicrons	LDL	LDL and VLDL	Chylomicron and VLDL remnants	VLDL	Chylomicrons and VLDL
S Triglycerides	++++	--	++	++ to +++	++	++++
Cholesterol	+ to ++	+++	++ to +++	++ to +++	-- to +	++ to +++
LDL- cholesterol						
HDL- cholesterol	+++	+	++	++	++	+++
Plasma appearance	Lactescent	Clear	Clear	Turbid	Turbid	Lactescent
Xanthomas	Eruptive	Tendon, tuberous	None	Palmar, tuberoeruptive	None	Eruptive
Pancreatitis	+++	0	0	0	0	+++
Coronary atherosclerosis	0	+++	+++	+++	+/–	+/–
Peripheral atherosclerosis	0	+	+	++	+/–	+/–
Molecular defects	LPL and apoC-II	LDL receptor, ApoB-100, PCSK9, ARH, ABCG5 and ABCG8	Unknown	ApoE	ApoA-V and Unknown	ApoA-V and Unknown
Genetic nomenclature	FCS	FH, FDB, ADH, ARH, sitosterolemia	FCHL	FDBL	FHTG	FHTG

Table 2 Classification of triglyceride levels.

TG Level, mg/dL	Classification
<150 mg/dL (<1.7 mmol/l)	Normal
150 - 199 mg/dL (1.7–2.3 mmol/l)	Borderline-high
200 - 499 mg/dL (2.3–5.64 mmol/l)	High
≥ 500 mg/dL (>5.64 mmol/l)	Very high

In case the secondary condition that raises triglyceride levels cannot be managed successfully, and if triglycerides are between 200-499 mg/dL, the non–HDL-c (total cholesterol - HDLc) can be used as the initial target of using LDL-lowering medication. The non–HDL-c denotes the sum of the cholesterol carried by the atherogenic lipoproteins, LDL, VLDL, and IDL.

The goals for non–HDL-c levels are similar to those for LDL-c levels and are dependent on the presence of risk factors. Risk factors include cigarette smoking, hypertension, low HDL cholesterol (<40 mg/dL).

The goals for non-HDL-c levels are 30 mg/dL higher than the corresponding LDL-c goals.

Role of lipids in atherogenesis and stroke

Atherosclerosis of arteries, extra cranial, and intracranial is the most prominent cause of stroke and hyperlipidemia is a major risk factor for atherosclerosis [5,7,8]. Most of the evidence specifically implicates hypercholesterolemia [3] and to a lesser extent, hypertriglyceridemia in the causation of atherosclerosis. The mechanisms by which hyperlipidemia contributes to atherogenesis are many:

1. Chronic hyperlipidemia, particularly hypercholesterolemia [3], impair endothelial function through increased production of superoxide and other oxygen-free radicals, which in turn deactivate nitric oxide which is the major endothelial- relaxing factor. Oxidative stress also activates the endothelial gene expression of numerous biologically active molecules and NF-κB.
2. Chronic hyperlipidemia causes the accumulation of lipoproteins within the intima at sites of increased endothelial permeability.
3. Free radicals are generated in macrophages or endothelial cells in the arterial wall which causes oxidative modification of lipid and yield oxidized (modified) LDL [9]. Oxidized LDL, in turn, contributes to lesion formation in several mechanisms:
   a) Macrophages readily ingest it through the scavenger
   b) It acts as a chemotactic factor for circulating monocytes.
   c) Oxidized LDL increases monocyte adhesion, through the induction receptor, thus forming foam cells of endothelial adhesion molecules.
   d) It inhibits the motility of macrophages already present in the lesion, hence favoring the recruitment and retention of macrophages in plaques.

The atherosclerotic plaques in the arterial walls contain large amounts of cholesterol. Increased levels of non-fasting triglycerides indicate the presence of increased levels of remnants from chylomicrons and very-low-density lipoproteins [10,11]. These triglyceride-rich lipoproteins are smaller and more abundant in cholesterol and thus penetrate the arterial endothelium [12] and may get trapped within the sub endothelial space [8,12-14].

