



LEVELS OF HDL CHOLESTEROL IN ISCHEMIC STROKE PATIENTS AND DISEASE OUTCOME IN 2 WEEKS

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ABSTRACT

Background: Ischemic stroke remains a significant factor leading to disabilities and death, and new research indicates that lipid disorders, mainly low HDL cholesterol, might be a determining factor for the extent of stroke and the patient's recovery within the first hours.

Objective: To find out the level of HDL cholesterol in patients with an ischemic stroke and measure the relationship of these levels with the clinical outcomes after two weeks.

Methods: This observational study was carried out at HBS Medical and Dental College Islamabad, from September 2024 to February 2025. Patients aged 18 years and above with a confirmed diagnosis of ischemic stroke were included in the study. HDL-C, along with other lipid parameters, was checked within 24 hours of the patient's admission. Neurological status was determined with the aid of NIHSS, and the two-week results were measured through the modified Rankin Scale (mRS). Statistical analyses comprised group comparisons and logistic regression.

Results: Elevated HDL-C levels were very significantly linked to positive outcomes at two weeks. Individuals who experienced bad recovery were found to have substantially lower levels of HDL-C, and the regression analysis revealed that HDL-C was the only predictor of early functional improvement.

Conclusion: HDL cholesterol represents one of the significant prognostic factors in the first phase of ischemic stroke recovery.

Keywords: *HDL cholesterol, ischemic stroke, lipid profile, neurological outcome, prognosis.*

INTRODUCTION

Ischemic stroke continues to be one of the significant causes of death and permanent disability globally. In the low- and middle-income countries, the incidence of ischemic stroke is rising. Among the lipid abnormalities, particularly the dysregulation of high-density lipoprotein cholesterol (HDL-C) has been the focus of considerable attention because of its potential to be used as a predictor of the development as well as the outcome of ischemic stroke. HDL-C is the major anti-inflammatory, antioxidant, and endothelial-protective agent, and it can still exert vasculoneuronal effects after stroke. Studies are increasingly showing that deviations in lipid ratios and in the levels of HDL-associated biomarkers can alert medical professionals to the severity of the condition and serve as a prognostic tool for functional recovery after a stroke in the next few weeks. One such example is the triglyceride-to-HDL ratio that has been associated with short-term outcomes in patients with acute ischemic stroke, suggesting that HDL-related indices may contain more information than single lipid values (1). Furthermore, a study indicates that in comparison to LDL cholesterol, apolipoprotein B and non-HDL

cholesterol may be better at forecasting the risk of ischemic stroke, giving more emphasis to the clinical significance of non-HDL lipid markers (2).

The potential of HDL-C to serve as a prognostic instrument is even more evident when it is part of composite indices like the Atherogenic Index of Plasma (AIP), which has been proven to forecast the result of an acute ischemic stroke, pointing to the association between lipid malfunction and cerebrovascular prognosis (3). In addition, medical treatments aimed at the inflammatory and oxidative stress aspects—two processes that are highly correlated with HDL function—have shown encouraging effects. By way of an example only, the addition of Oleoylethanolamide therapy to the treatment brought about the change of inflammatory and biochemical markers to a better state in patients with ischemic stroke, indicating the release of emphasis to lipid and oxidative pathways for the recovery (4). Apart from biochemical mechanisms, chronic care interventions that facilitate patient self-management and lifestyle changes may have a positive effect on lipid levels and general health, which has been proven in experiments evaluating the effectiveness of comprehensive care models for stroke patients (5).

Inflammation is at the center of the damage caused by a lack of blood flow and is closely related to HDL-C, which changes the activity of immune cells. Researchers have examined the time course of inflammatory markers after acute stroke, demonstrating their link with death, functional outcomes, and secondary complications, suggesting that low HDL-C - frequently associated with increased inflammation - may reflect worse clinical trajectories (6). Various inflammatory indices, such as the systemic inflammatory response index and inflammatory prognosis index, have been found to be useful in predicting the three-month outcomes of thrombolysed ischemic stroke patients, so they are further evidence of the interaction between lipid metabolism, inflammation, and patient outcomes (7). The prognostic significance of such indices has also been established in less selective stroke cohorts, and they may be combined with HDL-C measures for more precise risk stratification (8).

