Role of non-high-density lipoprotein cholesterol as a risk factor in ischemic stroke

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ABSTRACT

Introduction:

The present study highlights the significance of non-high-density lipoprotein cholesterol (non-HDL-C) as a key risk factor for ischemic stroke. A thorough analysis revealed a strong correlation

between elevated non-HDL-C levels and an increased risk of ischemic stroke. These findings underscore the importance of incorporating non-HDL-C testing into routine clinical practice to enhance risk assessment and preventive strategies. By identifying individuals at heightened risk based on non-HDL-C levels, healthcare providers can implement targeted interventions—such as lifestyle modifications and pharmacological treatments—to effectively reduce the likelihood of ischemic stroke.

Objectives:

To measure non-HDL cholesterol levels in ischemic stroke patients.

To evaluate non-HDL cholesterol and to establish non-HDL cholesterol as an independent risk factor for ischemic stroke.

Materials and methods:

Fasting venous sample of 5ml was drawn and lipid profile levels like Total Cholesterol (TC), Triglycerides (TGL), Low Density Lipoprotein Cholesterol (LDL-C) and High-Density Lipoprotein Cholesterol (HDL-C) were performed. Non-HDL-C was calculated.

Results:

All the patients in the study had experienced CVA-Infarct. A majority (70.1%) showed elevated levels of non-HDL cholesterol. Among patients with normal LDL cholesterol levels, 85.5% also had normal non-HDL levels, while 14.5% still had elevated non-HDL cholesterol. Notably, all patients with high LDL levels (100%) had elevated non-HDL cholesterol as well. The study found significant gender-based differences in mean total cholesterol, LDL, HDL, and VLDL levels. However, there was no significant difference in mean non-HDL cholesterol levels when comparing patients across different age groups. This suggests that non-HDL cholesterol levels remain consistent among stroke patients regardless of age.

Conclusion:

The present study emphasizes how important non-high density lipoprotein cholesterol (non-HDL-C) as a risk factor for Ischemic Stroke. The results further highlight the need for more investigation into the underlying mechanisms that connect non-HDL-C and ischemic stroke, as well as the effectiveness of particular non-HDL-C targeted therapies in lowering the incidence of stroke and enhancing outcomes.

INTRODUCTION

Stroke is of two types, ischemic stroke and hemorrhagic stroke that include subarachnoid and intracerebral haemorrhage. Globally, stroke is the main cause of mortality and disability. Ischaemic stroke accounts for approximately 71% characterized as an infarction of the brain, spinal cord, or retina [1,2]. Age, sex, and genetic variables are non-modifiable risk factors for ischemic stroke. The impact of age on the risk of ischemic stroke varies depending on a nation's level of development; for instance, developed nations have shown greater rises in incidence and prevalence after 49 and 39 years of age, respectively, when compared to developing nations [3]. Globally, the prevalence of ischemic stroke among people aged 20 to 64 approximately doubled between 1990 and 2013, and disability-adjusted life years increased by 37.3% during that same period [4].

Several modifiable risk factors for ischemic stroke have been identified. The INTERSTROKE study found that eight key factors accounted for 91.5% of the global population-attributable risk, consistent across age, sex, and regions [5]. Blood lipid profiles—including total cholesterol (TC), HDL-C, LDL-C, and triglycerides (TG)—are commonly used in diagnosing and assessing cardiovascular disease (CVD) risk [6]. Non-HDL-C levels are reported to strongly correlate with ApoB100, offering similar clinical insights. As a result, each could be used as a therapeutic proxy for the other. The majority of the variability (92%) in ApoB100 values may be captured by include LDL-C and non-HDL-C in normal lipid panels, according to data from UK Biobank research, and ApoB100 measurement does not provide any additional predictive value for ASCVD risk [7, 8,9].

ApoB100 testing is costlier and slower than standard lipid panels, while non-HDL-C is easily calculated and widely used as both a therapeutic target and prognostic marker [10,9]. Though studied as a risk factor for ischemic stroke, findings on non-HDL-C are inconsistent, warranting further investigation. This study aims to clarify its role in ischemic stroke risk. Hence, the present study aims at understanding non-HDL-C as a risk factor for Ischemic Stroke.