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In patients with type I disease, the chylomicrons cannot be converted to remnants and the lipoproteins are very large [15] and consequently not able to penetrate the intima of arteries [16]. Therefore they are not atherogenic.

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Serum triglyceride values are decreased following large doses of ascorbic acid and during the administration of halofenate, heparin, oral hypoglycaemic drugs like metformin and phenformin, and oxandrolone or oxymetholone.

Increased levels of triglyceride are seen commonly in secondary disorders of lipoprotein metabolism like Diabetes mellitus, obesity, alcoholism, nephritic syndrome and hypothyroidism [19].

Risk factors for stroke: The liability to stroke increased by several factors like hypertension, heart disease [11], atrial fibrillation, diabetes mellitus, cigarette smoking, and hyperlipidemia, and it is here that large-scale public health measures have had a substantial influence [2,20,18].

Blood pressure: Hypertension is a significant risk factor for stroke, and about 40% of strokes can be attributed to a systolic blood pressure >140 mm Hg [15,21,22].

Smoking: The Framingham study showed that smokers are at a three-fold risk of developing ischemic strokes as compared to non-smokers and this effect was greater at younger ages and paralleled the number of cigarettes smoked.

Diabetes mellitus: According to the Framingham study, DM was the sixth most important predictive factor for stroke [23,24].

Transient ischemic attacks: One out of six patients with TIA would suffer a thrombotic stroke, after 2-4 years [25,26].

Obesity: In both smokers and non-smokers, body mass index is predictive of stroke, as shown by the White hall study. It was estimated that having a body mass index above 25 kg/m^2 and smoking account for 60% of strokes in men up to 65 years [27].

Cardiovascular disease: According to the Framingham study electrocardiographic changes of left ventricular hypertrophy increases the risk of ischemic stroke by tenfold, Nonspecific STChronic atrial fibrillation increases the risk of embolic stroke by is 5 to 7 fold than an age-matched population with normal cardiac rhythm [2].

Age: It is the single most important risk factor for stroke [18,28]. For each successive ten years after the age of 55, the stroke rate more than doubles in both men and women [29,30]. Stroke incidence rates are 1.25 times greater in men.

Cholesterol: Hypercholesterolemia is a modifiable risk factor for ischaemic heart disease, the relation to ischemic stroke remains unsettled [9]. Shreds of evidence support the definite link between total and LDL cholesterol and protective influence of HDL cholesterol on extra cranial carotid atherosclerosis [2,31]. The connection between TGs and ischemic stroke remains controversial [17,32].

Alcohol: Alcohol consumption predisposes to stroke. In alcoholics, the occurrence of embolic strokes accounted for cardiac arrhythmias, and cardiac wall motion abnormalities, increased platelet aggregation, activation of the clotting cascade and hypertension [33]. Increasing alcohol consumption increases the risk for brain haemorrhage [34].

Anticoagulant therapy: Anticoagulant therapy is a significant risk factor for intracranial hemorrhage.

Hemoglobin: Polycythemia increases the risk of stroke [28].

Prior stroke: In the national survey of stroke, it found that the annual incidence of recurrent stroke rates was 142 per one lakh population for the first stroke and 56 for subsequent stroke.

Methodology

Source of data

Hundred consecutive patients presenting with acute ischemic stroke, occurring within 24 hours, confirmed by CT scan admitted in King George Hospital Visakhapatnam from November 2017 to September 2020 were included in this study, and in each patient fasting serum, TG levels estimated.

Study design

Observational study (CROSS SECTIONAL)

Study period

From Nov 2017-2020. The present study was carried out on 100 patients (cases) admitted in the Medicine department, King George Hospital, Visakhapatnam. The patients in this study satisfied the following inclusion criteria.

Inclusion criteria: Patients with a first-ever ischemic stroke occurring within 24 hours, confirmed by CT scan, admitted to King George hospital, Visakhapatnam, Andhra Pradesh.

Exclusion criteria: Patients admitted >24 hours after stroke onset, History of stroke, Hemorrhagic stroke, History of transient ischemic attack, Space occupying lesions, Patients with Cortical venous thrombosis.