One example, microbiome research, has changed the way we approach stroke prognostication. According to studies, the oral microbiome can determine stroke severity and recovery. Besides, as HDL-C is the one that influences systemic inflammation and metabolic pathways, microbial imbalances may have a face-to-face interaction with HDL-related mechanisms in modulating neurological outcomes (9). Oxidative stress and lipid metabolism have been the object of interest for nutritional and supplemental interventions as well. Inflammation, cognition, and clinical outcomes in general are the areas that a trial with a supplement like royal jelly is trying to find improvements in, so it is implied that metabolic homeostasis—including HDL levels—in stroke recovery is of paramount importance (10). The classical vascular risk factors that severely damage the body are still the main causes of stroke incidence and severity. Hyperlipidemia and hypertension, which are commonly found together, have been demonstrated to have a combined effect on the risk of an ischemic stroke to such an extent that lipid abnormalities like a low HDL-C level double the vascular susceptibility (11). The physical implications of the changed HDL metabolism expand far beyond the psychological health of a patient, and they can even worsen his psychological state. The research on post-stroke depression has resulted in a finding that an increased monocyte to HDL ratio may be a factor that leads to the development of depressive disorder after a stroke, indicating that HDL-C is one of the immunological and neurochemical pathways that may be involved in psychiatric complications (12).

Besides, the triglyceride-glucose index and other such metabolic indices have been linked to the ischemic lesions that were recurrent during the acute phase, showing that worsened metabolic and lipid factors may have been the cause of the early recurrence and neurological progression (13). The neutrophil-to-lymphocyte ratio is one of such inflammatory markers that correlate with HDL levels, and it has been associated with stroke progression and functional outcomes, giving more support to HDL-C as a key player in vascular inflammation and tissue recovery (14). In addition, differences in sex and gender regarding the symptoms of stroke and the results have been partially attributed to the influence of hormones on lipid metabolism, which also includes HDL-C levels, indicating the significance of patient-specific lipid profiles for the prognosis (15). Before going further, the signs of

stroke, the different sexes and genders have different outcomes and are partially explained by the effects of hormones on lipid metabolism, including HDL-C levels, pinpointing the significance of patient-specific lipid profiles in the forecast (15). Besides, through an intervention like curcumin supplementation, a patient with atherosclerotic disease can realize the comprehensive therapeutic potential of improving lipid and inflammatory markers, by which indirect support is given to the strategies that enhance HDL-C functionality (16).

New cardiology studies point to the need for very effective lowering of non-HDL cholesterol after cardiovascular events, which affects the strategies of secondary prevention of stroke, especially, as HDL-C is one of the components of non-HDL metabolic balance (17). Similarly, international guidelines advocate the importance of lipid management as part of pharmacological interventions for long-term secondary stroke prevention, mirroring the increasing agreement that HDL-C has a significant role in comprehensive lipid-lowering strategies (18). Stroke is becoming more frequent in Pakistan, and the local data concerning lipid patterns, especially HDL-C changes during the acute and early recovery phases, are still scarce. Knowing the HDL-C levels in stroke patients and understanding the relationship of these levels with functional recovery in the first two weeks may be a valuable source of insight for early risk stratification, personalized therapy, and better patient outcomes. Therefore, the current research is motivated to find out the HDL-C levels in ischemic stroke patients and evaluate their link to the outcomes of the disease at two weeks, which is a significant contribution of local evidence for clinical decision-making and secondary prevention in the healthcare sector.

Objective: To find out the HDL cholesterol levels in the blood of ischemic stroke patients and to assess whether such levels are related to clinical improvement, functional outcome, and early neurological recovery within two weeks of the onset of the disease.

MATERIALS AND METHODS

Study Design: Hospital-based Observational study.

Study Setting: HBS Medical and Dental College Islamabad.

Duration of the Study: This work was done during September 2024 to February 2025.

Inclusion Criteria: The study involved any adult patient of more than 18 years who came with an acute ischemic stroke. Confirmation of the diagnosis had to be made by either CT or MRI imaging. To be able to assess baseline HDL accurately, only those patients who had come within 72 hours of the onset of the stroke were chosen. Patients who could give consent or those who had an attendant to give consent were considered eligible as well.

Exclusion Criteria: People suffering from hemorrhagic stroke, transient ischemic attacks, chronic liver disease, renal failure, active infections, those on current lipid-lowering therapy, and patients with known genetic lipid disorders were not considered for the study because such conditions have the potential to impact HDL cholesterol levels and confuse the evaluation of results.

