A Study of Lipid Profile in Non Diabetic Ischemic Stroke in Adults

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Abstract
BACKGROUND:
Cerebrovascular accident is the most important non communicable disease resulting in 2nd leading cause of death and 3rd leading cause of disability worldwide. While blood lipids and lipoproteins are strongly related to coronary atherosclerosis, there association with cerebrovascular atherosclerosis is in doubt. Lipoproteins are considered as an independent risk factor for atherosclerosis. Due to distinctive structural homology with plasminogen, it interferes with function of plasminogen thus increasing thrombotic events. The amount of evidence relating to relation between serum lipids, lipoproteins and cerebrovascular accident is not adequate. The incidence rises steeply with age, and in many lower and middle income countries it is rising in association with less healthy lifestyles, prompted us to undertake this study. Hence the study has been taken up to study lipid abnormalities in nondiabetic stroke patients in our setup
AIM OF THE STUDY METHODOLOGY: The study will be conducted on 50 patients admitted to or attending out patient department Basaveshwar Teaching and General Hospital, attached to Mahadevappa Rampure Medical College, Kalaburagi. From 1st October 2019-31th March 2021 (18 months),prospective observational study
*RESULTS: Study observed that, majority of cases 24 (28.8%) were belongs to the age group of 31-40 years. Mean TC was 161 and abnormal 11 patients at onset , TG was abnormal in 11 patients at onset ,LDL was abnormal in 26 patients at onset , HDL was abnormal in 06 patients . **Correlation between variables (Spearmans Correlation test)** Statistically significant correlation was observed between **TC** & TG, HDL, LDL, VLDL, TC/HDL; **TG** & LDL ,VLDL, TC/HDL; **HDL** & LDL, , TC/HDL; **LDL &**, TC/HDL; **VLDL** & TC/HDL.*
CONCLUSION: Baseline high-density lipoprotein cholesterol, triglyceride, and total cholesterol levels were not associated with risk of ischemic stroke. Low-density lipoprotein cholesterol (LDL-C) cholesterol levels were associated with a paradoxical reduction in risk of stroke.
Key Words: *Ischemic stroke, Cerebro Vascular Accident, hemorrhagic stroke, lipoproteins, lipid profile*

I. Introduction:

Stroke is one of the most important non communicable diseases causing death and is responsible for 3.5% of disability adjusted life years (DALY) in India [1]. Cerebrovascular diseases include some of the most common and devastating disorders; ischemic stroke and hemorrhagic stroke [2].

Stroke or Cerebrovascular accident is defined as an "abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Thus the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis[3]. Stroke refers to any damage to the brain or spinal cord caused by the abnormality of the blood flow [4]. It is sometimes referred to as brain attack [5]. WHO defines stroke as "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 [6].

Stroke is difficult to treat and the treatment is still not effective. Prevention is the best option but ability to forecast the stroke is challenging making the detailed study of risk factors essential .[7] The risk factors of stroke include various fixed and modifiable risk factors, notable among them are age, gender, heredity, diabetes mellitus, hypertension, dyslipidemia, smoking, atherosclerosis, excessive intake of alcohol and other rare causes .[7]There is good evidence that modification of risk factors will reduce the risk of stroke.[7,8]

Studies have shown that elevated levels of serum lipids are important risk factors for the development of atherosclerosis which is the precursor of stroke.[9] Elevated plasma concentration of low density lipoproteins (LDL) and low levels of high density lipoprotein (HDL) concentrations are associated with an increased risk of atherosclerosis.[9] The relationship between atherosclerosis and elevated serum lipids is well established and aggressive treatment of dyslipidemia decreases the risk of stroke.[8] Numerous clinical trials have shown a

marked reduction in stroke incidence with use of cholesterol lowering drugs as in case of coronary artery disease, the level of low density lipoprotein (LDL) cholesterol has the most impact on incidence of stroke but elevated triglyceride (TG) may also confer risk.[10]

II. Materials And Methods:

Source of Data:
 The study will be conducted on 50 patients admitted to or attending out patient department Basaveshwar Teaching and General Hospital, attached to Mahadevappa Rampure Medical College, Kalaburagi.
 METHOD OF STUDY:
Study will be conducted on 50 patients of non-diabetic adult ischemic stroke patients
Data will be collected with meticulous history clinical examination with detailed neurological examination along with appropriate investigations.
PERIOD OF STUDY
1st October 2019-31th March 2021 (18 months)
INCLUSION CRITERIA:
Non diabetic ischemic stroke patients below   45years
 EXCLUSION CRITERIA:
• Diabetic stroke patients are excluded.
• Patients on diet or other modifications that would lower the plasma lipid levels are   excluded.
• Stroke patients > 45years
• Cerebral infraction associated with trauma and tumors.

