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Clinical evaluation of the lipid profiles of the patients suffering from strokes in PMCH, Patna

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Abstract
Dyslipidaemia is a major risk factor for cerebral infarction. The LDL targeting goal can significantly reduce the risk of cerebral infarction. 4 There has been a number of publications on the role of lipid disorders and outcome in stroke. 5-10HDL is known to promote the transport of extra-hepatic cholesterol back to the liver hence reducing serum cholesterol thereby preventing Ischaemic stroke. It therefore shows that, HDL cholesterol level has an inverse correlation with the risk of stroke Therefore this study was designed to find out the patterns of dyslipidaemia in cases of strokes.
The present study was planned in the Department of Pathology, Patna Medical College and Hospital, Patna from Feb 2018 to July 2018. The diagnosis of stroke was confirmed by taking CT scan of brain. The total 75 patients were enrolled in the present study. Out of that 25 cases were diagnosed with haemorrhagic stroke and 25 cases were diagnosed with ischemic strokes. To compare the parameters 25 control patients were also enrolled in the present study. The lipid profiles of the patients were done on fasting state. The samples were sent for the analysis and results were compiled and studied further.
The data generated from the reported literate suggest that stroke is a multifactorial disease, there are multiple risk factors involved for the disease occurrence. Hence lipid profile assessment is proven to be of help to alert patients. Early recognition and treatment is helpful for reduction in morbidity and mortality.

Keywords: Lipid profile, Strokes, HDL, LDL, Cholesterol, etc

1. Introduction
Stroke (also known as Brain Attack) occurs when blood supply to the brain is affected due to either blockage or leakage (or both blockage and leakage) of a blood vessel responsible for supplying or draining blood to and from the brain, thereby, causing brain damage leading to difficulty in movements, sensation, speaking, vision etc. or at times to death.
A stroke is a medical condition in which poor blood flow to the brain results in cell death. There are two main types of stroke: ischemic, due to lack of blood flow, and hemorrhagic, due to bleeding. Both result in parts of the brain not functioning properly. Signs and symptoms of a stroke may include an inability to move or feel on one side of the body, problems understanding or speaking, dizziness, or loss of vision to one side. Signs and symptoms often appear soon after the stroke has occurred. If symptoms last less than one or two hours it is known as a transient ischemic attack (TIA) or mini-stroke. A hemorrhagic stroke may also be associated with a severe headache. The symptoms of a stroke can be permanent. Long-term complications may include pneumonia or loss of bladder control [1].
The main risk factor for stroke is high blood pressure. Other risk factors include tobacco smoking, obesity, high blood cholesterol, diabetes mellitus, a previous TIA, and atrial fibrillation. An ischemic stroke is typically caused by blockage of a blood vessel, though there are also less common causes. A hemorrhagic stroke is caused by either bleeding directly into the brain or into the space between the brain's membranes. Bleeding may occur due to a ruptured brain aneurysm. Diagnosis is typically based on a physical exam and supported by medical imaging such as a CT scan or MRI scan. A CT scan can rule out bleeding, but may not necessarily rule out ischemia, which early on typically does not show up on a CT scan. Other tests such as an electrocardiogram (ECG) and blood tests are done to determine risk factors and rule out other possible causes. Low blood sugar may cause similar symptoms [2].
Prevention includes decreasing risk factors, as well as possibly aspirin, statins, surgery to open up the arteries to the brain in those with problematic narrowing, and warfarin in those with atrial fibrillation. A stroke or TIA often requires emergency care. An ischemic stroke, if detected within three to four and half hours, may be treatable with a medication that can break down the clot. Aspirin should be used. Some hemorrhagic strokes benefit from surgery. Treatment to try to recover lost function is called stroke rehabilitation and ideally takes place in a stroke unit; however, these are not available in much of the world [3].
Strokes can be classified into two major categories: ischemic and hemorrhagic. Ischemic strokes are caused by interruption of the blood supply to the brain, while hemorrhagic strokes result from the rupture of a blood vessel or an abnormal vascular structure. About 87% of strokes are ischemic, the rest being hemorrhagic. Bleeding can develop inside areas of ischemia, a condition known as "hemorrhagic transformation." It is unknown how many hemorrhagic strokes actually start as ischemic strokes [3].
Ischemic stroke occurs because of a loss of blood supply to part of the brain, initiating the ischemic cascade. Brain tissue ceases to function if deprived of oxygen for more than 60 to 90 seconds [citation needed], and after approximately three hours will suffer irreversible injury possibly leading to the death of the tissue, i.e., infarction. (This is why fibrinolytics such as alteplase are given only until three hours since the onset of the stroke.) Atherosclerosis may disrupt the blood supply by narrowing the lumen of blood

