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RESEARCH ARTICLE

A STUDY OF LIPID PROFILE AND ITS CORRELATION WITH CLINICAL OUTCOME AND IN-HOSPITAL MORTALITY IN PATIENTS WITH INTRA CRANIAL HAEMORRHAGE

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ABSTRACT

Introduction: Stroke is an emergency requiring urgent investigation and treatment. It remains a major cause of mortality and disability worldwide. The association between lipid profile and stroke remains uncertain. This study therefore investigated whether changes in lipid profile might contribute to the risk of ICH. ***Materials and Methods****:* This is a case control which included 50 patients of ICH as cases and 50 persons of same age and sex as controls. Serum lipid profile was done which consisted of Total Cholesterol, High density lipoprotein cholesterol, Low density lipoprotein cholesterol and Triglycerides. The diagnosis was ascertained based on Non-Contrast Computed Tomography of Head, done at the time of admission. The correlation of lipid profile and clinical outcome was studied. ***Result***: In our study, 68% were males and 32% were females in case and in control group 58% were males and 42% females. All the levels of different lipid components were significantly different except HDL. The mean LDL for death patients was 109.62±38.17 and for discharged patients was 89.23±28.01. The mean level of triglycerides for discharged group was 110±45.76 and for death group was 85.14±37.20. ***Conclusion***: Our study concluded that there is significant correlation between lipid profile, specifically LDL-C and Triglycerides and clinical outcome of ICH patients in terms of death or discharge. Low levels of LDL-C and Triglycerides are associated with poor outcome in patients with ICH.

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INTRODUCTION

Stroke is a rapidly developing phenomenon of symptoms and signs of focal and at times global loss of cerebral function with no apparent cause other than vascular origin. Stroke is an emergency requiring urgent investigation and treatment (WADE, 2015; Amanullah, 2009). It remains major cause of mortality and disability worldwide among middle aged and elderly people (LI et al. 2011). The main pathological types are cerebral infarction, Primary intracranial haemorrhage and subarachnoid haemorrhage. In developed counties 85%-90% of strokes are due to cerebral infarction and 10%-15% due to intracranial haemorrhage (Sergio Gonzalez Garcia, 2008). Spontaneous intracerebral haemorrhage (ICH) accounts for 10% to 20% of all strokes (Keir *et al.,* 2002) and has higher morbidity and mortality than cerebral infarction or subarachnoid haemorrhage (Caplan, 1996) (Broderick *et al.,* 1993; Jorgensen *et al.,;* Qureshi *et al.,* 2001). Short term prognosis of patients with ICH is poor, approximately 35% to 50% of them die within first month after bleeding (Poungvarin amd Viriyavejakul, 1990; Nilsson *et al.,* 2002). Spontaneous ICH accounts for highest mortality of all strokes. An early and reliable prognostic indication in ICH patients is potentially useful in initiating individual treatment and for informing patients and families (Feng-zeng, 2011). Considering the high mortality rate and the paucity of effective treatments prevention of ICH is of paramount importance. Identification of risk factors for ICH especially modifiable risk factors is the first step in prevention. Several modifiable risk factors such as hypertension and excessive alcohol consumption have been demonstrated to increase the risk of ICH but not all patients with ICH have these identifiable risk factors (Xinguo Wang, 2011). It is important to examine lipid profiles in patients with different stroke subtypes separately since different subtypes may have different risk factors (Sergio Gonzalez Garcia, 2008; Woo, 1990). However, it is unclear whether the acute stroke affects the serum lipid profile or at what stage after ictus serum lipid values can be effectively compared with those from Controls subjects (Woo, 1990).

These limitations can be summarized as follows

- Stroke has been studied as a single entity, without distinguishing between cerebral infarction (CI) and cerebral haemorrhage (CH);

- Strokes of ischemic origin have been studied without separate consideration of each etiopathogenic subtype;
- Populations have been studied that were selected according to other criteria such as those with high cardiovascular risk not necessarily representative of normal stroke behaviour; and
- Blood lipid levels have been considered a nominal, rather than a continuous, variable using arbitrary lipid level classification categories (Sergio Gonzalez Garcia, 2008).

The association between cholesterol and stroke remains uncertain. Epidemiological studies have failed to associate cerebral infarction and cholesterol, but they have found an inverse relation with the incidence of ICH. Additionally, higher cholesterol levels have been associated with better short-term health outcome after stroke, including ICH.[14] This study therefore investigated whether changes in lipid profile might contribute to the risk of ICH.

MATERIALS AND METHODS

This is a prospective case control study. This study included 50 patients of stroke diagnosed as ICH of non-traumatic aetiology as cases and 50 of same age and sex matched healthy persons as controls.

