## ORIGINAL ARTICLE

# The Effect of Total Cholesterol and Serum Triglycerides Level on Recovery from Acute Ischemic Stroke

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### ABSTRACT

**Objective:** To determine the effect of serum total cholesterol and triglyceride levels on stroke recovery in patients with acute ischemic stroke.

**Study Design:** This was an observational cross sectional study.

**Place and Duration of Study:** The study was conducted at Shifa International Hospital Islamabad. Total duration of the study was 6 months starting from 5th August 2011 up till 4th February 2012.

**Materials and Methods:** A total of 100 consecutive stroke patients fulfilling the inclusion criteria were recruited over a period of 6 months. Stroke severity was clinically assessed using the National Institute of Health Stroke Scale (NIHSS) at the time of admission and then again at the time of discharge from the hospital. Their blood sample were collected for Serum Cholesterol and Triglyceride estimation within first 24 hours of admission. Neurological improvement was assessed by the reduction in NIHSS score at discharge and was defined as good if it was ≥3. The data analysis was done by using SPSS version 20. Cross tabulation and Chi Square tests were applied to analyze the data.

**Results:** Out of the 100 patients, 63 were males and 37 were females with a mean age of 63.7 years (SD 11.9). Patients with a normal or low cholesterol showed good recovery at the time of discharge in 41.3% of cases as compared to 68% of patients showing good recovery with a high total cholesterol levels. For the triglycerides level, there was good recovery in 49.2 % of patients with normal or low triglycerides levels while in patients with high triglyceride levels, good recovery was seen in 46.3% of patients.

**Conclusion:** Our study shows a positive effect of high total cholesterol on early recovery following acute ischemic stroke but no positive or negative effect was evident with high serum triglycerides. This shows a possible role of serum cholesterol in prognosticating patients with acute ischemic stroke.

**Key Words:** Acute Ischemic Stroke, Cholesterol and Triglycerides, Stroke Recovery.

## Introduction

Stroke is a common disease worldwide resulting in significant morbidity and mortality. It is the second leading cause of death above the age of 60 years and the fifth leading cause in patients aged 15 to 59 years old.[1] Globally the number of stroke patients each year is on the rise. According to WHO, up to 15 million people worldwide suffer from stroke each year. Out of these 5 million die and another 5 million are left permanently disabled.[1] Paradoxically, 80% people who suffer from stroke live in areas of low and mid income countries.[2] In Pakistan also, stroke is becoming the leading cause of morbidity and mortality.[3] Among the risk factors for stroke, hypertension and diabetes are more prevalent risk factors in the Asians (44% and 35 % respectively) as compared to the Caucasians (14% and 8% respectively).[4] Dyslipidemia was also found to be more common among Asian stroke population as compared to the Western, but it was not statistically significant.[2]

Relation of high total cholesterol and triglycerides with ischemic heart disease is well established worldwide. High cholesterol level are estimated to cause 56% of ischemic heart disease.[5] However, dyslipidemia as a risk factor for ischemic stroke has been quite controversial in recent times. It has been observed in several studies that higher cholesterol and triglyceride levels are associated with better outcome after ischemic stroke.[6,7] Many studies have demonstrated that patients with acute ischemic stroke who had a high serum cholesterol and triglycerides on admission showed a better recovery from stroke related disability as compared to those

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stroke patients who had normal or low cholesterol and triglycerides at the time of admission. By determining a relationship of cholesterol and triglycerides with recovery of acute ischemic stroke; in terms of clinical improvement, we will be able to prognosticate the outcome of ischemic stroke in our patients. The purpose of this study is to find the effect of serum total cholesterol and triglyceride levels in patients with acute stroke on their recovery.

## Materials and Methods

An observational cross sectional study was conducted at Shifa International Hospital Islamabad which is a tertiary care Hospital with 500 beds. The total study period was six months from August 2011 to February 2012. The sample size was calculated with the help of WHO sample size calculator and it was 100 patients. The study was started after permission from the Hospital's ethical committee. Consecutive sampling was done. All the patients who were admitted in the neurology and medical departments of the hospital with the diagnosis of acute stroke were checked for the following inclusion and exclusion criteria. Patients included in study were 18 years of age or above, having signs and symptoms of acute stroke within previous 48 hours and it was diagnosed radiologically as ischemic stroke confirmed by diffusion positive stroke on MRI brain. Patients with previous history of major stroke, hemorrhagic stroke, venous stroke and focal neurological deficit lasting for less than an hour were excluded from study. The two most common reasons for exclusion of patients from the study were delayed presentation after acute stroke (more than 48 hrs. after the onset of symptoms) and patients with history of previous stroke.

