

# FASTING LIPID PROFILE IN ACUTE ISCHEMIC STROKE PATIENTS WHO ARE ALREADY ON LIPID-LOWERING DRUGS: AN OBSERVATIONAL STUDY

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## ABSTRACT

**Objectives.** Stroke or cerebrovascular accident is a global health problem. It is the second leading cause of morbidity and mortality worldwide. The relationship between dyslipidemia and acute ischemic stroke is intricate and varies according to the type of stroke and lipid levels. Given the inconsistent results of existing studies on the association of stroke with dyslipidemias, there is a need to further explore this relationship and to establish the role of lipid abnormalities in stroke incidence, severity, and prognosis. We aimed this study to know the lipid derangements in acute ischemic stroke patients who were already on lipid-lowering drugs for a substantial duration of time.

**Material and methods.** This study was conducted as a descriptive, retrospective, observational study involving patients admitted in the Stroke Unit, with acute ischemic stroke included those who were using lipid-lowering drugs (most preferably statins) for more than a year with a continuous use for a period of at least 3 months prior to the event of stroke. A total of 153 individuals met the inclusion criteria, and the sampling was done via non-probability consecutive methods.

**Results.** The mean age of the study population is  $58.86 \pm 14.02$ . The study population included 52.9% males ( $n = 81$ ) and 47.1% females ( $n = 72$ ), with a similar mean age ( $p = 0.855$ ). The mean total cholesterol was  $175.64 \pm 51.41$ , with females had a slightly higher mean ( $p = 0.349$ ). The mean total triglycerides were  $134.01 \pm 69.85$ , with a slightly higher value in males ( $p = 0.392$ ). The mean LDL levels were found to be  $118.41 \pm 45.56$ , slightly higher in females ( $p = 0.308$ ). The mean HDL levels were  $36.76 \pm 9.06$  with equal values among the gender ( $p = 0.295$ ). The mean VLDL was  $26.78 \pm 13.94$  with slight variation among gender ( $p = 0.406$ ). The mean non-HDL cholesterol was found to be  $138.94 \pm 48.02$  and was slightly higher in females ( $p = 0.425$ ). The most frequently deranged lipid marker in the study population was HDL, non-HDL, and LDL.

**Conclusions.** Despite the utilization of statins, frequent derangements of lipid markers are reported among acute stroke patients in our study with LDL/HDL ratio was the most prominently deranged lipid marker.

**Keywords:** lipid, cholesterol, stroke, ischemia, frequency

## INTRODUCTION

Stroke or cerebrovascular accident is a global health problem. It is the second leading cause of morbidity and mortality worldwide [1]. The World Health Organization defined stroke in 1970 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 vascu-

lar origin” [2]. This definition has recently been revised by the American Heart Association, incorporating the clinical and tissue criteria of stroke. The new broader definition includes any impartial sign of permanent brain, spinal cord, or retinal cell death due to a vascular cause based on pathological or imaging evidence with or without the presence of clinical symptoms [3]. Around 85% of strokes are ischemic while 15% are due to hemorrhage either intracerebral or subarachnoid [4].

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The incidence of stroke is continuously on the rise in developing countries in contrast to a recent decline seen in the western world [5]. This rising incidence can be attributable to a variety of risk factors and lifestyle changes secondary to urbanization [6]. In Pakistan, stroke accounts for approximately 7% of deaths making it the fourth leading cause of death in the country, with 3.12% in Disability Adjusted Life Years (DALYs) [7]. It is a major cause of lifelong disability and adds considerably to the disbursement of resources of finances, manpower, and health services.

The common modifiable risk factors associated with acute ischemic stroke include hypertension, diabetes mellitus, hypercholesterolemia, atrial fibrillation, smoking, drug abuse, and alcohol intake [8]. The fasting lipid profile has many determinants including total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), and non-high-density lipoprotein (non-HDL). The relationship between dyslipidemia and acute ischemic stroke is intricate and varies according to the type of stroke and lipid levels [9]. For instance, in some studies, severe ischemic strokes with grave prognosis have been observed in patients with lower levels of total cholesterol and on the other hand, some studies report no association between total cholesterol, or LDL levels, and stroke outcome [10]. Similarly, severe strokes have been reported in patients with both high and low levels of total triglycerides [11,12]. Still, other studies report no association between stroke-related mortality and triglyceride level [13].

Given the inconsistent results of existing studies on the association of stroke with dyslipidemias, there is a need to further explore this relationship and to establish the role of lipid abnormalities in stroke incidence, severity, and prognosis. This would help in targeting specific lipid-lowering therapy in the primary and secondary prevention of stroke and to decrease the overall burden of cerebrovascular disease. We aimed this study to know the lipid derangements in acute ischemic stroke patients who were already on lipid-lowering drugs for a substantial duration of time.