INFORMED CONSENT
Written and informed consent will be taken from the patient in patient's own vernacular language.
The investigations like
Random Blood sugar, FBS and PPBS if RBS elevated and Hba1c
• 12 hours fasting Lipid profile for
• Serum Total Cholesterol
• Serum Triglycerides
• Serum High Density Lipoproteins (HDL)
• Serum Very Low-Density Lipoproteins (VLDL)
• Serum Low Density Lipoproteins (LDL)
• Computed tomography (CT) scan of the brain/ MRI brain:

III. Results

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Results on continuous measurements were presented on Mean ± SD (Min-Max) & categorical as Frequency (Percentage). Normality of the data was assessed using Shapiro Wilk test/ Kolmogorov-Smirnov test. Inferential statistics like Chi-square test/Fischer Exact test, Mann-Whitney U test and Kruskal-wallis test was used to check difference between the groups. The significance of level adopted was 5%.

Table No.1: Age and sex wise distribution of cases

Age in years	Male		Female		Total	
	No.	%	No.	%	No.	%
21—30	4	13.8	3	14.3	7	14.0
31—40	12	41.4	12	57.1	24	48.0
41—45	13	44.8	6	28.6	19	38.0
Total	29	100.0	21	100.0	50	100.0
Mean ± SD	38.10 ± 4.95		37.47 ± 6.20		37.65 ± 12.14	
t-test value and P-value	t = 0.397 P = 0.693 NS					

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

Study observed that, majority of cases 24 (28.8%) were belongs to the age group of 31-40 years, followed by 19 (38.0%) of cases were belongs to the age groups of 41-45 years and 7 (14.0%) of cases were belongs to the age group of 21-30 years
There was no statistical significant difference of mean age of cases between males and females (P>0.05)

Multiple bar diagram represents age and sex wise distribution of cases
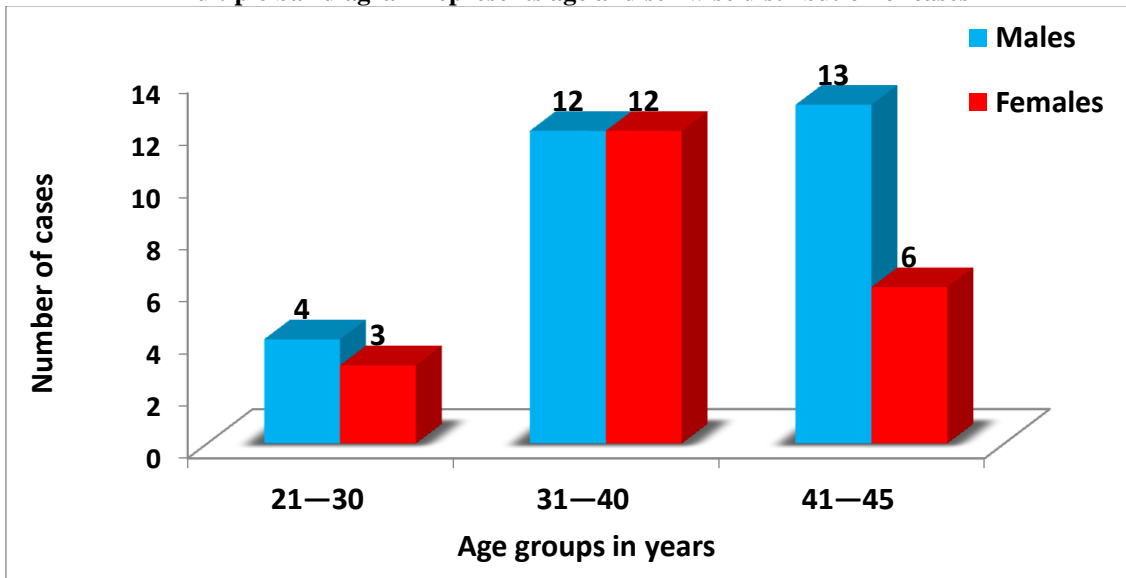

Table No.2: Height ,Weight and BMI distribution of cases

Age	Mean±SD	Range
Height	158.96±7.21	147-177
Weight	63.88±8.09	44-84
BMI	25.11±3.01	18.66-34

In our study, the mean height of patients with stroke is 158.96 cms with standard deviation 7.21.