All patients presenting to Department of Neurology or Medicine at Shifa International Hospital, meeting the sample selection criteria were included in the study. Written consent was taken from all the patients or their families. As a routine, all patients with stroke admitted at Shifa International Hospital undergo a set pattern of investigations according to the stroke pathway developed by a multidisciplinary team of our hospital. This includes fasting lipid profile and MRI of brain with stroke protocol. Other variables which have been included in data collection were age, gender, type and site of stroke, history of diabetes mellitus, ischemic heart disease, hypertension and smoking, duration of stay in the hospital and the stroke severity. For describing the type of stroke TOAST classification was used. For stroke severity, an initial clinical assessment of these patients was done by using NIHSS. On the day of discharge these patients were reassessed using the NIHSS score to measure clinical improvement. The data analysis was done by using SPSS version 20. Cross tabulation and Chi Square tests were applied to analyze the data.

## Results

More than 170 patients were seen before the required sample size of 100 patients was met.

Out of the 100 patients who were selected for the study, 63 were males and 37 were females. The mean age of the patients was 63.7 years. The range of age was between the minimum of 36 and a maximum of 95 years.

The total cholesterol level was normal or low in 75% of the patients and high in 25%. Triglycerides levels were low or normal in 59% and high in 41%. (Table II and III).

Regarding the stroke severity, 39% of the patients had a minor stroke, 44% had a moderate intensity stroke while 17% of the patient had a severe stoke.

At the time of discharge, good recovery was seen in 48 patients while poor recovery was seen in 52 patients. When we compared the level of cholesterol and Recovery, we found that 41.3% of patients with a normal or low cholesterol showed good recovery at discharge as compared to 68% of patients showing good recovery with a high total cholesterol levels (Table II).

For the triglyceride levels, there was good recovery in 49.2 % of patients with normal or low triglyceride levels while in patients with high triglyceride levels, good recovery was seen in 46.3% of patients. (Table III).

A total of 66% of patients had a history of hypertension. Diabetes Mellitus was seen in 54% of the patients. 18% of patients had a history of ischemic heart disease while 27% had a current or recent history of smoking.

**Table I: Details of lipid levels in the study group (n=100)**

| Plasma Lipids | Mean (mg/dL) | Maximum (mg/dL) | Minimum (mg/dL) | SD (mg/dL) |
|---|---|---|---|---|
| Total Cholesterol | 178.4 | 311 | 80 | 44.4 |
| Triglycerides | 168.6 | 483 | 182 | 103.5 |

**Table II: Cross tabulation between serum cholesterol (high vs. low)  and recovery (good vs. poor) (n= 100)**

| Total Serum Cholesterol | Number of Patients (Out of 100) | Recovery at discharge by NIHSS scoring | |
|---|---|---|---|
| | | **Good Recovery** | **Poor Recovery** |
| Normal Count (<200 mg/dl) | 75 | n=31 | n=44 |
| | | 41.3% | 58.7% |
| High Count (≥ 200mg/dl) | 25 | n=17 | n=8 |
| | | 68.0% | 32.0% |

**Table III: Cross tabulation between serum triglycerides (high vs. low) and recovery (good vs. poor (n= 100)**

| Total Serum Triglycerides | Number of Patients (Out of 100) | Recovery at discharge by NIHSS scoring | |
|---|---|---|---|
| | | **Good Recovery** | **Poor Recovery** |
| Normal Count (< 150 mg/dl) | 59 | n=29 | n=30 |
| | | 49.2% | 58.8% |
| High Count (≥ 150 mg/dl) | 41 | n=19 | n=22 |
| | | 48.0% | 52.0% |

## Discussion

Stroke is a common neurological emergency presenting to the tertiary care hospitals all over the world. The risk factors and the factors affecting the stroke outcome are still poorly understood and controversial.