Data collection

Method of collection of data: A CT scan head (MRI brain where required) taken <24 hours after stroke onset for all patients with the first-ever stroke admitted in King George Hospital, Visakhapatnam.

Scandinavian stroke scale is used to measure the severity of stroke. The patients divided into two groups: those with severe stroke SSS >25 and those with mild/moderate stroke SSS <25.

Arterial hypertension was diagnosed when at least two readings of blood pressure were ≥ 140 mmHg (systolic) or ≥ 90 mmHg (diastolic) after the acute phase of the stroke. Ischemic heart disease was diagnosed when a history of angina pectoris or myocardial infarction was present. Smoking is considered if there is a history of cigarette/beedi smoking during the past 5 years. Abdominal obesity diagnosed if the waist circumference was >102 cm in men and >88 cm in women.

In addition to routine investigations as per standard protocol in the evaluation of stroke patients, fasting serum triglyceride level and total cholesterol were measured between 12 and 36 hours after stroke onset using commercially available kits. Hyper triglyceridemia was diagnosed if TG >2.3 mmoL/L. Patients were followed up until they were discharged from the hospital.

Parameters

The following parameters were tested:

- Age
- Sex
- Abdominal circumference (obesity)
- Diabetes
- Hypertension
- Smoking
- Atrial fibrillation
- IHD

Statistical method

1. Diagrammatic representation
2. Mean ± SD
3. a) X2 test

b) T-test

Procedure

A detailed history, clinical examination, and relevant laboratory investigations were done as per proforma. Fasting serum triglyceride levels were estimated in patients, quantitatively by GPO-TOPS method.

The intensity of chromogen (Quinoneimine) formed is proportional to the triglycerides concentration in the sample when measured at 505 nm (500-540 nm) **(Table 3).**

Testing

Plasma separation: Venous blood is collected from the patient after a 9-12 hour fasting, in a clean container, and centrifuged at 360rpm for two minutes for separation of serum.

Assay: 10 µL of the serum obtained is added to 1 mL of triglyceride reagent. This mixture is incubated for 10 minutes at 37°C, which yields Quinoneimine dye (red). The absorbance of standard (TG=2.3 mmmoL/L) and test sample are read at 505 nm on bichromatic analyzers against reagent blank.

Calculation: TG (mg/dl)=absorbance of test sample × concentration absorbance of standard of standard(mg/dl) (Converted to mmol/L by multiplying by 0.01129).

Results

The **Table 4** shows various parameters, their frequency, percentage, and mean and standard deviation (wherever possible).

In this study, the number of patients with severe stroke (SSS ≤ 25) was 32, of which 31 had TG ≤ 2.3 mmol/L, and only one patient had TG >2.3 mmol/L. The number of patients with mild to moderate stroke (SSS>25) was 68 of which 48 had TG ≤ 2.3 mmol/L, and 20 patients had TG >2.3 mmol/L **(Table 5).**

There is an association between TG Level and SSS at a 5% level of significance **(Figure 1).**

The mean of TG levels in patients with severe stroke is 1.057 ± 0.50 mmol/L, whereas in patients with mild to moderate stroke is 1.809 ± 0.79 mmol/L. A statistically significant difference present between TG levels, which are associated with lower and higher values of SSS (severe and mild to moderate stroke) **(Table 6)**.

The number of patients <65 years was 57, of which 43 had TG ≤ 2.3 mmol/L, and 14 patients had TG levels >2.3 mmol/L. The total number of patients in the age group ≥ 65 was 43, of which 36 had TG ≤ 2.3 mmol/L, and seven patients had TG levels >2.3 mmol/L **(Table 7)**.

The youngest age was 40 years, and the oldest age was 84 years **(Figure 2).** There is no association between TG Level and age at a 5% level of significance.

Table 3 The intensity of chromogen (Quinoneimine) proportional to the triglycerides concentration in the sample when measured at 505 nm.

Triglycerides +H_2O (In the presence of lipoprotein lipase)	→	Glycerol + Free fatty
Glycerol +ATP (In the presence of glycerol kinase and magnesium)	→	Glycerol-3-Phosphate + ADP
Glycerol-3-Phosphate + O_2 (In the presence of glycerol phosphate oxidase)	→	DAP + H_2O_2
H_2O_2 + 4AAP +3,5-DHBS (In the presence of peroxidase)	→	Quinoneimine dye + $2H_2O$

Table 4 Table of statistical measures.