   •**The mean weight is 63.88kg with standard deviation 8.09**
   •**The mean BMI is 25.11kg/m² with standard deviation of 3.01**

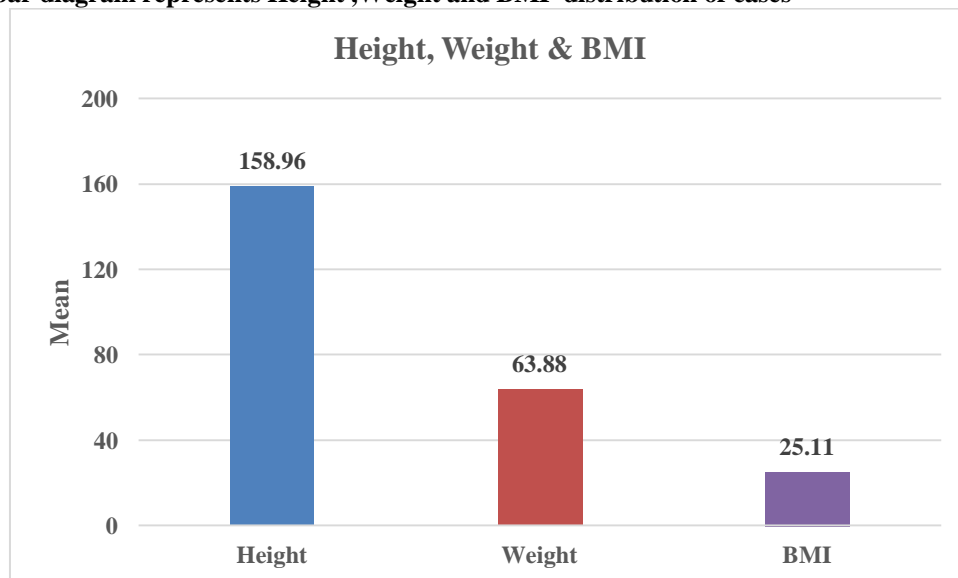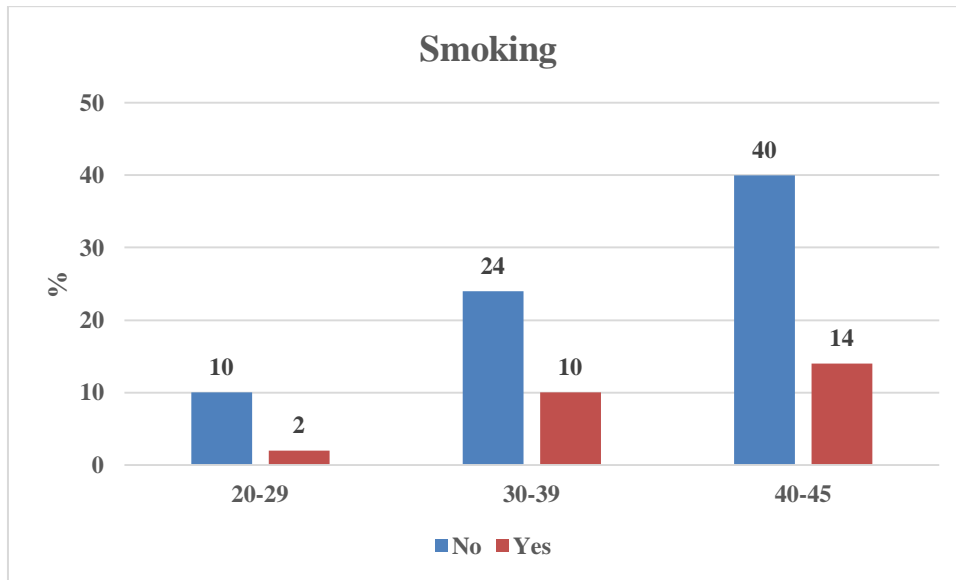**Multiple bar diagram represents Height ,Weight and BMI distribution of cases**

Table No.3: Smoking wise distribution of cases

Smoking	No N(%)	Yes N(%)	P value
20-29	05(10)	01(02)	0.346
30-39	12(24)	05(10)	
40-45	20(40)	07(14)	
Total	37(74)	13(26)	

Smoking

Table No.4: Hypertension wise distribution of cases

Hypertension	No N(%)	Yes N(%)	P value
20-29	03(06)	03(06)	0.99
30-39	09(18)	08(16)	
>40	14(28)	13(26)	
Total	26(52)	24(48)	

Hypertension
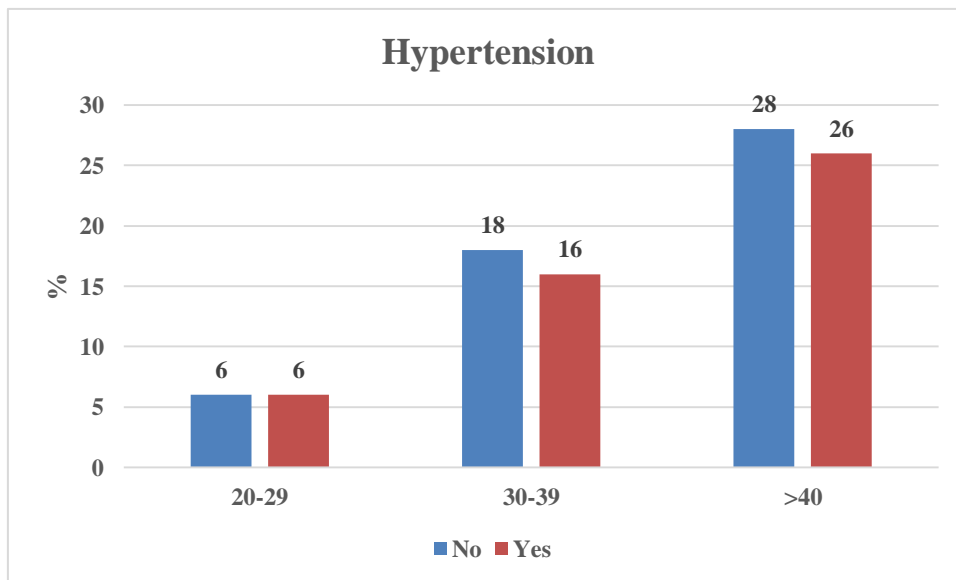
Table No.5: Stroke based on clinical examination distribution of cases