## MATERIAL AND METHODS

This study was conducted as a descriptive, retrospective, observational study involving patients

admitted in the Stroke Unit, with acute ischemic stroke in the last year. The study included all those patients with a diagnosis of acute ischemic stroke. The diagnosis was reaffirmed by a radiological and clinical assessment of all the patients with informed consent. The inclusion criteria were the use of lipid-lowering drugs (most preferably statins) for more than a year with continuous use for a period of at least 3 months prior to the event of the stroke. The study excluded all those patients who were either not taking lipid-lowering agents, not been diagnosed with ischemic stroke, or had a hemorrhagic stroke on imaging. A total of 153 individuals met the inclusion criteria, and the sampling was done via non-probability consecutive methods.

All analysis was conducted by using the Statistical Package for Social Science (SPSS) version 25. The sample size was not required due to the retrospective nature of the study. All continuous variables were described as mean & standard deviation which were then compared using an independent sample t-test. The categorical data were described as frequency and relative percentages. A p-value of < 0.05 was considered statistically significant (2-tailed).

## RESULTS:

The mean age of the study population is  $58.86 \pm 14.02$ . The study population included 52.9% males ( $n = 81$ ) and 47.1% females ( $n = 72$ ), with a similar mean age ( $p = 0.855$ ). The frequent comorbidities were diabetes, hypertension, ischemic heart disease, and chronic kidney disease as shown in Table 1.

**TABLE 1.** Demographic data of the study population ( $n = 153$ )

Characteristics	Frequency/Mean $\pm$ SD	
Age (years)	58.86 $\pm$ 14.02	
Gender	<b>Males:</b> 81 (52.9%)	<b>Females:</b> 72 (47.1%)
Age among gender	58.66 $\pm$ 12.93	59.08 $\pm$ 15.24
Comorbidities	Diabetes	73 (47.71%)
	Hypertension	71 (46.40%)
	Ischemic heart disease	48 (31.37%)
	Chronic kidney disease	21 (13.72%)
	Chronic liver disease	11 (7.18%)

**TABLE 2.** Comparison of lipid markers amongst the patients of stroke with respect to gender

#	Laboratory investigations	All patients (n = 153)	Grouping variables		p-value
			Male (n = 82)	Females (n = 71)	
1	Serum Total Cholesterol (mg/dl)	175.64 ± 51.41	171.96 ± 54.06	179.79 ± 48.30	0.349
2	Low density lipoprotein (mg/dl)	118.41 ± 45.56	114.86 ± 46.83	122.41 ± 44.08	0.308
3	High density lipoprotein (mg/dl)	36.76 ± 9.06	36.04 ± 8.96	37.58 ± 9.16	0.295
4	Triglycerides (mg/dl)	134.01 ± 69.85	138.59 ± 72.16	128.87 ± 67.27	0.392
5	Very low density lipoprotein (mg/dl)	26.78 ± 13.94	27.67 ± 14.40	25.79 ± 13.43	0.425
6	Non-high density lipoprotein (mg/dl)	138.94 ± 48.02	136.01 ± 50.70	142.25 ± 44.94	0.676
7	Total cholesterol to HDL ratio	4.89 ± 1.32	4.88 ± 1.42	4.90 ± 1.21	0.908
8	LDL to HDL ratio	3.29 ± 1.17	3.24 ± 1.20	3.34 ± 1.15	0.585
9	Triglycerides to HDL ratio	3.89 ± 2.20	4.12 ± 2.38	3.63 ± 1.96	0.161
10	Non-HDL to HDL ratio	3.89 ± 1.32	3.88 ± 1.41	3.90 ± 1.21	0.910

P-value calculated by independant sample t-test

Table 2 has shown the fasting lipid profile markers among the study population. The mean total cholesterol was  $175.64 \pm 51.41$ , with females had a slightly higher mean ( $p = 0.349$ ). The mean total triglycerides were  $134.01 \pm 69.85$ , with a slightly higher value in males ( $p = 0.392$ ). The mean LDL levels were found to be  $118.41 \pm 45.56$ , slightly higher in females ( $p = 0.308$ ). The mean HDL levels were  $36.76 \pm 9.06$  with equal values among the gender ( $p = 0.295$ ). The mean VLDL was  $26.78 \pm 13.94$  with slight variation among gender ( $p = 0.406$ ). The mean non-HDL cholesterol was found to be  $138.94 \pm 48.02$  and was slightly higher in females ( $p = 0.425$ ). Coming to the ratios, the mean TC/HDL ratio was  $4.89 \pm 1.32$  with no difference in gender ( $p = 0.908$ ). The TG/HDL ratio was quite higher in males but not statistically significant ( $p = 0.166$ ) with a total mean value of  $3.89 \pm 2.20$ , while the LDL/HDL ratio was found to be  $3.29 \pm 1.17$  with indifferent variation among gender ( $p = 0.585$ ). Lastly, the non-HDL/HDL ratio was  $3.89 \pm 1.32$  with almost equal values in males and females ( $p = 0.910$ ).