Parameter	n	%	Mean	Standard Deviation(SD)
Age	100	100	62.06	10.24
Age <65	57	57	54.47	6.04
Age ≥ 65	43	43	71.77	5.41
TG level ≤ 2.3	79	79	1.25	0.45
TG level >2.3	21	21	2.74	0.67
SSS ≤ 25	32	32	13.73	5.84
SSS >25	68	68	38.6	10.08
Male	60	-	-	-
Female	40	-	-	-
DM-Yes	28	-	-	
DM-No	72	-	-	-
Smoking –Yes	30	-	-	-
Smoking –No	70	-	-	-
Obesity-Yes	20	-	-	-
Obesity-No	80	-	-	-
Hypertension-Yes	66	-	-	-
Hypertension-No	34	-	-	-
IHD –Yes	13	-	-	-
IHD-No	87	-	-	-
Atrial fibrillation-Yes	4	-	-	-
Atrial fibrillation –No	96	--	-	-

Table 5 Association between TG Level and SSS.

TG Level (mmol/l)					
		≤ 2.3	>2.3	Total	X^2 Value
SSS	≤ 25	31	1	32	9.063
	>25	48	20	68	
	Total	79	21	100	P value-0.003

In the present study, 66 patients are hypertensive, of which 52 had TG ≤ 2.3 mmol/L, and 14 patients had TG levels >2.3 mmol/L. Of the remaining 34 Non-hypertensive patients 27 had TG ≤ 2.3 mmol/L, and seven patients had TG levels >2.3 mmol/L **(Table 8).**

There is no association between TG Level and hypertension (HTN) at a 5% level of significance **(Figure 3).**

In this study, 13 patients were found to have IHD, of which 12 had TG ≤ 2.3 mmol/L, and one patient had TG levels >2.3 mmol/L. Out of the remaining 87 patients, 67 had TG ≤ 2.3 mmol/L, and 20 patients had TG levels >2.3 mmol/L **(Table 9).**

These differences were not statistically significant at 5% level of significance **(Figure 4).**

Of the 100 patients in this study, 28 were diabetic, and 23 had TG ≤ 2.3 mmol/L, and 5 had TG >2.3. of the remaining 72 non-diabetic patients, 56 had TG ≤ 2.3 mmol/L, and 16 had TG levels >2.3 mmol/L **(Table 10).**

There is no association between TG Level and DM at a 5% level of significance **(Figure 5).**

Of the 100 patients studied, 60 were males, and 40 were females. Among the males, 46 had TG ≤ 2.3 mmol/L, and 14 had TG levels >2.3 mmol/L. Of the 40 females, 33 had TG ≤ 2.3 mmol/L, and seven patients had TG levels >2.3 mmol/L **(Table 11).**

There is no association between TG Level and Sex of an individual at a 5% level of significance **(Figure 6).**

In this study, of the 100 patients studied, 20 were found to have abdominal obesity. The TG levels were ≤ 2.3 mmol/L in 16 of the obese patients. Of the 80 non-obese, 63 patients had TG ≤ 2.3 mmol/L, and 17 patients had TG levels >2.3 mmol/L **(Table 12).**

There is no association between TG levels and Obesity at a 5% level of significance **(Figure 7).**

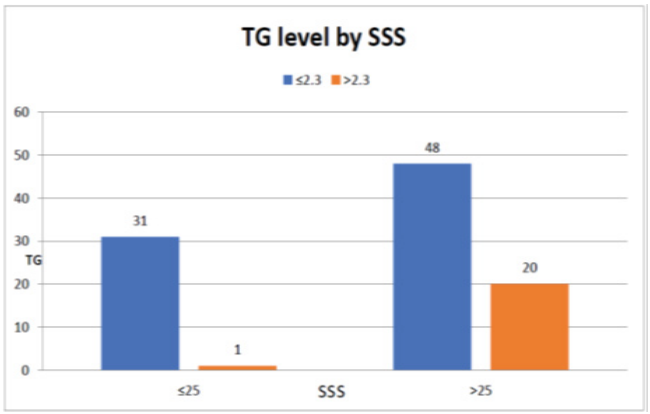

Figure 1 Bar diagram showing the association between TG Level and SSS.