vessels leading to a reduction of blood flow, by causing the formation of blood clots within the vessel, or by releasing showers of small emboli through the disintegration of atherosclerotic plaques. Embolic infarction occurs when emboli formed elsewhere in the circulatory system, typically in the heart as a consequence of atrial fibrillation, or in the carotid arteries, break off, enter the cerebral circulation, then lodge in and block brain blood vessels. Since blood vessels in the brain are now blocked, the brain becomes low in energy, and thus it resorts to using anaerobic metabolism within the region of brain tissue affected by ischemia. Anaerobic metabolism produces less adenosine triphosphate (ATP) but releases a by-product called lactic acid. Lactic acid is an irritant which could potentially destroy cells since it is an acid and disrupts the normal acid-base balance in the brain. The ischemia area is referred to as the "ischemic penumbra [4].

Hemorrhagic strokes are classified based on their underlying pathology. Some causes of hemorrhagic stroke are hypertensive hemorrhage, ruptured aneurysm, ruptured AV fistula, transformation of prior ischemic infarction, and drug induced bleeding [58]. They result in tissue injury by causing compression of tissue from an expanding hematoma or hematomas. In addition, the pressure may lead to a loss of blood supply to affected tissue with resulting infarction, and the blood released by brain hemorrhage appears to have direct toxic effects on brain tissue and vasculature. Inflammation contributes to the secondary brain injury after haemorrhage [5].

Triglycerides are lipid compounds composed of a glycerol esterified to 3 fatty acid chains of varying length and composition. These fatty acid chains can be saturated or unsaturated, and the chemical composition of each chain is different. Each chain consists of carbon and hydrogen atoms with varying single or double-bonded chains, depending on the degree of saturation or unsaturation. Triglycerides are formed of mixed chains, and the structural comparison between the chains is heterogenous in nature.

Triglyceride is the most abundant dietary lipid compound found throughout the diet and is the method with which energy is stored in the body. Initial digestion of dietary triglycerides takes place with pancreatic lipase, which hydrolyzes one fatty acid chain at a time to form 2 free fatty acid (FFA) chains and one 2-monoglyceride (2MG) compound per each triglyceride. Bile salts are released in the duodenum in response to cholecystokinin release occurring in the presence of lipid compounds within the ingesta. Bile salts aid in forming lipid micelles, which create a hydrophilic surface with a hydrophobic core of lipid molecules, including FFA.

Absorption of lipid compounds into the enterocyte for biochemical usage occurs through diffusion across the cellular membrane and also through lipid transporters that are located on the luminal side of the enterocyte. Once in the enterocyte, FFA chains and 2MG compounds are transported to the endoplasmic reticulum, where they are reformed into triglycerides and packaged into chylomicrons in the golgi apparatus to receive chylomicron specific apolipoproteins, namely apo B48, which is a marker for TG chylomicron. These newly formed chylomicrons are then released from the enterocyte and transported to circulation by the lymphatic system [6].

Once in the circulation, the triglyceride-rich chylomicrons pass through the vasculature, where they undergo a complex process of protein exchange mediated by HDL and, based upon this protein exchange process, are either received in the liver for further metabolism and packaging or undergo delipidation at the vascular endothelial surface by lipoprotein lipase (LPL) [6]. The largest proportion of chylomicrons containing dietary triglycerides undergo hepatic uptake, where triglycerides are packaged into very-low dense lipoprotein (VLDL) for transport to peripheral tissues.