CVA type	Ischemia	%
Left hemiparesis	22	44
Right hemiparesis	15	30
Left hemiplegia	3	6
Right hemiplegia	8	16
Brain stem stroke	1	2
Multi infarct	1	2
total	50	100

In my study majority of the cases have left hemi paresis followed by right hemi paresis with 44% and 30% respectively. 16% of the patient and 6 % of the patient had right and left hemiplegia respectively. 2% of my study population had brain stem stroke. 2 %of my study population had multi infarct state.

Table No.5: Comparison of the variables based on age groups (Kruskal-Wallis test)

|		N	Mean	SD	Minimum	Maximum	P value
TC	**20-29**	06	155.67	57.59	106	255	0.626
	30-39	17	169.12	48.73	107	269	
	40-45	27	157.78	41.82	106	235	
	Total	50	161.38	45.53	106	269	
TG	**20-29**	06	150.83	83.01	52	267	0.757
	30-39	17	162.00	84.39	79	404	
	40-45	27	148.26	89.52	37	437	
	Total	50	153.24	85.56	37	437	
HDL	**20-29**	06	38.83	8.08	32	53	0.778
	30-39	17	37.12	11.11	20	58	
	40-45	27	36.67	13.49	11	82	
	Total	50	37.08	12.00	11	82	
LDL	**20-29**	06	105.83	41.65	64	180	0.405
	30-39	17	106.06	36.95	60	199	
	40-45	27	91.78	27.23	57	143	
	Total	50	98.32	32.67	57	199	
VLDL	**20-29**	06	28.66	17.14	10.0	53.0	0.638
	30-39	17	33.52	15.28	16.0	81.0	
	40-45	27	31.57	17.92	5.4	87.0	
	Total	50	31.88	16.71	5.4	87.0	
TC/HDL	**20-29**	06	3.93	1.09	2.60	5.18	0.501
	30-39	17	4.81	1.66	2.76	8.15	
	40-45	27	4.76	2.31	2.42	14.60	
	Total	50	4.68	1.98	2.42	14.60	
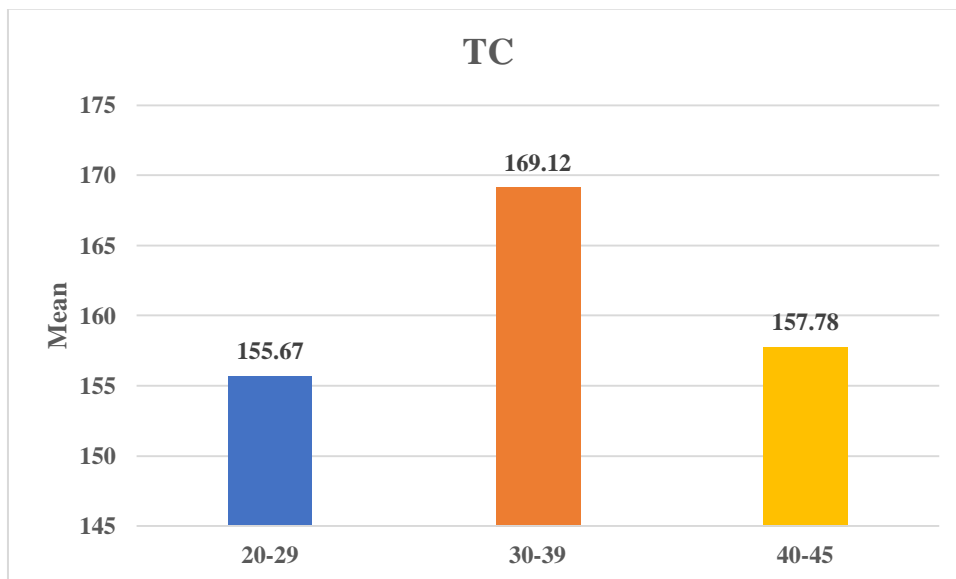
In my study the mean total cholesterol is 161mg/dl with a standard deviation of 45.53mg/dl.
The minimum value of total cholesterol in my study is 106mg/dl and maximum value is 269 mg/dl.
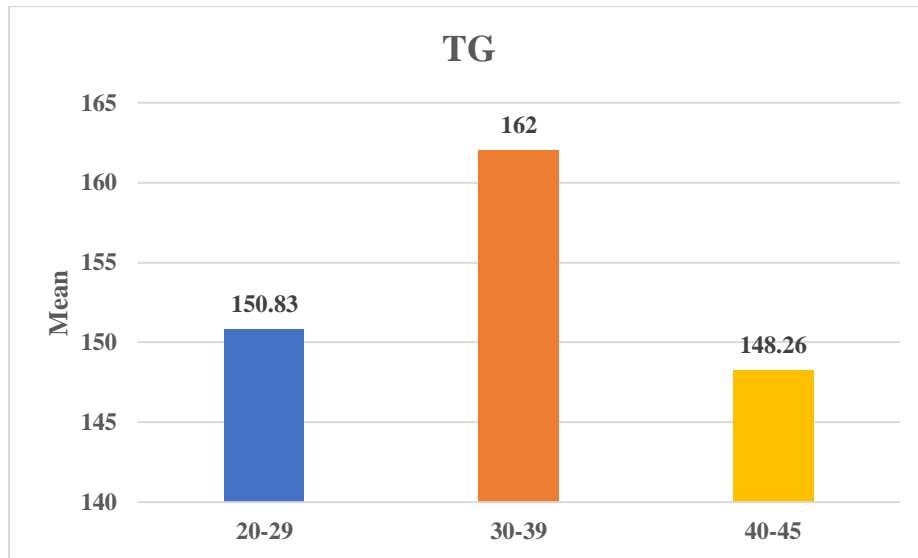
The mean value of triglycerides is 153.24 mg/dl in my study population with a standard deviation of 85.56mg/dl. The minimum and maximum Triglycerides observed in my study is 37and 437 mg/dl.
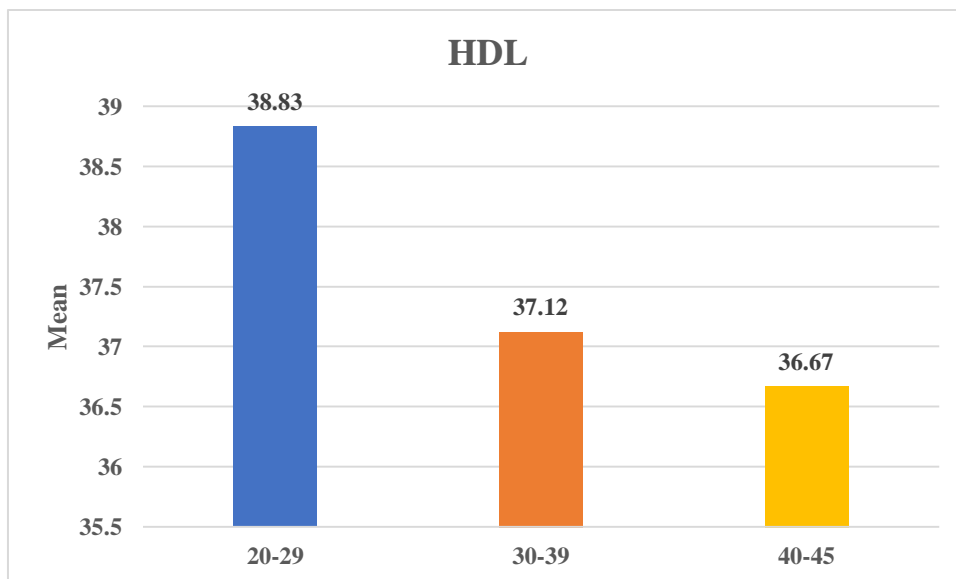