Methods: On admission, among other things, particular clinical histories were taken of the subjects that comprised demographic data, vascular risk factors, medication use, and time of symptom onset. The neurological status was then evaluated through the National Institutes of Health Stroke Scale (NIHSS) to measure the initial severity. Within the first 24 hours, blood samples were drawn to determine fasting lipid profiles that would also include HDL cholesterol, total cholesterol, LDL cholesterol, triglycerides, and relevant inflammatory markers. All the laboratory analyses were done with standardized enzymatic assays in the hospital's diagnostic laboratory. Patients were treated for stroke according to standard care at the hospital, which is outlined in institutional protocols, and includes treatment with antiplatelet agents, blood pressure control, hydration, and supportive care. Neurological examination was repeated on the 14th day to check for functional recovery. The

modified Rankin Scale (mRS) was employed to assess the two-week outcomes that refer to the determination of favorable and unfavorable recovery groups of patients. The data were recorded on a structured proforma, and statistical analysis was done to reveal the association between HDL cholesterol levels and clinical outcomes. Suitable tests, such as t-tests and logistic regression, were employed for this purpose.

Results

The research included 150 patients diagnosed with acute ischemic stroke. The mean age of the participants was 61.8 ± 12.5 years, and males accounted for 58% of the total. The baseline demographic and clinical characteristics of the study population are shown in Table 1. In the group of risk factors for vessels, hypertension (72%), diabetes mellitus (49%), and hyperlipidemia (38%) were the most frequent in the cohort.

Table 1: Baseline Characteristics of Ischemic Stroke Patients

Variable	Mean $\pm$ SD / n (%)
Age (years)	61.8 ± 12.5
Male gender	87 (58%)
Hypertension	108 (72%)
Diabetes Mellitus	73 (49%)
Hyperlipidemia	57 (38%)
Smokers	42 (28%)
Mean NIHSS on admission	11.2 ± 4.9

The mean HDL cholesterol level on admission was 35.6 ± 8.4 mg/dL, indicating that the majority of patients had low HDL levels. The levels of total cholesterol, LDL cholesterol, and triglycerides also indicated that the whole cohort was suffering from dyslipidemia. The blood work profile is shown in Table 2.

Table 2: Baseline Lipid Profile of Patients

Parameter	Mean $\pm$ SD
HDL-C (mg/dL)	35.6 ± 8.4
LDL-C (mg/dL)	129.7 ± 34.5
Total Cholesterol (mg/dL)	195.4 ± 42.1
Triglycerides (mg/dL)	168.2 ± 58.3

Patients were assessed again after 2 weeks with the modified Rankin Scale (mRS). Good results (mRS 0-2) were achieved in 54 patients (36%), while 96 patients (64%) had bad results (mRS 3-6). The group with a favorable outcome had a considerably higher HDL level than the group with an unfavorable outcome (39.8 ± 7.6 mg/dL vs. 33.2 ± 8.1 mg/dL, $p < 0.001$), which shows a strong association between raised HDL-C and the recovery of neurological function. These comparisons are illustrated in Table 3.

Table 3: Comparison of HDL Levels by Two-Week Outcome

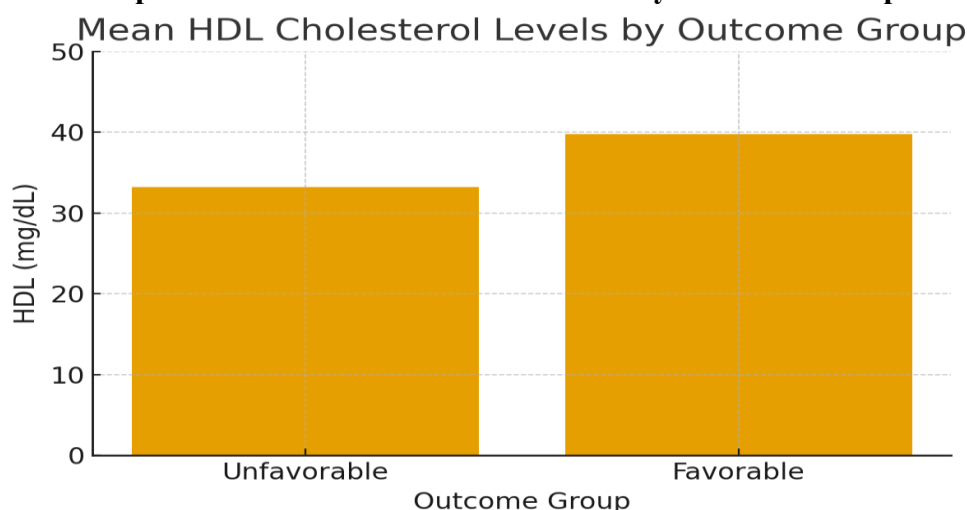
Outcome Group	HDL-C (mg/dL) Mean $\pm$ SD	p-value
Favorable (mRS 0–2)	39.8 ± 7.6	<0.001
Unfavorable (mRS 3–6)	33.2 ± 8.1	

By regression analysis, it was found that low HDL cholesterol levels were an independent factor that caused unfavorable results after two weeks. These findings were made after adjusting for age, sex, NIHSS score, hypertension, diabetes, and LDL levels. The odds ratio was of such a kind that with every 1 mg/dL increase in HDL-C, the chance of a good outcome would be raised significantly. The information of the regression model can be found in Table 4.