VLDL is the major carrier of triglycerides and FFA in serum and is synthesized within the hepatocyte, while a smaller percentage of FFA travels in a unesterified form, which is complexed to albumin for transport [7]. Once the VLDL is release into serum, it travels to peripheral tissues where it undergoes a delipidation cascade, and triglyceride is removed by LPL at multiple LPL receptor sites along the endothelium [6]. Following delipidation, a VLDL remnant (IDL) is formed, which has released the bulk of triglyceride originally packaged and is cleared by the liver or transformed to LDL by serum protein exchange process.

Triglyceride is the major high-energy compound for energy storage supplying 9 Kcal/g of FFA. Those lipids that are intended for storage are recognized by and are removed from VLDL by LPL as well as storage specific transmembrane proteins that aid in a process of lipid droplet formation within adipocytes and muscle tissue for use later as an energy source [6, 8]. Liberation of triglycerides from lipid stores begins under metabolic stressors when circulating systemic nutrient supply is not sufficient to meet metabolic energy demand.

Regulation of enzymes needed for lipolysis occur through cyclic adenosine monophosphate (cAMP)–mediated and cAMP-independent pathways that activate adipose triglyceride lipase, hormone-sensitive lipase, and monoacylglycerol lipase, which hydrolyzes the ester bonds of stored triglyceride producing glycerol and FFA chains. Glycerol undergoes cellular removal through transcellular aquaporins, and FFAs are either moved to serum, esterified or metabolized into signaling molecules [9].

Once FFA has been liberated from adipocytes for use in energy production they are transported and received by cells for metabolism and mobilized to intracellular mitochondria and peroxisomes for use. These lipid compounds undergo fatty acid oxidation, providing acetyl-CoA for hepatic ketogenesis and substrates for energy production through oxidative phosphorylation [7].

The role of lipids profiles at the aspect of stroke status and risk assessment also needs to further discuss. At the same time, it is lacking in the aspect of using large-scale prospective cohort study to verify the role of lipids profiles of prediction for stroke, especially in Chinese hypertensive patients. Simultaneously, few studies compared the power of traditional and non-traditional lipids indicators in predicting the risk of stroke in hypertensive patients.

Dyslipidaemia is a major risk factor for cerebral infarction. The LDL targeting goal can significantly reduce the risk of cerebral infarction. 4 There has been a number of publications on the role of lipid disorders and outcome in stroke. 5-10HDL is known to promote the transport of extra-hepatic cholesterol back to the liver hence reducing serum cholesterol thereby preventing Ischaemic stroke. It therefore shows that, HDL cholesterol level has an inverse correlation with the risk of stroke Therefore this study was designed to find out the patterns of dyslipidaemia in cases of strokes.

Methodology

The present study was planned in the Department of Pathology, Patna Medical College and Hospital, Patna Feb 2018 to July 2018.The diagnosis of stroke was confirmed by taking CT scan of brain. The total 75 patients were enrolled in the present study. Out of that 25 cases were diagnosed with haemorrhagic stroke and 25 cases were diagnosed with ischemic strokes. To compare the parameters 25 control patients were also enrolled in the present study. The lipid profiles of the patients were done on fasting state. The samples were sent for the analysis and results were compiled and studied further.

The patients suffering from diseases like which can alter the lipid profiles are not involved in the study. The examples of the lipid lowering diseases like diabetes mellitus, cancer, acute pancreatitis, recent parenteral nutrition and acute gastrointestinal bleeding, renal failure, patients who were on glucose or lipid lowering drugs.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results & Discussion

Stroke is a serious life threatening condition which continues to be a major public health problem leading to death and severe neurologic disability. Nikolai Anichkov first proposed a link between cholesterol and atherosclerosis in 1912 by proving that obstructive pathophysiology in atherosclerosis occurs as a result of increased cholesterol levels [10]. Dyslipidemia is a major risk factor for cerebral infarction is the presence of abnormal levels of lipids in the blood, characterized by an elevation of the serum level of TC, LDL, and TG, and a decrease in the serum level of HDL [11-12].

Stroke events were confirmed according to the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) criteria: cases with significant non-vascular etiologic events, including local or global brain disorders that lasted longer than 24 h, but it contained stroke events that had duration of fewer than 24 h due to death or surgery [13].