Table 6 Statistical analysis for the significance of the TG levels associated with SSS ≤ 25 and SSS >2.

TG levels associated with SSS ≤ 25 Mean ± SD	TG levels associated with SSS >25 Mean ± SD	T-value	P-Value
1.057 ± 0.50 Mmol/L	1.809 ± 0.79 Mmol/L	4.889	0.00008

Table 7 Association between TG Level and age.

TG Level (mmol/l)					
Age		≤2.3	>2.3	Total	X^2 Value
	<65	43	14	57	1.013
	≥65	36	7	43	
	Total	79	21	100	P value- 0.336

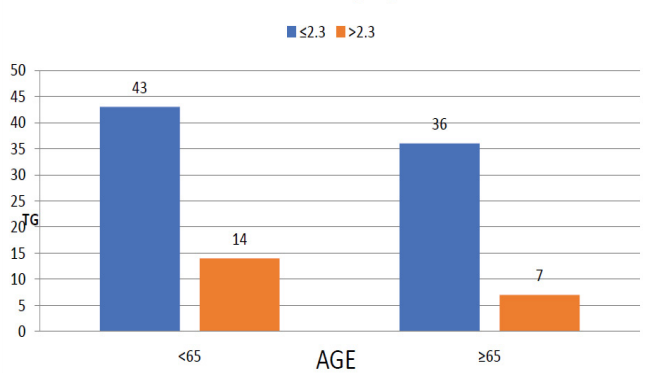

Figure 2 Bar diagram showing the association between TG Level and age.

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Table 8 Association between TG Level and hypertension.

		TG Level (mmol/L)			
		≤ 2.3	>2.3	Total	X^2 Value
HTN	Yes	52	14	66	0.05
	No	27	7	34	
	Total	79	21	100	P value-0.942

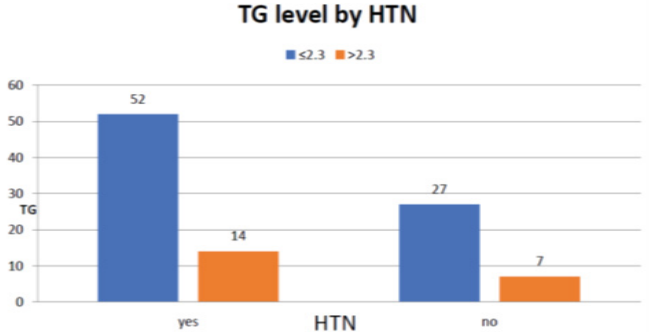

Figure 3 Bar diagram showing the association between TG Level and hypertension.

Table 9 Association between TG Level and IHD.

		TG Level (mmol/L)			
		≤ 2.3	>2.3	Total	X^2 Value
IHD	Yes	12	1	13	1.63
	No	67	20	87	
	Total	79	21	100	P value-0.442

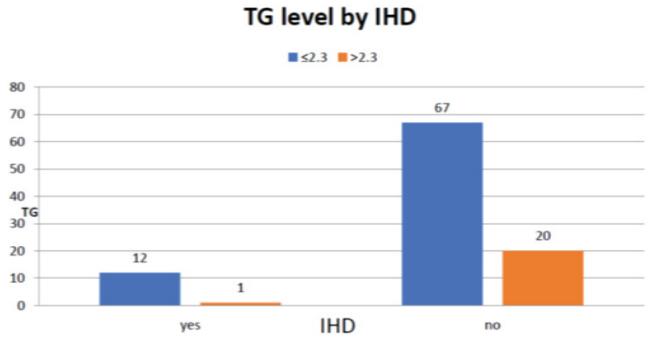

Figure 4 Bar diagram showing the association between TG Level and IHD.

Table 10 Association between TG Level and DM.