AIM AND OBJECTIVES:

- To measure non-HDL-Cholesterol levels in Ischemic Stroke.
- To assess the levels of non-HDL-Cholesterol and to establish non-HDL-Cholesterol as an individual risk factor for Ischemic Stroke.

MATERIALS AND METHODS:

This is an 18-month prospective cross-sectional study conducted on ischemic stroke patients admitted to tertiary care hospital at Puducherry, using defined inclusion and exclusion criteria.

Ischemic stroke patients over 45 years diagnosed via clinical evaluation, CT, and MRI (if needed) were included in the study. Patients under the age of 45 years, those with secondary stroke causes, hemorrhagic, traumatic, or thrombo-embolic strokes, on lipid-lowering drugs, or unwilling to participate are excluded from the study.

A 5 ml fasting venous sample was collected to measure lipid profile parameters: Total Cholesterol (TC), Triglycerides (TGL), Low Density Lipoprotein Cholesterol (LDL-C), and High-Density Lipoprotein Cholesterol (HDL-C).

Non-HDL-C was calculated by using the formula:

Non-HDL-C (mg/dl) = TC – HDL-C

The normal value of Non-HDL-Cholesterol is less than 130mg/dl

DATA COLLECTION METHOD:

Patients' demographic data including age and sex along with relevant medical history and other comorbid conditions were noted. Further, they were subjected to thorough clinical examination. All these data were recorded in a predesigned proforma.

STATISTICAL ANALYSIS:

Data were entered in Excel and analyzed using SPSS v23. Statistical methods included frequency analysis, cross-tabulation, t-tests, and ANOVA. Results are presented as frequencies, percentages, means, SD, and 95% CIs. A p-value < 0.05 was considered significant. Results are shown in the following tables.

RESULTS AND DISCUSSION:

Half of the patients (50%) are aged 45-60, 40.9% are 60-75, and 9.1% are over 75. Males make up 56.7%, females 43.3%. Sacco et al., reported 67% over 65 and 55% female, while Guangyao et al., and Yinghui et al., found a male majority. Regarding BMI, 41.5% are obese, 36.6% overweight, and 22% normal. [11, 12, 13]

On the physical parameters such as age, height, weight and BMI, the mean age of the patients in the study is 60.890±11.0031 falling between 46-94 years similar to Yinghui et al., mean age of 61.2±7.35 years [13]. Average height is 160.701 ± 10.7339 cm with a range of 141-180 cm and 75.189 ± 10.0810 kg with a range of 55-90 kg. Similarly, average BMI is 29.493±5.5902 kg/m^2 ranging 19-44.1 kg/m^2 and 29.493±5.5902 kg/m^2 with a range of 19-44.1 kg/m^2; whereas in the study by Guangyao et al the median BMI was 24.1 kg/m^2 [12].

Table 1 presents the lipid profile of the patients in the study. The mean total Cholesterol level was 192.283±50.7543 mg/dL (range: 110 mg/dL-309 mg/dL), triglycerides 125.378±61.1922 mg/dL(range: 46-426 mg/dL). Mean LDL level was 123.311±43.2304 mg/dL (range: 51-231 mg/dL). Mean VLDL level was 25.037±12.2384 mg/dL (Range 9-85 mg/dL). Mean HDL level was 40.683±6.2572 mg/dL (range: 26-57 mg/dL). The Non-HDL level was 152.140±50.5913 mg/dL (range: 67-270 mg/dL). Similarly, non-HDL-C levels ranged from 0.59 to 10.03 mmol/L (mean value, 3.14 mmol/L) in a study by Wang et al., and the median level was 3.41 (2.78-4.10) mmol/L in a study by Guangyao et al. [14, 12].

Table 1: Descriptive Statistics on Lipid profile

Parameters	N	Minimum	Maximum	Mean	Standard Deviation
Total Cholesterol	164	110.0	309.0	192.823	50.7543
Triglycerides	164	46.0	426.0	125.378	61.1922
LDL	164	51.0	231.0	123.311	43.2304
VLDL	164	9.0	85.0	25.037	12.2384
HDL	164	26.0	57.0	40.683	6.3572
Non-HDL Cholesterol	164	67.0	270.0	152.140	50.5913

Distribution of patients based on BMI:

Majority of the patients (41.5%) are obese, 36.6% are overweight and 22% are normal based on BMI. Distribution of patients based on gender and BMI; majority of the male patients (40.9%) are overweight, 33.3% are Obese and 25.8% have normal weight. In case of female patients, 52.1% are obese, 31% are overweight and 16.9% are normal in BMI.