The incidence and mortality of stroke vary greatly among the different population of world and has declined considerably in several foreign countries probably due to better preventive measurements. According to World Health Organization, stroke is second largest cause of mortality throughout the world. Recent studies conducted on Indian population have shown that age-adjusted prevalence rate of stroke is between 250-350/100,000 [14-15]. In developed countries, more than 80% of cases of CVA occur in individuals who are above 60yrs of age, whereas in India about 1/5th of the all strokes occur in individuals who are below the age of 60 year [16].

There are various non modifiable risk factors like age, sex, familial trends, ethnic groups, race and modifiable risk factors like cardiac diseases, diabetes mellitus, dyslipidemia, hypertension, smoking, alcohol abuse & physical inactivity [17]. Though substantial differences are there in occurance of frequency from place to place, cerebral thrombosis is the most frequent form of stroke in studies done by clinical researchers followed by hemorrhage. Cerebral hemorrhage and cerebral embolism comes next as regards the mortality and morbidity [14].

Table 1: Demographic Details prevalence of Stroke

Sex	Number of Cases with Haemorrhagic stroke	Number of Cases with Ischemic stroke	Control number
Males	14	15	16
Females	11	10	9
Age group in years			
31 – 40 years	1	3	2
41 – 50 years	3	4	3
51 – 60 years	4	6	6
Above 60 years	17	12	14
Total	25	25	25

Table 2: Lipid Profile in Different Patients

Lipid Profile	Haemorrhagic stroke	Ischemic stroke	Control number
Total Cholesterol	191.2 ± 24.5	193.5 ± 21.9	168.3 ± 11.5
LDL Cholesterol	112.7 ± 15.9	121.5 ± 12.8	95.6 ± 23.6
HDL Cholesterol	51.2 ± 12.9	43.9 ± 2.9	41.2 ± 3.5
Triglycerides	120.5 ± 29.2	132.6 ± 21.5	129.1 ± 32.5

Table 3: Lipid profile of patients with stroke and control Patients

Lipid	No. of Cases of Strokes	No. of Cases of Haemorrhagic Strokes	No. of Cases of Ischemic Stroke	No. of Control Cases
Cholesterol >200mg%	10	11	9	4
LDL-C >100 mg%	16	15	15	11
Triglyceride >150 mg%	5	4	5	3
HDL-C <40mg%	6	3	8	5

Amarenco and Steg [18] conducted 61 prospective observational studies, and concluded that no association exists between total cholesterol and stroke mortality. They concluded that stroke was a multifactorial disease and that its various causes are not equally associated with blood cholesterol levels. Study done by Millions *et al*. [19] showed a strong relation between serum total cholesterol and nonhaemorrhagic strokes with an inverse association to intracranial haemorrhage. Similar findings were observed in the present study. Study done by Park *et al*. [20] showed negative results whereas others showed a positive association with high serum triglyceride concentrations. Copenhagen City Heart Study [21] showed a log linear association between serum triglyceride concentrations and non-haemorrhagic stroke while similar relation was found of high triglyceride levels as a risk factor for stroke in this study

Cynthia *et al*. [22] reported that 56% of stroke patients had dyslipidemia, in the present study 79.5% of cases showed similar findings. Cynthia *et al* also stated that most of them had high triglycerides and low HDL levels, which is in accordance to present study data. Denti *et al*. [23] reported that LDL-C concentrations over 100 mg/dl along with low HDL-C levels were associated with higher risk for stroke,

similar findings were observed in present study. Korean Morang *et al*. [24] in their study observed that the mean value of Apo B was higher, that of Apo A1 was lower, similar findings were observed in the present study.

This study considered one of the risk factor for stroke, therefore dyslipidaemia may reflect a cluster of other risk factors for stroke. It is a hospital based study, so the data may not represent the whole population. Some of the patients were from poor socio-economic background hence some of them couldn't afford CT scan investigation therefore affecting study duration.

Conclusion

The data generated from the reported literate suggest that stroke is a multifactorial disease, there are multiple risk factors involved for the disease occurrence. Hence lipid profile assessment is proven to be of help to alert patients. Early recognition and treatment is helpful for reduction in morbidity and mortality.

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