Inclusion criteria: 1. Patients who are willing to participate in the study

2. Patients with Intracranial Haemorrhage in age group more than 12 years

Exclusion criteria: Intracranial haemorrhage due to

1. Traumatic brain injury 2. Neurosurgical procedure. 3. Anti-Coagulant therapy

50 patients of intracranial haemorrhage were enrolled in the study after taking informed consent and 50 person of same age and sex matched were enrolled as Controls. Along with the complete medical history of the patient a thorough General and Neurological examination of the patient which consisted at

- Vitals Score on Glasgow Coma scale. the diagnosis was ascertained based on Computed Tomography (CT) scan of Brain, done at the time of admission.
- Location of the bleed: capsuloganglionic: cerebral: Cerebellar: Brainstem: Others
- Type of Haemorrhage Parenchymal: Subdural: Sub arachnoid
- Size of the bleed
- Midline shift
- Intraventricular Extension
- Same age and sex matched 50 persons were enrolled as Controls and lipid profile was done.
- Lipid profile was done at the time of admission (within 48 hours) which consisted of: 1. Total cholesterol 2. High-density lipoprotein cholesterol (HDL-C) 3. Low density lipoprotein cholesterol (LDL-C) 4. Triglycerides

Observation and Results

50 patients each of controls and cases were included in the study. The demographic data revealed that 58% of sample size were males and 42% females. (29/50 and 16/50 respectively) in cases. Maximum number of Patients (92%) were in the age group of 21 to 80 years of age among cases and 96% among controls. Among 50 patients each of cases and controls, 30% were hypertensive and 20% were associated with Diabetes Mellitus in case group. 22% were hypertensive and 16% were associated with Diabetes Mellitus in control group. At the time of hospitalization, on a Glasgow coma scale, 64% had a score 5-12, 30% had 13-15 and 6% had 3-4. Out of 50 patients of cases, 21 (42%) died and 29 (58%) were discharged. Maximum number of patients (71.43%) died in the age group of 51-80 years followed by 23.81% in 21-50 years and 4.76% in more than 80 years of age. Maximum discharge was in 51-80 years age group (58.62%) followed by 37.93% in the 21-50 years age group and a 3.45% in more than 80 years of age. In our study, highest affected area was capsuloganglionic regions which represents 78% of the sample size (39/50) followed by corona radiata (56%), cerebrum (52%), Brain stem (10%). The association between clinical outcome and location of the bleed was also found to be not significant ($p<0.05$). Midline shift was observed in 50% of the cases and another 44% had Intra-ventricular extension. The association between clinical outcome and midline shift was also significant. 66.67% of the patients having midline shift died ($p<0.04$). In our study, the difference in lipid profile between cases and controls was statistically significant except for HDL levels. That is, lipid profile was found to be raised in cases than in controls. The comparison among study group for clinical outcome and levels of LDL C was significant. The mean LDL for discharged patients was 109.62±38.17 and for death it was 89.38±28.01. The difference was statistically significant. ($p<0.05$). The cholesterol and HDL levels were significant in discharged and death patients. In our study, the association between Hypertension and clinical outcome was not statistically significant. ($p=0.66$). 27.59% of the discharged patients wee hypertensive and 33.33% of the dead were hypertensives. The association between Diabetes Mellitus and the clinical outcome was not statistically significant ($p=0.31$). 6.89% of discharged were Diabetic and 28.57% of the dead were diabetic. The correlation between size of the bleed and other parameters like Age, Total Cholesterol, LDL Cholesterol, HDL Cholesterol was not statistically significant, but correlation with Triglyceride was found to be statistically significant.

DISCUSSION

This study tested the hypothesis whether changes in lipid profile might contribute to the risk of ICH. It supports the idea that serum lipid profile can influence the clinical outcome and mortality in patients with ICH. Sethi 2002 et al has noted that stroke incidence may vary considerably from country to country. The male to female ratio of the study patients was 1.54:1; further, the most common age group experienced stroke was between 60-69 years. This may be due to differences in risk factors such as smoking and alcohol intake which are more prevalent among men in India compared with women (Sethi, 2002). In our study which was conducted in 50 patients of ICH and same age and sex match 50 Controls, 68% were males and 32% females. (34/50 and 16/50, respectively) in case and in Controls group 58% were male and 42% female (21/50 and 29/50, respectively). This supports the fact that Men are more likely to have a stroke than women: the male/female sex ratio in our study is 212:1 case and in Controls group is 1.38:1.