Distribution of patients by Age and BMI:

The majority of patients aged 45-60 years are obese (45.1%), followed by overweight (35.4%) and normal BMI (19.5%). Among those aged 60-75 years, 41.8% are obese, 37.3% overweight, and 20.9% have normal BMI. In patients over 75 years, 40% are either normal or overweight, while 20% are obese.

Based on gender and Obesity:

Majority of (66.7% & 52.1%) the male and female patients are obese; (33.3% & 47.9%) are not obese.

Distribution of patients based on age and obesity:

In the age group 45 and 60 years; majority of them are (54.9%) are not obese and 45.1% are obese, who are between 60 and 75 years, 41.8% are obese and 58.2% are not obese. Among the patients above 75 years, 80.0% are not obese and 20% are obese.

Distribution of patients based on smoking and drinking habits:

About 27.4% of the patients are smoker and 72.6% are non-smokers. Majority of (54.3%) the patients consume alcohol and 45.7% are non-alcoholic.

Distribution of patients based on gender and smoking habit:

Majority of the male patients (51.6%) are non-smokers and 48.4% have smoking habit. All female patients are non-smokers.

Distribution of patients based on gender and drinking habit:

Majority of the male patients (83.9%) have the habit of drinking and 16.1% do not consume alcohol, whereas (84.5%) female patients do not consume alcohol and 15.5% alcohol consumers.

Distribution of patients based on age and smoking habit:

Majority of the patients in the age group 45- 60 years (82.9%) do not smoke and 17.1% are smokers. Patients in between 60 and 75 years (65.7%) do not smoke and 34.3% are smokers. Patients who are above 75 years, 53.3% are smokers and 46.7% are non-smokers.

Distribution of patients based on age and drinking habit:

Majority of the patients in the age group 45 and 60 years (51.2%) drinks alcohol and 48.8% do not consume alcohol. Patients in between 60 and 75 years (55.2%) consume alcohol and 44.8% do not drink alcohol. Patients above 75 years (66.7%) have the habit of drinking and 33.3% are non-alcoholic.

Distribution of patients based on prevalence of Diabetes:
Most of the patients (56.7%) has Diabetes and (78.7%) have hypertension; 43.3% are non-diabetic and 21.3% do not have hypertension.

Distribution of patients based on gender and prevalence of diabetes:
Majority of the male patients (62.4%) do not have Diabetes and 37.6% have Diabetes, whereas majority of the patients (81.7%) have Diabetes and 18.3% do not have Diabetes.

Distribution of patients based on gender and prevalence of hypertension:
Majority of the male patients (77.4%) have hypertension and 22.6% do not have hypertension. Similarly, majority of female patients (80.3%) have hypertension and 19.7% do not have Hypertension.

Distribution of patients based on age and prevalence of Diabetes:

Patients in between 45 and 60 years; 54.9% have diabetes and 45.1% do not have diabetes. The patients in between 60 and 75 years, 62.7% have diabetes and 37.3% do not have Diabetes. Among the patients who are above 75 years, 40% have diabetes and 60% do not have Diabetes.

Distribution of patients based on age and prevalence of Hypertension:
Table 2 depicts patients in the age group of 45 and 60 years (68.3%) have hypertension and 31.7% do not have hypertension; in between 60 and 75 years (91%) have hypertension and 9% do not have hypertension. Among the patients who are above 75 years, 80% have hypertension and 20% do not have hypertension. All the patients in the study have CVA-infarct.

Table 2: Distribution of Patients based on Age and Hypertension

Age		Hypertension		Total
		Yes	No	
45-60 years	Frequency	56	26	82
	%	68.3%	31.7%	100.0%
60-75 years	Frequency	61	6	67
	%	91.0%	9.0%	100.0%
>75 years	Frequency	12	3	15
	%	80.0%	20.0%	100.0%
	Total	129	35	164
	%	78.7%	21.3%	100.0%

Distribution of patients based on total Cholesterol level:
50% patients have normal total Cholesterol level, 40.9% have borderline high level of Cholesterol and 9.1% have High level of Total Cholesterol.