In my study group the mean HDL-C is 37.08 mg/dl with a standard deviation of 12 .00mg/dl. The minimum and maximum HDL –C value observed is 11mg/dl and 82 mg/dl respectively.
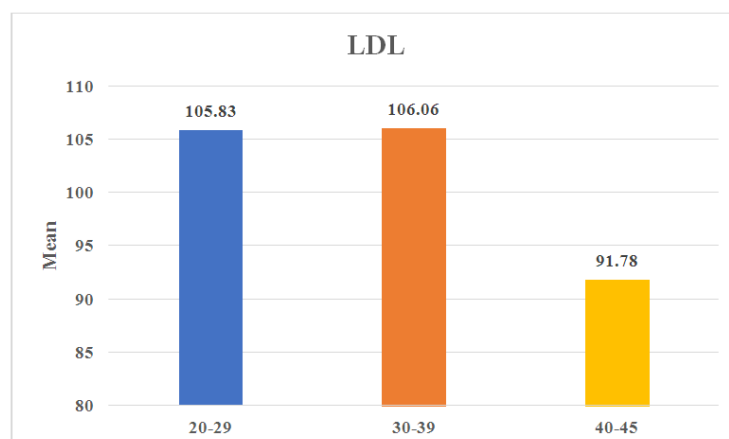
In my study population the mean LDL-C among the stroke population is 98.32mg/dl with a standard deviation of 32.67mg/dl and values range from 57mg/dl to 1999mg/dl.
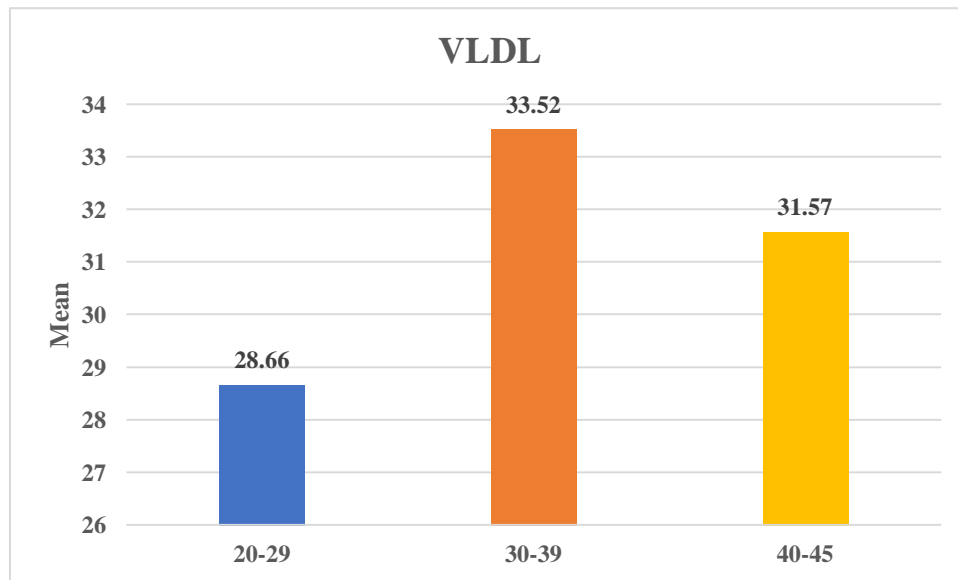