The most frequently deranged lipid marker in the study population was lower HDL in 70.6% ( $n = 108$ ), higher non-HDL in 52.9% patients ( $n = 81$ ) followed by LDL in 43.1% of the patients ( $n = 66$ ), total cholesterol in 37.3% ( $n = 57$ ), and triglycerides in 33.3% ( $n = 51$ ). Among the ratios, non-HDL/HDL and LDL/HDL were most frequently deranged (both in 78.4%), while TG/HDL was higher in 56.9% and TC/HDL in 37.3% of the acute ischemic stroke patients, as shown in Table 3.

**TABLE 3.** Frequency of deranged lipid markers amongst the patients of stroke ( $n = 153$ )

#	Laboratory investigations	Above/below given value n (%)
1	Total cholesterol (> 200 mg/dl)	n = 57 (37.3%)
2	LDL (> 130 mg/dl)	n = 66 (43.1%)
3	HDL (< 40 mg/dl)	n = 108 (70.6%)
4	Triglycerides (>150 mg/dl)	n = 51 (33.3%)
5	VLDL (>30 mg/dl)	n = 51 (33.3%)
6	Non-HDL (>130 mg/dl)	n = 81 (52.9%)
7	Total cholesterol to HDL ratio(>5)	n = 57 (37.3%)
8	LDL to HDL ratio (>2.5)	n = 120 (78.4%)
9	Triglycerides to HDL ratio (>3)	n = 87 (56.9%)
10	Non-HDL to HDL ratio (>3)	n = 120 (78.4%)

## DISCUSSION

Our study showed mean total cholesterol levels of 175 mg/dl, which was compared with another study that compared lipid markers of acute stroke patients with healthy controls as well as distinguishes lipid markers among hemorrhagic and ischemic stroke. Their findings suggested high total cholesterol levels of 226 mg/dl in ischemic stroke patients, and their mean triglyceride levels were also higher than ours (134 vs. 164). Our study had lower HDL levels, which was significantly higher in their study, but lower when compared with healthy controls. In their study, triglycerides were indifferent among ischemic stroke patients and healthy controls but were found significantly lower in hemorrhagic stroke. With respect to LDL levels, they reported no difference in ischemic and hemorrhagic stroke patients, but LDL was signifi-

cantly higher when compared with healthy controls [14]. They concluded high LDL and total cholesterol levels increase the risk of ischemic stroke contrary to triglycerides. While a review article summarized the relationship between lower total cholesterol and LDL levels increasing the risk of hemorrhagic stroke. They also linked triglycerides inversely with the risk of hemorrhagic stroke [15]. With respect to HDL, there is a decreased risk of ischemic stroke with high levels. In one prospective cohort study conducted in China, TC/HDL was most significantly associated with an increased risk of ischemic stroke, especially in the male gender. The same study also concluded high triglyceride levels are significantly associated with ischemic stroke in females [16]. While they found no association of lipid markers with hemorrhagic stroke in either sex. They had a mean age of 41 years in males and 43 years in females which was significantly lower than our mean age of 58 and 59 years respectively. In their study, all the lipid markers were found significantly higher in males, except for HDL which was higher in females. This finding was contrary to our results having no discrimination of lipid markers among the gender. Concerning the ratios, TC/HDL was 4.03 in males and 3.45 in females, which was significantly lower than our mean TC/HDL of 4.89 [16]. Similarly, their TG/HDL ratio of 1.59 in males and 0.91 in females was significantly lower than our mean of 3.89. Lastly, our reported LDL/HDL of 3.29 was slightly higher than their mean of 2.35 in males and 1.98 in females. They concluded higher triglycerides, non-HDL, TC/HDL, and TG/HDL are all associated with ischemic stroke [16].