Bhattacharya et al 2005 found out that the mean age was 66 yrs. SD ±13.60 and women were older compared with men (mean age 68.9 yrs. SD ±13.12 Versus 63.4 yrs. SD ±13.53). The mean onset of stroke for men in India ranges from 63-65 and 57-68 for women. (Bhattacharya et al 2005. Dalal et al 2008 (Sridharan *et al.,* 2009). In our study mean age of male was 56.65±13.41 and for female was 60.25±12.85 and in Controls group was for male 52.93±19.52 yrs. For females 47.33±15.40 yrs. In our study, comparison of various parameters of lipid profiles was done among study and Controls group. The total cholesterol level in Controls was 155±41.71 as compared to 174.24±37.44 in study group. similarly, total triglyceride in Controls was 100.04±51.41 and 136.72±82.88 in study group, HDL was 46.14±19.98 and 50.26±12.78, LDL was 96.10±28.95 and 109.48±32.29 respectively in Controls and study groups. All the levels were significantly different except HDL. Rodriguez-Luna D et al studied that lower LDL-C levels were associated with Hematoma Growth (98.1±33.7 mg/dL versus 117.3±25.8 mg/dL; P=0.003), early neurological deterioration (89.2±31.8 mg/dL versus 112.4±29.8 mg/dL; P=0.012), and 3-month mortality (94.9±37.4 mg/dL versus 112.5±28.5 mg/dL; P=0.029), but not with poor long-term outcome (109.5±31.3 mg/dL versus 108.3±30.5 mg/dL; P=0.875). Moreover, LDL-C levels were inversely related to the amount of hematoma enlargement at 24 hours (F-0.31; P=0.004). In multivariate logistic regression analysis, LDL-C level <95 mg/dL emerged as an independent predictor of Hematoma Growth (OR, 4.24; 95% Cl, 1.26-14.24; P=0.020), early neurological deterioration (OR, 8.27; 95% Cl, 1.66-41.16; P=0.010), and 3-month mortality (OR, 6.34; 95% Cl, 129-313; P=0.023. The study concluded that lower serum LDL-C level independently predicts Hematoma Growth, early neurological deterioration, and 3-month mortality after acute ICH (Rodriguez-Luna *et al.,* 2011).

Our study also shows that the association between clinical outcome and levels of LDL-C was significant. The mean LDL for death patients was 89.38±28.01 and for discharged patient was 109.62±38.17. The difference was statistically significant (p<0.05). Renske G et al studied that Triglycerides were strongly and inversely associated with intracerebral haemorrhage, independently of HDL-cholesterol, LDL-cholesterol. and potential confounders [HR for highest versus lowest quartile: 0.20 (906-969)]. Triglycerides were also associated with deep or infratentorial microbleeds [odds ratio for highest versus lowest quartile: 0.37 (0.14-0.96)], but not with strictly lobar microbleeds (Renske, 2011). Bonaventure A et al During a mean follow-up of 5.0 years, 36 haemorrhagic strokes, 143 ischemic strokes and 393 coronary events occurred. An increased level of triglycerides was associated with an increased risk of ischemic vascular events. Conversely, a low level of triglycerides (< or = 0.94 mmol/L) was associated with an increased risk of haemorrhagic stroke (adjusted hazard ratio 2.35; 95% confidence interval 1.18-4.70). The relationship with haemorrhagic stroke was mainly apparent in men, in individuals with high blood pressure, and in those with low levels of cholesterol (Bonaventure, 2009). In our study also the comparison among study group for clinical outcome and levels of Triglyceride was found to statistically significant (P<0.05). The difference is significant in that the levels were lower in patients whose clinical outcome was death, than those who discharged (P<0.05). The mean for discharged patient was 110.95±45.76 and for death was 85.14±37.20 suggesting low levels of Triglycerides in patients with clinical outcome of death. The role of cholesterol in the organization of biological membranes and in disease is well documented (Maxfleld and Tabas, 2005). The fine-tuned composition of lipid and cholesterol at the cellular membrane, have been suggested to play crucial role in compartmentalizing various membrane proteins for specific cellular activities (Mukherjee and Maxfield, 2004). Cholesterol helps maintain the membrane stability of vessels. This might explain the low levels of triglycerides and LDL-C in patients with intracranial Haemorrhage. Cholesterol is required in the neurons for synaptic function and in the neuronal membrane fusion pores. (Jeremic A, Jin Cho W, Jena BP.). The correlation between size and bleed and the levels of triglyceride was significant (P<0.05).