VLDL

In my study population the average mean of VLDL-C levels is 31.88 mg/dl with standard deviation of 16.71 mg/dl. The minimum value of VLDL –C is 5.4mg/dl and maximum value is87 mg/dl
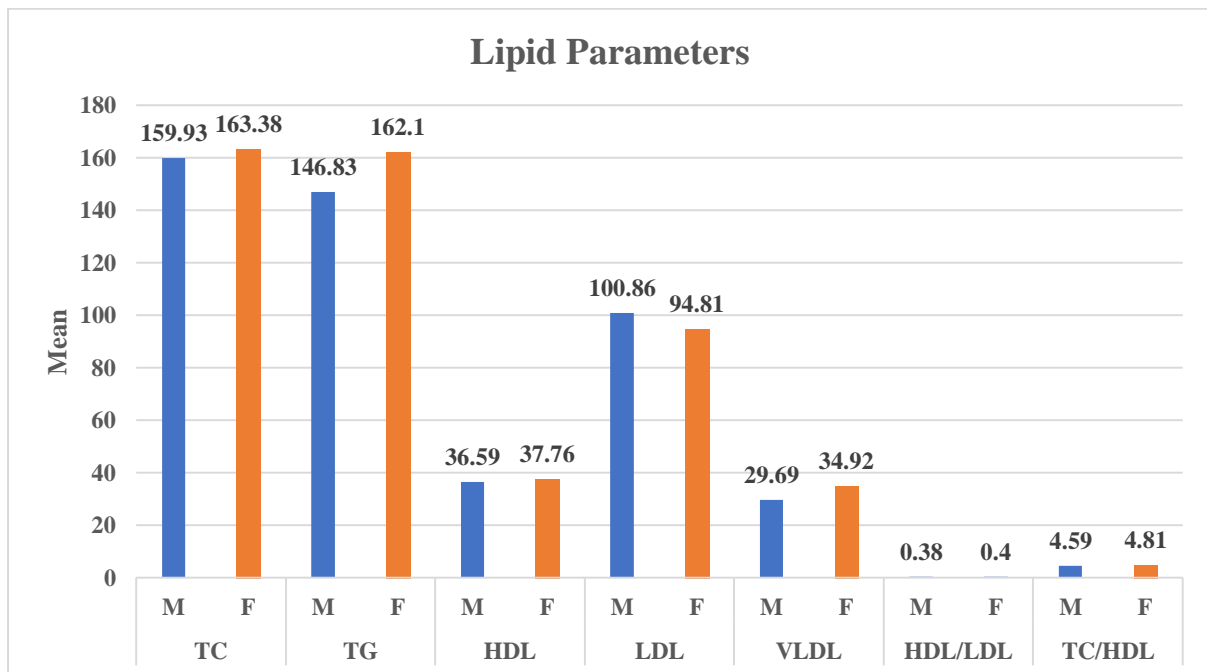
TC/HDL
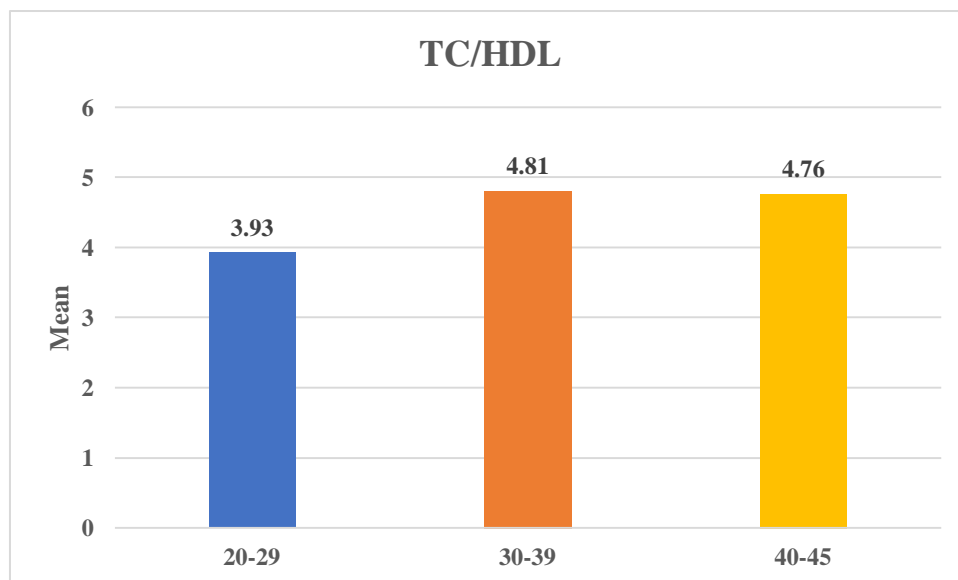
In my study the mean TG:HDL-C value is 4.68 with a standard deviation of 1.98and range extendsfrom2.00to11.60.