Distribution of patients based on gender and total Cholesterol level:
Majority of the male patients (62.4%) have normal level of total Cholesterol, 34.4% have borderline high level of total Cholesterol and 3.2% have high level of total Cholesterol. In case of female patients, majority of the patients (50.7%) have normal level of

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Total Cholesterol, 16.9% have borderline high level of Total Cholesterol and 32.4% have high level of Total Cholesterol.

Distribution of patients based on age and total Cholesterol level:
Table 3 shows that most patients aged 45-60 (63.4%) have normal total cholesterol, with 20.7% high and 15.9% borderline high levels. In the 60-75 age group, 46.3% have normal, 41.8% borderline high, and 11.9% high cholesterol. Among those over 75, 73.3% have normal, 20% borderline high, and 6.7% high cholesterol levels.

Table 3: Distribution of patients based on Age and total cholesterol level

Age		Total Cholesterol			Total
		Normal	Borderline High	High	
45-60 years	Frequency	52	13	17	82
	%	63.4%	15.9%	20.7%	100.0%
60-75 years	Frequency	31	28	8	67
	%	46.3%	41.8%	11.9%	100.0%
>75 years	Frequency	11	3	1	15
	%	73.3%	20.0%	6.7%	100.0%
	Total	94	44	26	164
	%	57.3%	26.8%	15.9%	100.0%

Distribution of patients based on triglycerides level:
Majority of the patients (72%) have normal triglycerides, 15.9% have borderline high level of triglycerides and 12.2% have high level of triglycerides.

Distribution of patients based on gender and triglycerides level:

Table 4: Distribution of patients based on gender and Triglycerides level

Table 4 shows that most male patients (78.5%) have normal triglyceride levels, with 9.7% borderline high and 11.8% high. Among females, 63.4% have normal levels, 23.9% borderline high, and 12.7% high.

Gender	Triglycerides			Total
	Normal	Borderline High	High	

Male	Frequency	73	9		11	93
	Male%	78.5%	9.7%		11.8%	100.0%
Female	Frequency	45	17		9	71
	Female%	63.4%	23.9%		12.7%	100.0%
	Total	118	26		20	164
	Total%	72.0%	15.9%		12.2%	100.0%

Distribution of patients based on age and triglycerides level:
Most of the patients aged between 45 and 60 years (69.5%) have normal level of triglycerides, 14.6% have high level of triglycerides and 15.9% have borderline high level of triglycerides. Among the patients aged between 60 and 75 years, 70.1% have normal level, 19.4% have borderline high level and 10.4% have high level of triglycerides. Patients who are above 75 years, 93.3% have normal level of triglycerides and 6.7% have high level of triglycerides.

Distribution of patients based on LDL level:

Most of the patients (51.8%) have high LDL level, 33.5% have normal level and 14.6% have borderline High level of LDL.

Distribution of patients based on gender and LDL level:
Table 5 shows that majority of the male patients 47.3% have high, 14% borderline high and 38.7% normal level of LDL. In case of female patients, most 57.7% have high, 15.5% borderline high and 26.8% normal level of LDL.

Table 5: Distribution of patients based on gender and LDL level

Gender		LDL			Total
		Normal	Borderline High	High	
Male	Frequency	36	13	44	93
	Male%	38.7%	14.0%	47.3%	100.0%
Female	Frequency	19	11	41	71
	Female%	26.8%	15.5%	57.7%	100.0%
	Total	55	24	85	164
	Total%	33.5%	14.6%	51.8%	100.0%

Distribution of patients based on age and LDL level:
Most of patients aged 45 and 60 years 57.3% have high level of LDL, 6.1% border line high and 36.6% normal level. Patients in between 60 and 75 years, 50.7% have high level of LDL, 28.4% have borderline high, and 20.9% have normal level. Among the patients who are above 75 years, 73.3% have normal and 26.7% have high level of LDL.