The comparison among study group for clinical outcome and levels of total cholesterol (172.48±143.92 and 175.52±132.73) and HDL (48±12.82 and 51.90±0.13) was not significant (p>0.05) in death and discharged patients respectively. Debabrata Goswami et al found that Clinical parameters that can predict outcome are state of consciousness at presentation, Glasgow coma sale score, systolic and diastolic blood pressure with mean arterial blood pressure, elevated body temperature and increased respiratory rate, vertical and horizontal gaze palsies, pupillary abnormalities and severity of motor weakness. Presence of comorbidities increased the likelihood of poor outcome. CT findings including the ICH scone can also accurately predict the outcome are- volume of hematoma>30ml, a mid-line shift of >5 mm and Intraventricular extension of bleed. Finally, the ICH Score was found to be a better predictor of short-term outcomes in patients with spontaneous Intracerebral bleed (WADE, 2015; Debabrata Goswami *et al.,* ?). The association between clinical outcome and Glasgow Coma Scale was calculated using Chi-Square Test. 100% of patients having a score of 3-4 died and 100% of patients having a score of 13-15 were discharged. The difference for significant for scores (P<0.001).

In our study group for clinical outcome and size of Intra cranial bleed was highly significant (P<0.001). The mean for discharge was 0.03±0.04) The mean for death was 0.06±0.04.
In our study the association between clinical outcome and midline shift was significant. 66.67% of the patients having midline shift died (P<0.04). There Is no association between clinical outcome and intra-ventricular extension, which was not statistically significant. 11 (37.93%) were discharged and 11 (47.62%) died in our study. In our study there is no association found between clinical outcome and location of the bleed It was found to be statistically not significant (P>0.05). Out of 50 cases, 13 were (61.90%) males and 8 (38.10%) were females who died in our study. There is no significant difference between outcome and sex of the patient (p value-0.043). In our study out of 50 cases, 21 were (42%) died and 29 (58%) cases were discharged. Maximum number of patients (71.43%) died in the age group of 51-80 yrs. followed by 23.81% in 21-50 yrs. group and 4.76% in more than 80 yrs. age group. Maximum discharge was in the age group of 51-80 years (58.62%), followed by 37.93% in the age group of 21-50 years and 3-45% in more than 80 years group, which was statistically not significant(p>0.05). Enlargement of the size of the haemorrhage is a major concern, as the size of the blood clot may impact survival, or at least the degree of neurological disability if the patient survives. It is well established that enlargement of the blood clot occurs in the first 24 hours after onset in about one-third of patients.

Although blood pressure elevation is suspected as a contributing cause of the enlargement, this remains unproven. Other comorbid factors like Hypertension and Diabetes were not statistically significant for clinical outcome. Our results contribute new evidence in the quest for an answer to the long-standing question: Is there an association between blood lipids levels and occurrence of Intracranial Haemorrhage? According to our findings, the answer is that low levels of LDL and triglycerides are associated with the clinical outcome of intracranial Haemorrhage. These preliminary results may shed light on the scientific debate, since they point to the need to stratify the importance of lipid profile and their role in etiopathogenesis of intracranial Haemorrhage. In order to determine the real association between lipid alterations and occurrence of intracranial Haemorrhage, this study may also help guide future trials attempting to relate lipid alterations with occurrence of vascular events.

Summary and Conclusion

This study aimed at establishing a correlation of lipid profile with clinical outcome in intra-cranial haemorrhage and understanding in hospital mortality in intra cranial haemorrhage with reference to size, site of the bleed and presence of co-morbid conditions like Diabetes, Hypertension. The Study included 50 patients of ICH and 50 Controls of same age and sex match. Along with the complete medical history, General and Neurological examination of the patient, the lipid profile was done which consisted of Total cholesterol, High-density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C) and Triglycerides. The diagnosis was ascertained based on Computed Tomography (CT) scan at Brain. done at the time of admission. The results showed a significant association between low levels of Triglycerides and LDL-C with poor outcome in ICH patients.

The levels of Triglycerides are inversely related with the size of the intracranial bleed, which further supports the fact that the significant association between levels of Triglycerides and Intracranial Haemorrhage exists. It was concluded that a significant association between lipid profile and in hospital mortality of ICH patients exists. As the alterations in lipid profile affects the clinical outcome in patients with ICH. a detailed evaluation of lipid profile should be done, and it is further recommended that overzealous treatment of Stroke patients with Anti-Lipidemic therapy should be avoided. Our study concluded that there is a significant correlation between lipid profile, specifically LDL-Cholesterol and Triglyceride and clinical outcome of intracranial Haemorrhage patients in terms of death or discharge. Low levels at LDL-cholesterol and Triglyceride are associated with poor outcome in patients with ICH. It is thus recommended that care should be taken while administrating lipid-lowering therapy to Stroke patients and attention should be paid to the levels of lipids in patients with Intracranial Haemorrhage.

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