		TG Level (mmol/L)			
		≤ 2.3	>2.3	Total	X^2 Value
DM	Yes	23	5	28	0.232
	No	56	16	72	
	Total	79	21	100	P value-0.787

30 of the 100 patients are smokers, and 21 out of these 30 had TG ≤ 2.3 mmol/L, and 9 had TG levels >2.3 mmol/L. In the remaining 70 patients (non-smokers), 58 had TG ≤ 2.3 mmol/L, and 12 patients had TG levels >2.3 mmol/L **(Table 13).**

There is no association between TG levels and Smoking at a 5% level of significance **(Figure 8).**

Discussion

Triglyceride levels correlation to severity of stroke

The present study involved 100 patients of acute ischemic stroke. The mean triglyceride levels amongst them are 1.578 mmol/L. However, the mean triglyceride levels amongst patients with severe stroke (SSS ≤ 25) was found to be 1.057 ± 0.50 mmol/L and that in patients with mild to moderate stroke (SSS>25) was 1.809 ± 0.79 mmol/L. There is a statistically significant difference

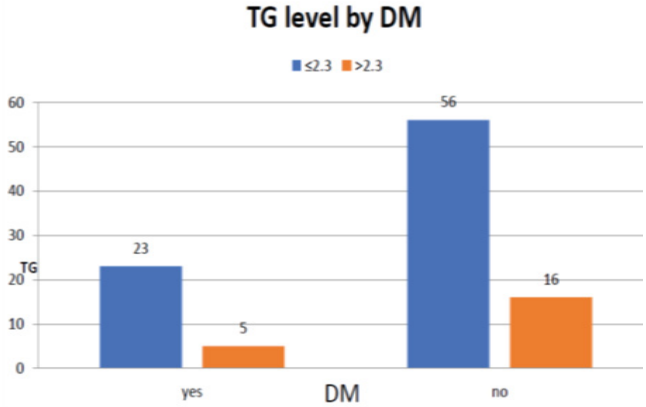

Figure 5 Bar diagram showing the association between TG Level and DM.

Table 11 Association between TG Level and Sex of an individual.

		TG Level (mmol/L)			
		≤ 2.3	>2.3	Total	X^2 Value
Sex	Male	46	14	60	0.492
	Female	33	7	40	
	Total	79	21	100	P value-0.483

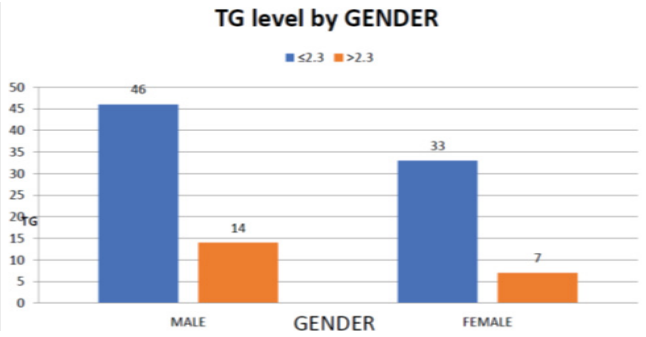

Figure 6 Bar diagram showing the association between TG Level and sex of an individual.

Table 12 Association between TG Level and Obesity.

TG Level (mmol/L)					
		≤ 2.3	>2.3	Total	X^2 Value
Obesity	Yes	16	4	20	0.015
	No	63	17	80	
	Total	79	21	100	P value-1.00

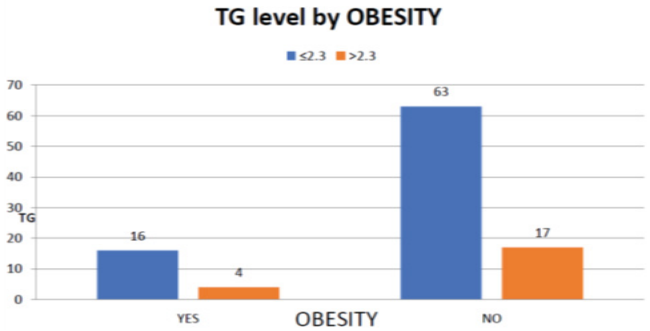

Figure 7 Bar diagram showing the association between TG Level and obesity.

Table 13 Association between TG Level and smoking.