Distribution of patients based on VLDL level:
Majority of the patients 72% have normal level of VLDL and 28% have high level. Among, the male patients 78.5% have normal

level of VLDL and 21.5% high level. In case of female patients, most patients 63.4% have normal level of VLDL.

Distribution of patients based on age and VLDL level:
Table 6 presents that most of the patients aged 45 and 60 years 69.5% have normal level of VLDL and 30.5% have high level. Patients aged between 60 and 75 years, 70.1% have normal level of VLDL and 29.9% have high level. Among the patients who are above 75 years, 93.3% have normal level and 6.7% have high level of VLDL.

Table 6: Distribution of patients based on Age and VLDL level

Age		VLDL		Total
		Normal	High	
45-60 years	Frequency	57	25	82
	%	69.5%	30.5%	100.0%
60-75 years	Frequency	47	20	67
	%	70.1%	29.9%	100.0%
>75 years	Frequency	14	1	15
	%	93.3%	6.7%	100.0%
	Total	118	46	164
	%	72.0%	28.0%	100.0%

Distribution of patients based on HDL level:
Most of the patients 79.9% have normal level of HDL and 20.1% high level. Majority of the male patients 76.3% have normal level of HDL and 23.7% have high level; in case of female patients, most of the patients 84.5% have normal and 15.5% high level of HDL.

Distribution of patients based on age and HDL level:
It can be depicted from the table 7 that most of the patients aged between 45 and 60 years (85.4%) have normal level of HDL and 14.6% have high level. Patients between 60 and 75 years (70.1%) have normal level of HDL and 29.9% have high level.

Among the patients who are above 75 years 93.3% have normal level of HDL and 6.7% have high level.

Table 7: Distribution of patients based on Age and HDL level

Age		HDL		Total
		Normal	High	
45-60 years	Frequency	70	12	82
	%	85.4%	14.6%	100.0%
60-75 years	Frequency	47	20	67
	%	70.1%	29.9%	100.0%
>75 years	Frequency	14	1	15
	%	93.3%	6.7%	100.0%
	Total	131	33	164
	%	79.9%	20.1%	100.0%

Distribution of patients based on non-HDL level and based on gender and non-HDL level:

Most of the patients 70.1% had high level of non-HDL Cholesterol and 29.9% had normal level.

Most of male patients 67.7% have high level of Non-HDL and 32.3% have normal level of Non-HDL. In case of female patients, most of the patients 73.2% had high level of Non-HDL and 26.8% have high level of Non-HDL. Thus, non-HDL is high in majority of the patients irrespective of gender. Thus, Serum Non-HDL cholesterol level is a predictor for the risk of ischemic stroke as per the study by Zetuo et al., irrespective of gender [15].

Distribution of patients based on age and Non-HDL level:

It can be depicted from the table 8 that most of the patients aged between 45 and 60 years 63.4% have high level of Non-HDL and 36.6% have normal level. Patients who are between 60 and 75 years, 77.6% have high level of Non-HDL and 22.4% normal level. Similarly, patients above 75 years, 73.3% have high level of Non-HDL and 26.7% have normal level of Non-HDL. Thus, non-HDL is high in most of the patients. Most patients with normal LDL 85.5% have normal level of Non-HDL, but 14.5% with normal LDL have elevated non-HDL. Majority of the patients with Border line high LDL 91.7% elevated Non-HDL, 8.3% border line high LDL has normal non-HDL. All the patients with high LDL (100%) have elevated Non-HDL.

Table 8: Distribution of patients based on Age and Non-HDL level

Age		Non-HDL		Total
		Normal	High	
45-60 years	Frequency	30	52	82
	%	36.6%	63.4%	100.0%
60-75 years	Frequency	15	52	67
	%	22.4%	77.6%	100.0%
>75 years	Frequency	4	11	15
	%	26.7%	73.3%	100.0%
	Total	49	115	164
	%	29.9%	70.1%	100.0%

Distribution lipid profile of the patients based on gender:

It can be inferred from the table 9 that the mean total Cholesterol level in patients differed significantly based on gender with highly significant 't' value of -3.907 (p<0.01). Similarly, mean triglycerides level differed significantly based on gender with high significant 't' value of -3.266 (p<0.01). Mean LDL level differed significantly with 't' value of -3.887 (p<0.01). Mean VLDL level differed significantly based on gender as with high significant 't' value of -3.337 (p<0.01). However, there was no significant difference in the mean HDL level and non-HDL level. This implies the level of non-HDL Cholesterol is same in all patients who had stroke irrespective of their gender.