Table No.6: Comparison of the variables based on gender (Mann-Whitney U test)

	Gender	N	Mean	SD	P value
TC	**Male**	29	159.93	43.57	0.922
	Female	21	163.38	49.14	
TG	**Male**	29	146.83	69.37	0.969
	Female	21	162.10	105.15	
HDL	**Male**	29	36.59	9.46	0.929
	Female	21	37.76	15.05	

LDL	**Male**	29	100.86	32.15	**0.340**
	Female	21	94.81	33.85	
VLDL	**Male**	29	29.69	13.79	**0.360**
	Female	21	34.92	20.02	
HDL/LDL	**Male**	29	0.38	0.15	0.644
	Female	21	0.40	0.14	
TC/HDL	**Male**	29	4.59	1.58	0.99
	Female	21	4.81	2.46	

Inference: No statistically significant difference is observed when checked gender-wise

Table No.7: Correlation between variables (Spearmans Correlation test)

		TG	HDL	LDL	VLDL	TC/HDL
TC	**Correlation Coefficient**	0.610	0.383	0.808	0.427	0.489
	P value	0.001*	0.006*	0.001*	0.002*	0.001*
TG	**Correlation Coefficient**	-	0.043	0.435	0.817	0.488
	P value	-	0.765	0.002*	0.001*	0.001*
HDL	**Correlation Coefficient**	-	-	0.348	-0.052	-0.587
	P value	-	-	0.013*	0.718	0.001*
LDL	**Correlation Coefficient**	-	-	-	0.184	0.349
	P value	-	-	-	0.200	0.013*
VLDL	**Correlation Coefficient**	-	-	-	-	0.413
	P value	-	-	-	-	0.003*

Inference: Statistically significant correlation was observed between **TC** & TG, HDL, LDL, VLDL, TC/HDL; **TG** & LDL ,VLDL, TC/HDL; **HDL** & LDL, , TC/HDL; **LDL &**, TC/HDL; **VLDL &** TC/HDL;

IV.   Discussion:

Epidemiological studies suggest that patients with elevated lipid levels are at higher risk for atherothrombotic brain infarction than those with normal values and this applies mainly to premature ischaemic stroke.Serum lipids have been incriminated in the pathogenesis of

atherosclerosis, but very little is known concerning the possible interrelationship between abnormal levels of serum lipids and development of vascular complications. Lipid composition of the intima of the arteries resembles that of serum, therefore it is believed that there should be possibility of inter-relationship between abnormal lipid levels and ischaemic stroke. Hence Dyslipidemia has emerged clearly as a major risk factor associated with increased risk of atherosclerosis.