TG Level(mmol/L)					
		≤2.3	>2.3	Total	X^2Value
Smoking	Yes	21	9	30	2.092
	No	58	12	70	
	Total	79	21	100	P value-0.148

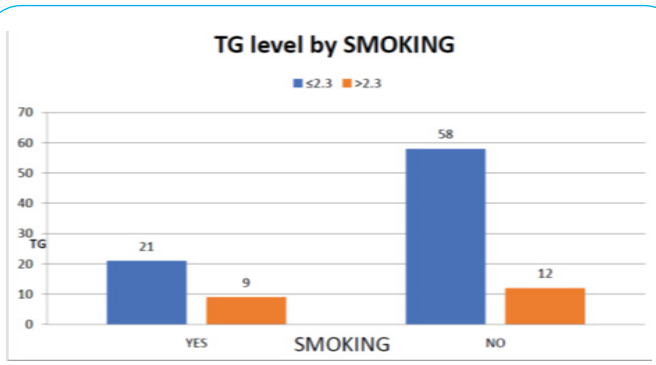

Figure 8 Bar diagram showing the association between TG Level and smoking.

between TG levels, which are associated with lower and higher values of SSS (severe and mild to moderate stroke, respectively) with p-value being 0.00008.

Tomasz Dziedzic, Agnieszka Slowik, and others in their study on 863 patients with acute ischemic stroke found that those with lower serum triglycerides had a severe stroke compared to those with higher serum triglyceride levels (1.4 ± 0.6 *vs.* 1.7 ± 1.3 mmol/L). They concluded that after adjusting for age, sex, atrial fibrillation, diabetes mellitus, obesity, and ischemic heart disease, patients with triglyceride >2.3 mmol/L had a less severe stroke. Weir in his study, showed that low TG concentration strongly and independently predicts higher mortality six months after stroke.

Another study consisting of 121 consecutive acute ischemic stroke patients showed that a higher (≥ 1.70 mmol/L) fasting serum triglyceride level (within 24 h after admission) was associated with a lower infarct volume (p=0.014) [9].

The biological mechanism responsible for the association between TG level and stroke severity is unknown. Low TG levels may reflect the poor nutritional status of the patient.

Though malnutrition in acute stroke patients is a risk factor for poor outcomes [35] at admission itself, it does not explain stroke severity. Therefore, different explanations focusing on potentially neuroprotective properties of cholesterol becoming evident. Higher cholesterol levels may be protective by increasing gamma-glutamyltransferase. Gamma-glutamyltransferase plays a role in amino acid uptake and transport and could reduce the neurotoxic effects of amino acids [36]. Cholesterol can also provide antioxidantprotection [37]. In one study higher cholesterol levels remained an independent predictor of better functional outcome in patients with first-ever ischemic stroke [38].

Triglyceride levels and age: Triglycerides gradually increase in men until about age 50 years and then decline slightly, but in women, they continue to increase with age. The prevalence of mild hypertriglyceridemia is slightly more in men beginning at age 30 years and women starting at age 60 years. The present study did not show any statistically significant association between TG level and age [28].

Sex and triglyceride levels: In the Prospective Munster Study (PROCAM), a large observational study, high triglycerides (triglycerides >200 mg/dL) was more prevalent in men (18.6%) than in women (4.2%). However, in the present study, no statistically significant association between TG level and sex of an individual could be noticed.

Smoking and triglyceride levels: The increased level of malondialdehyde in smokers is evidence of the intensification of lipid peroxidation processes, which may cause chronic stress for endothelial cells. However, it can also reorientate enzymatic systems of the arachidonic acid cascade towards intensified TXA2 synthesis [38].

Cigarette smoking has been found to increase the concentrations of triglycerides and lowers the level of HDL cholesterol [39,40]. These changes were found to contribute towards the atherogenic potential of cigarette smoking. But in another study, a significant difference in triglycerides between smokers and controls was not found [41]. Our study also did not show any significant association between TG level and Smoking.

Obesity and triglyceride levels: Mild-to-moderate hypertriglyceridemia is common in obese patients, mostly secondary to reduced efficacy of LPL and overproduction of VLDL. But this study did not show any association between TG levels and obesity.