High serum cholesterol and triglycerides have always been considered as a risk factor for the cardiovascular diseases including the ischemic stroke.[5] However, many studies conducted in patients with acute stoke have shown an opposite effect of these risk factors on recovery from stroke.[5] The patients with higher cholesterol and triglyceride did better in terms of recovery and mortality when compared with patients having normal or lower level of these substances. High admission cholesterol may be associated with increased long-term survival after IS.[8,9] The data already available from other studies on this particular aspect of the stroke has mainly come from studies on patient population whose genetics and demographics are very different from the patients presenting in the hospitals of Pakistan.[10]

The severity of the stroke on admission was assessed using the NIHSS system. Only 17% of the strokes fell under the category of severe stroke with NIHSS greater than 15. Moderate intensity stroke was 44% with NIHSS score between 5 and 15. The percentage of minor stroke was 39% having a NIHSS stroke between 1 and 4. The recovery from the stroke at the time of discharge, which was the main outcome measure, was assessed by the improvement in NIHSS score on the day of discharge. An improvement of 3 or more points from the admission NIHSS score was considered as a good recovery while those showing improvement of 2 or less points on NIHSS at discharge were categorized as having a poor recovery.

The results of this study showed that acute stroke patients with higher total cholesterol had a better recovery at the time of discharge as compared to the patients who had normal or low cholesterol on admission. Out of the 100 patients, 25 had cholesterol that was higher than 200 mg/dl. Out of these 25 patients, 17 (68%) patients showed good recovery from stroke that was improvement in NIHSS score by 3 or more points. When we compared this with the patients having normal or low serum cholesterol we saw a marked difference, with good recovery seen in only 41.3% of the patients and a poor recovery in 58.7% of patients (p value < 0.05). This is a significant finding and has also been seen in other studies.

Data from a Chinese study on acute stroke patients showed that the levels of serum cholesterol in the good outcome group were significantly higher as compared to the patients with normal or low cholesterol.[11] Although this study also included patients of intracranial hemorrhage, the beneficial effect was seen in both types of stroke independently. Another major difference of this study from the current one is that the prognosis of the patients with acute stroke was assessed at 3 months' interval after the stroke but in my study the outcome has been measured at the day of discharge which is somewhere between 5 to 7 days after admission.

The effect of serum triglyceride on recovery from acute stroke was also compared with recovery from stroke. The results did not show any statistically significant difference in this regard. A total of 19

(48%) of patients with high triglyceride levels showed good recovery from acute ischemic stroke. Similar good outcome (49.2%) was seen for patients with normal or low cholesterol levels.

The mean hospital stay for the patients was 5.9 days. Some patient stayed for 48 hours while the maximum hospital stay was 24 days. The reason of early discharge was usually because of less severity of stroke or early recovery, however many patients were discharged on request as their families wanted to take the patient home or shift to some other hospital due to personal and economic reasons.

One study speculates a potential neuroprotective mechanism of high cholesterol by increasing gama-glutamyltransferase. Gamma-glutamyl transferase (GGT) mediates intracellular intake of extracellular glutathione which is an important component of antioxidant mechanisms. Glutathione is produced during normal metabolic processes and plays an important role in the protection of cells against oxidative stress.[12] Another study suggested that this effect could be seen due to cofounding effect of other prognostic factors.[13] A study done by M Jane et al concluded that Lower triglyceride levels seem to be associated with a worse prognosis in AIS.[14] low level of triglycerides predicts poor outcome following stroke and may be used as a prognostic marker for early mortality. Some of the studies suggested that higher cholesterol level was associated with less severe stroke and hence a better outcome as compared to patients with normal or low cholesterol levels. The reason for this association was given that cholesterol played a role in the development of small vessel disease of the brain which results in minor strokes as compared to the disease process leading to occlusion of large vessels of brain which results in more severe stroke.[9,11]

In our study, we have not catered for the other confounding factors that is age, presence or absence of modifiable risk factors for example smoking, HTN, DM, IHD, diet and weather the patient was on lipid lowering drugs or not. All of these factors can have an independent as well as combined effect on stroke recovery which is difficult to measure. Length of hospital stay is also an issue which needs to be looked into as it is difficult to assess the recovery of a patient in less than 6 days following acute stroke. Although a positive correlation is seen between high cholesterol and good recovery following stroke, further studies are needed to confirm or reject this association. A better study design would be required with larger number of patients in both groups' i.e. acute stroke patients with and without high cholesterol levels.

## Conclusion

The study shows a positive relationship of high total cholesterol with early recovery following acute ischemic stroke but no positive or negative effect was evident of high serum triglyceride on early recovery from acute ischemic stroke. These findings are not likely to change the clinical practice regarding prevention and management of acute strokes any time soon, however there may be a role of serum cholesterol in prognosticating patients with acute ischemic stroke. This needs to be further investigated in larger studies.

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