Table 9: Lipid Profile and association with gender

	Gender	N	Mean	Std. Deviation	't' Statistic
Total Cholesterol	Male	93	179.849	38.2156	-3.907 p<0.01
	Female	71	209.817	59.6862	
Triglycerides	Male	93	112.129	59.9404	-3.266 p<0.01
	Female	71	142.732	58.8096	
LDL	Male	93	112.312	33.7230	-3.887 p<0.01
	Female	71	137.718	49.8584	
VLDL	Male	93	22.333	11.9540	-3.337 p<0.01
	Female	71	28.577	11.7700	

HDL	Male	93	40.527	6.7753	-0.359 p>0.05
	Female	71	40.887	5.8053	
Non HDL Cholesterol	Male	93	139.323	37.4297	-3.869 p>0.05
	Female	71	168.930	60.1204	

Distribution of the lipid profile of the patients based on gender:

It can be inferred from the table 10; the mean total Cholesterol level in patients did not differ significantly based on age with insignificant 'F value of 0.261 (p>0.05), but the mean triglycerides, mean LDL, and mean VLDL differed significantly. There was a significant difference in the mean HDL level with significant 'F' value of 12.513 (p<0.05) and no significant difference in the mean non-HDL level. This implies that the level of non-HDL Cholesterol is the same in all the patients who had stroke irrespective of their age similar to the findings by Sacco et al, Yinghui et al [11, 13].

Table 10: Lipid Profile and association with age

		N	Mean	Std. Deviation	F Statistic
Total Cholesterol	45-60 years	82	195.549	60.7171	0.261 p>0.05
	60-75 years	67	190.716	39.0512	
	>75 years	15	187.333	37.0977	
	Total	164	192.823	50.7543	
Triglycerides	45-60 years	82	134.134	66.3436	4.412 p<0.05
	60-75 years	67	123.851	52.8526	
	>75 years	15	84.333	51.9294	
	Total	164	125.378	61.1922	
LDL	45-60 years	82	125.329	46.9563	3.748 p<0.05
	60-75 years	67	127.224	35.4280	
	>75 years	15	94.800	46.0096	
	Total	164	123.311	43.2304	
VLDL	45-60 years	82	26.793	13.3025	4.560 p<0.05
	60-75 years	67	24.761	10.4607	
	>75 years	15	16.667	10.5198	
	Total	164	25.037	12.2384	
HDL	45-60 years	82	41.122	6.0008	12.513 p<0.05
	60-75 years	67	38.716	5.7150	
	>75 years	15	47.067	6.7025	
	Total	164	40.683	6.3572	
Non HDL Cholesterol	45-60 years	82	154.427	59.2486	0.494 p>0.05
	60-75 years	67	152.000	40.7531	
	>75 years	15	140.267	38.4475	
	Total	164	152.140	50.5913	

CONCLUSION

The study suggests that there is a strong correlation between raised non-HDL-C levels and a higher chance of having an ischemic stroke. This emphasizes how crucial it is to use non-HDL-C testing in regular clinical practice in order to improve risk assessment and preventative measures. The risk of ischemic stroke can be reduced by lifestyle adjustments and pharmacological interventions, by identifying individuals who exhibit increased risk based on non-HDL-C levels. The results further highlight the need for more investigation into the underlying mechanisms that connect non-HDL-C and ischemic stroke, as well as the effectiveness of particular non-HDL-C targeted therapies in lowering the incidence of stroke. In the end, incorporating non-HDL-C screening into standard clinical care can enhance public health outcomes and lead to more successful stroke prevention measures. The accuracy and usefulness of current ischemic stroke risk prediction models may be improved by including non-HDL-C and can more accurately identify people who are at high risk and adjust preventive measures by improving these models. The findings of the study have important implications for public health given the high prevalence of ischemic stroke and its related morbidity and mortality Worldwide.

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