IHD and triglyceride levels: In the Copenhagen Male Study on 2906 white men who were initially free of overt cardiovascular disease, an 8-year follow-up period showed that a clear gradient of risk of IHD found with increasing triglyceride levels within each level of HDL cholesterol, including high HDL cholesterol level,

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which are thought to protect against IHD. However, the present study did not show a significant association between TG Level and IHD [2,39].

Hypertension and triglyceride levels: Essential hypertension is frequently associated with metabolic abnormalities including glucose intolerance, hypertriglyceridemia, and enhanced postprandial lipemia [42,43].

Triglycerides are catabolized in the circulation at both muscle cells and adipocytes by endothelial-bound lipoprotein lipase, which in turn determines triglyceride catabolic rate, postprandial lipemia and, ultimately, fasting TG level [44,45]. As this lipase expressed at the vascular lumen surface, its activity is diminished with decreased microvascular density. Hence vascular rarefaction occurring in essential hypertension [19] may be directly responsible for impairing triglyceride catabolic rate. But this study failed to show an association between TG level and hypertension.

Diabetes and triglyceride levels: Uncontrolled type 1 and type 2 diabetes mellitus is one of the most common causes of hypertriglyceridemia and is often severe in patients presenting with ketosis. Insulin is deficient in patients with type 1 diabetes mellitus, and LPL is mostly ineffective. Administration of insulin will restore LPL function, reducing triglyceride levels and regaining diabetes mellitus control [19].

In uncontrolled type 2 diabetes mellitus with hyperinsulinemia, triglycerides elevated due to many reasons.

- LPL is less effective in the insulin-resistant states.
- Excess VLDL production by the liver is standard in patients with diabetes who are often overweight.

Diabetes mellitus leads to incomplete metabolism of VLDL, causing increased remnant VLDL or IDL observed in dysbetalipoproteinemia. However, this study did not show any association between TG level and diabetes mellitus.

Conclusion

In this study, mean serum triglyceride levels were significantly lower in patients with severe stroke when compared to the levels in patients with mild to moderate stroke.

As per this study, smoking, obesity, hypertension, IHD, diabetes mellitus, age, and sex of an individual do not influence levels of serum triglyceride levels.

Summary

This study was done to identify if serum TG levels predict the severity of stroke at admission. Scandinavian Stroke Scale (SSS) used for the assessment of the severity of stroke. The patients divided into two groups: those with severe stroke (SSS ≤ 25) and those with mild/moderate stroke (SSS >25). Fasting serum TG levels were estimated in each patient.

The total number of patients studied was 100 of which 60 were males, and 40 were females. Of the 100 patients, 43 were aged ≥ 65 years, and the rest were below 65 years of age. The commonest risk factor in the patients studied was hypertension, 66 patients out of 100patients (66%) were hypertensive. Other risk factors included DM in 28 patients (28%), smoking in 30 patients (30%), IHD in 13 patients (13%), abdominal obesity in 20 patients (20%) and atrial fibrillation in 4 patients (4%). However, this study did not show a significant association between triglyceride levels and smoking, obesity, hypertension, IHD, diabetes mellitus, age, and sex of an individual.

In this study, the number of patients with severe stroke was 32 of which 31 had TG ≤ 2.3 mmol/L, and only one patient had TG>2.3 mmol/L while those with mild to moderate stroke were 68 of which 48 had TG ≤ 2 .3 mmol/L, and 20 patients had TG>2.3 mmol/L.

The mean triglyceride levels amongst the patients were found to be 1.578 mmol/L (SD 0.790). The mean triglyceride levels amongst patients with severe stroke was found to be 1.057 ± 0.50mmol/L and that in patients with mild to moderate stroke was 1.809 ± 0.79mmol/L. There is a statistically significant difference between TG levels, which are associated with lower and higher values of SSS (severe and mild to moderate stroke respectively) with p-value being 0.00008.

Therefore according to this study, lower serum TG levels, at admission, are associated with severe stroke. Lower triglyceride levels may reflect the poor nutritional status of the patient.

Conflicts of Interest

The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.

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