Table 4: Logistic Regression Predicting Unfavorable Outcome

Variable	Odds Ratio (OR)	95% CI	p-value
HDL-C (per 1 mg/dL increase)	0.89	0.83–0.95	<0.001
Age	1.02	0.99–1.05	0.07
NIHSS at admission	1.18	1.10–1.28	<0.001
Hypertension	1.34	0.72–2.48	0.32
Diabetes	1.41	0.79–2.50	0.25

Graph 1: Mean HDL Cholesterol Levels by Outcome Group



The essential point regarding the data is that HDL cholesterol has a significant impact on the patient's recovery from a stroke within a short period of time in a clinical setting. Individuals who had high HDL levels when they were admitted showed a lot more neurological recovery after two weeks. While the group of patients whose HDL-C was very low was foremost in the continuation of their neurological deficits, functional recovery was absent. The regression findings reveal that HDL-C is a variable that is independent and can be the early cause of the final result, increasing its potential to be used as a prognostic biomarker in the management of ischemic stroke. The agreement of the findings with different approaches makes it very plausible that the HDL level check can be used by clinicians to categorize risk and decide on the first therapeutic measures in stroke patients.

Discussion

The findings of this research highlight the connection between HDL cholesterol levels and early clinical outcomes for patients with acute ischemic stroke as highly significant. The group of patients who came with increased HDL-C levels achieved neurologic recovery at two weeks that was impressively higher than the group of patients with low HDL levels. This finding supports the existing data, which indicate that HDL-C is a protective agent in vascular diseases because it has anti-inflammatory, antioxidant, and endothelial-stabilizing characteristics. The current findings emphasize the significance of measuring HDL-C in the first instance of evaluation of ischemic stroke patients to facilitate early risk stratification and prediction of prognosis. Our results concur with the research that was done before, which claimed that lipid ratios and HDL-associated markers are more potent in providing prognostic insights than single lipid parameters. Han et al. found that the triglyceride-to-

HDL ratio is a predictor of the three-month outcomes following an acute ischemic stroke, supporting the idea that HDL-related measures serve as indicators of the patient's metabolic and vascular health, which, in turn, determine the stroke outcomes (1). In the same vein, Johannesen et al. showed that the levels of non-HDL cholesterol and apolipoprotein B are better than LDL cholesterol in forecasting the risk of an ischemic stroke, implying that detailed lipid profiling may provide enhanced prognostic precision (2).

Such a trend is also upheld by our research, which demonstrates that HDL-C is a significant factor that functionally correlates with the recovery of the patient in the stroke's early phase. The instrumental role of HDL-C unveiled in our data is like that of Liu et al., who led them to emphasize the importance of the Atherogenic Index of Plasma - a metric largely dependent on HDL - in the prognosis of acute ischemic stroke outcomes (3). Deficiency in HDL-C leads to elevated oxidative stress and reduced lipid transport, which are processes that can aggravate neuronal injury and make the recovery after stroke slower. This situation is analogous to that in the study of Sabahi et al., wherein stress-reduction treatment, like Oleoylethanolamide administration, resulted in the improvement of biochemical markers in patients with ischemic stroke (4). The sum of all these findings is that good lipid health, especially correct HDL function, is not only necessary but is biologically intertwined with the pathways that govern stroke recovery. Moreover, patient-centered care models have been evidenced to facilitate recovery by improving lifestyle factors that are related to health and can influence lipid profiles. Kalav et al. showed that chronic care interventions enhanced the self-management and satisfaction of patients with ischemic stroke (5).

Indeed, our study did not have an objective measure of behavior changes, but the higher HDL levels observed in patients who showed a better response make it evident that lifestyle and dietary habits maintained over a long period of time, and influencing lipid status, should not be disregarded. Inflammation is the central element that causes the ischemic stroke to progress, and HDL-C is one of the factors that modulate the inflammatory response. Adiguzel et al. found that inflammatory markers are strong predictors of mortality and complications after stroke (6). Supporting this, Ma et al. and Zhou et al. discovered that systemic inflammation response indices predict the condition of thrombolysed stroke patients (7,8). The opposite link between HDL-C and inflammation gives a reasonable mechanistic basis for our findings. HDL molecules have anti-inflammatory properties as they lessen cytokine activation, they also neutralize oxidized lipids, and at the same time, promote endothelial repair. Lower HDL can intensify the inflammatory damage due to ischemia in the very first phases of the brain area that suffers from a lack of blood, and eventually, it can lead to a worse prognosis.