Cholesterol-

The study showed no relationship with cholesterol levels and stroke incidence which co- relates with studies conducted by Prospective studies collaboration 1995; Dauber et al, Kagan et al, Harmisenet a. Benfanteet al and Di Mascio et al had found positive co-relation between serum cholesterol and stroke incidence which is not corelated in the present study.

Rastenyte et al and Hart et al found that serum cholesterol levels are not related to risk of death from stroke which co-relates with the present study.

TRIGLYCERIDES-

Several studies such as Nubiolaet al, Sulonen and Puska et al, Qizildach et al, Tanne et al and Iso et al indicated high incidence of ischaemic stroke with hyper-triglyceridaemia which is contradicted in the present study.
Njolstalet al study states hypertriglyceridemia is weekly associated with ischaemic stroke in women but not in men which is not seen in the present study.
Albucher J.K et al 2000 has showed serum triglycerides in normal range in his study on stroke.

LDL-

William W B Kannelet al referred that relatively a large amount of cholesterol in the LDL fraction was atherogenic, whereas the HDL fraction was protective. Studies revealed the severity of stroke is more in patients with high LDL levels at onset as per mNIHSS.
Few studies such as Garg RK et al12 showed patients with thrombotic stroke to have high LDL levels which is statistically significant . study done by Hachinski et al which states patients have a high risk of thrombotic stroke with high LDL levels at onset.

Sreedharan - et al showed raised levels of serum LDL cholesterol had significant risk of ischemic stroke in non-diabetics.
Bolet et al and Hachinski et al have showed positive correlation between LDL cholesterol levels and risk of stroke.
Anseil B.J et al in 2000 showed patients with established atherosclerosis showed are treated with statins to lower LDL cholesterol levels < 100 mg to decrease the incidence of stroke.
Kurth T6 et al 2007 showed remarkable increase in serum LDL levels in ischemic stroke patients.
Lipid profile in Cerebrovascular Accidents" by Mansoureh Tagha et al concludes that LDL-C can be considered as a risk factor for both ischemic and hemorrhagic cerebral events ,high Total Cholesterol is a risk for ischemic stroke, whereas high TG had a protective against hemorrhagic events. In my study both high total cholesterol and high LDL-C is associated with ischemic stroke compared to hemorrhagic stroke and triglyceride levels are not a major risk factor for ischemic or hemorrhagic cerebral events.
In a study by Raju Talenar "A Study of lipid profile in Non-diabetic patient with CVA at tertiary health care centre" concludes that abnormal TG,VLDL,LDL are associated with stroke, and this study did not mention about both ischemic and hemorrhagic stroke separately . In our study both TG and VLDL are in a normal range for both ischemic and hemorrhagic stroke, but then it is compared higher levels are associated with ischemic stroke.Alok Mohankar, Ravindrakumar in 1993 showed increased LDL levels and low HDL levels were associated with atherosclerosis.

HDL

Severalstudies such as Qizilbach et al, sjd haram et al, lindgren et al,linden storm et al, tanne et al9, Wannamathe et al Sacco et al and Koren Morag et al indicated ischaemic stroke was associated with low levels of HDL which was not significant in the present study.
Simons et al in his study concluded that increase in HDL cholesterol is protective in ischaemic stroke which was similar to study conducted by Northern Manhattan study group which stated significant reduction in Ischaemic stroke with increase in HDL levels which was contradicted in the present study.

Simons et al study revealed HDL cholesterol had protective effect on ischemic stroke. The northern Manhattan study on stroke in 2001, concluded higher values of HDL cholesterol was associated with reduced risk of stroke. Wanna Mithee S.G et al had shown high HDL levels were associated with decreased non fatal stroke risk

VLDL
the present study high VLDL levels at onset did not show co-relation with severity of stroke.
Garg RK et al stated increased risk of thromboembolic stroke with high serum VLDL levels which is not relevant in the present study.
Bidyadhar et al 1984 showed that VLDL was raised in their study on stroke. Sreedharan - et al in his study showed high VLDL was not associated with risk of stroke in non-diabetic patients.

V. Conclusions:
1. The study showed no significant co - relation between the serum cholesterol &ischaemic stroke incidence.
2. The study showed no significant co-relation between the serum Triglycerides/VLDL and ischaemic stroke incidence.
3.Baseline lipid panel components were not associated with an increased stroke risk in this cohort. Treatment with cholesterol-lowering medications and changes in LDL-C level over time may have attenuated the risk in this population, and lipid measurements at several points
may be a better marker of stroke risk.
4.Baseline high-density lipoprotein cholesterol, triglyceride, and total cholesterol levels were not associated with risk of ischemic stroke. Low-density lipoprotein cholesterol (LDL-C) and non–high-density lipoprotein cholesterol levels were associated with a paradoxical reduction in risk of stroke.

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