A similar study reported mean total cholesterol levels of 191 as compared to 175 in our study, mean LDL of 114 (118 in our study), mean HDL of 52 (36 in our study) mean triglycerides of 126 (134 in our study), and non-HDL of 139 (138 in our study). The mean age of their study participants was 64 years as compared to 58 years in our study [17]. They concluded LDL and non-HDL significantly increasing the risk of ischemic stroke. Another study compared lipid markers in ischemic and hemorrhagic stroke and reported higher total cholesterol and lower HDL levels in ischemic stroke. The rest of the markers had no associations with the outcome. Total cholesterol was elevated in 42% of their stroke patients while HDL was

below normal in 31% of their stroke patients [18]. In our study, total cholesterol was elevated in 37% patients, TG in 33%, LDL in 43%, VLDL in 33%, non-HDL in 53%, while HDL was lower in 70% of the cases. Similarly, a study conducted in India reported 54% of stroke patients having abnormal lipid markers, out of which 30% had deranged total cholesterol, 35% had deranged LDL, 34% had deranged TG, and 53% had deranged non-HDL [19]. A study conducted on young stroke patients concluded lower HDL being the only risk factor among the lipid makers increasing the risk of stroke [20]. Similarly, another study showed lower HDL in 61% of the studied cases, followed by high LDL in 28%, high TC in 17%, and high TG in 15% [21]. Although their mean age was higher than ours (68 years), mean total cholesterol of 163, mean LDL of 114, mean HDL of 42, and mean TG of 133, all were closer to our results.

Now coming to hemorrhagic stroke, lower total cholesterol and triglycerides were found associated with higher risk [22]. According to one study, the reported mean total cholesterol in hemorrhagic stroke was 157, mean TG was 103, mean LDL was 112, mean VLDL was 20, and mean HDL was 26 [22]. TC, TG, and HDL were found significantly lower when compared to healthy controls. In comparison, our study had higher VLDL, HDL, TC, and TG levels, but LDL levels were the same. So far, TG is the only lipid marker that was least associated with the incidence of stroke. A review article negates this thought and found significant plausibility of TG contributing to increased risk of ischemic stroke [23]. Another study found the lowest elevation of triglycerides in their subjects, with lower HDL was the most associated lipid marker followed by non-HDL, LDL, and TC [24]. A large scale study conducted in China to know age and sex-related changes of lipid markers in acute stroke patients found high LDL and low HDL mostly associated with stroke. With respect to the elderly population, lower levels of TG, TC, and LDL were observed. Females had higher TC, HDL, and non-HDL, while higher LDL in elderly females was reported. A higher level of TC/HDL, LDL/HDL, and TG/HDL was observed in non-elderly males [25]. All of the above findings were contrasting with our results. Their mean TC/HDL of 4.41 in non-elderly and 4.22 in elderly was lower than our mean of 4.89, similarly, LDL/HDL of 2.77 in

non-elderly and 2.66 in elderly was lower than our 3.29, and their TG/HDL of 1.73 and 1.46 was significantly lower than our mean of 3.89 [25]. Another study gave a similar finding of high LDL and low HDL as the common most lipid abnormalities in stroke patients, with high TG was a feature of ischemic stroke as compared to hemorrhagic stroke [26]. However, their triglycerides levels were significantly lower than our study population. The rest of the lipid markers were in close range with our mean values.

A nation-wide cohort survey conducted in Korea linked the mildly abnormal lipid levels with less variability also associated with myocardial infarction and stroke, even in the young population with statin use [27]. This study had mean TC levels of 188 and mean HDL 56 (higher than our study), while mean LDL of 108 and mean TG of 104 (lower than our study). Another study compared lipid markers in ischemic stroke by gender and found females had higher total cholesterol and LDL than males [28]. This finding was again contrasting to our results with no lipid marker was indifferent with respect to gender except for higher TG/HDL ratio in males (which was also statistically insignificant). Lastly, a study conducted in Cameroon in newly diagnosed stroke patients, showed low

HDL, with high LDL/HDL and TC/HDL ratios [29]. The mean HDL reported in the study was similar to our reported values (37 vs. 36), LDL/HDL was reported 4.0 which was higher than our reported value of 3.29, and mean TC/HDL 5.9 which again was higher than our mean value of 4.89 [29]. All the above markers were found higher in female stroke patients, which was contrasting to our results. Similarly, ischemic stroke patients had a higher HDL (46 vs. 36) and a higher TG (185 vs. 134) than our study and a lower LDL (118 vs. 88) without any gender discrepancy.

## CONCLUSIONS

Despite the utilization of statins, frequent derangements of lipid markers are reported in acute stroke patients of our study. The pattern of those derangements were similar to previously reported studies. LDL/HDL ratio was the most prominently deranged lipid marker in our study results. However, the differences of lipid markers among gender was not found in our study which was evident in previous literature. Hence, further exploration is required in to the usage of lipid lowering drugs and its protective mechanisms for stroke.

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