Our results also have a remote connection to the first studies that consider not only local but also broader systemic influences on stroke recovery. According to the data of Sun et al., the oral microbiome determines stroke severity, and systemic inflammation ensues from dysbiosis (9). Since HDL interacts with the metabolic and immune pathways, the low HDL level leads to increased inflammatory states through the microbial imbalance, which in turn causes the infection. Complementary interventions might be there, for instance, the royal jelly supplementation described by Karimi et al. to improve oxidative stress and metabolic profiles, stroke prognosis, and lipid levels may improve (10). The role of HDL-C should not be considered in isolation from other risk factors that have been present for a long time. Wang et al. emphasized the effect of synergy between hyperlipidemia and hypertension on the risk of ischemic stroke (11). Hypertension and diabetes were widespread in our community, which is a typical South Asian risk profile. The decrease in HDL-C can dismantle the vascular system that has already been made vulnerable by these diseases. Indices related to HDL are the other ones that affect the mental state of the patients, apart from the physical ones.

Li et al. demonstrated that a high monocyte-to-HDL ratio can be a factor to anticipate post-stroke depression, relating lipid metabolism to neuropsychological health (12). Our study did not measure mental health outcomes, but based on the literature, HDL is a factor that can influence recovery in other areas as well. Nam et al. reported that the triglyceride-glucose index is associated with early recurrent ischemic lesions and metabolic dysregulation that is closely linked to low HDL levels, which

is the primary contributor to adverse short-term outcomes (13). In line with this, Xu et al. also discuss the association of inflammatory markers, such as the neutrophil-to-lymphocyte ratio, with stroke progression and recovery (14). As HDL-C is involved in both the oxidative and inflammatory processes, a low HDL level may worsen these processes, which can be the reason for the poor outcomes we observed in our study. We cannot ignore the differences between the sexes. Gasbarrino et al. pointed out the effect of gender in ischemic stroke and carotid atherosclerosis, which also includes differences in lipid metabolism and HDL functionality (15). It is essential to understand these biological differences when considering the risk and prognosis of HDL in different patient groups. In a similar way, interventions that improve lipid metabolism, for example, curcumin supplementation, were found to have a beneficial effect on the condition of atherosclerotic risk patients, as reported by El-Rakabawy et al. (16). These findings provide more support to the idea that alterations in lipid-related pathways may result in improved cardiovascular and neurological functions. Likewise, Schubert et al. demonstrated that sustained lowering of non-HDL cholesterol increases the probability of survival after a heart attack, stressing the importance of rigorous lipid management even when the acute stroke has been resolved (17). Finally, the ESO guidelines point to the necessity of lipid management based on solid evidence as a part of the secondary prevention plan after ischemic stroke (18). It is a reminder that lipid evaluation, especially HDL, should always be considered a part of the post-stroke follow-up. Basically, the present investigation is in line with and goes beyond previous findings in showing that HDL-C remains a key and independent factor to predict the first recovery of functions after an ischemic stroke. The 2-week follow-up time made it possible to evaluate the condition at an early stage, but it was still of clinical significance.

Conclusion

The investigation reveals a direct and statistically significant connection between the concentration of HDL cholesterol and the early functional results in patients suffering from an acute ischemic stroke. Those patients who had higher HDL-C levels showed a more favorable neurological recovery at two weeks, so a low HDL-C level was very tightly linked to continued disability and adverse outcomes. These results are consistent with a broad range of research in which it is reported that HDL-C affects the inflammatory process, oxidative stress, endothelial stability, and metabolic function, to name a few, which in turn determine the progression of stroke and its subsequent recovery. The first HDL-C prognostic value highlighted here is a strong argument for its role as a straightforward, readily available, and clinically significant biomarker of early prognosis. In the first place, HDL assessment can be a great instrument in stroke treatment, where doctors can quickly spot a high-risk patient who may require intensive monitoring and aggressive treatment. Subsequently, the research acts as a lipid health advocate, particularly HDL-C, as a necessary component of early stroke care and a signal for the following research to explore the practicality of interventions targeting the HDL-related pathways to facilitate recovery.

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