Original Research Article

Correlation between HbA1c level and LDL cholesterol level in ischemic stroke patients

Gaurav Gupta, Mohammad Aquiqe*, Richa Giri, Shivendra Verma

Department of Medicine, G. S. V. M. Medical College, Kanpur, Uttar Pradesh, India

*Correspondence:
Dr. Mohammad Aquiqe,
E-mail: dr.akeek2013@gmail.com

ABSTRACT

Background: Defects in insulin action and hyperglycemia could lead to Dyslipidemia in patients with diabetes.
Methods: Cross sectional study carried out in patients presenting with ischemic stroke to medicine emergency unit of the LLRH Hospital from January 2018 to October 2019.Patient of age group 40-80 years The subjects in the present study were 450 patient comprised of 235 cases with ischemic stroke of age group of 40-80 years and 215 health y controls of age group of 40-80 years.
Results: The correlation between these two variable as elicited from data obtained from study and, is significant (p<0.0001). The sensitivity of this correlation in the context of ischemic stroke is 75%, while the specificity is 60%. However, an impressive negative predictive value of 91% suggests a beneficial effect of normal or well controlled diabetes and Dyslipidemia. Conversely, a modest positive predictive value of 29% does not appear to help in utilizing this correlation as a measure of future likelihood of ischemic stroke. p value 0.00005 inference-highly significant.
Conclusions: Study show statistically significant association (p < 0.001) of increased levels of HbA1c and LDL-C in patients of ischemic stroke.

Keywords: Diabetes, Dyslipidemia, Infarct, Ischemia

INTRODUCTION

Stroke or cerebrovascular accident (CVA) is defined as an abrupt onset of a neurological deficit attributable to a focal vascular cause. Thus the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis. The focal vascular event may include cerebral infarction, intra-cerebral haemorrhage (ICH), and subarachnoid haemorrhage (SAH).[1] Acute ischemic stroke (AIS) occurs as a result of an event that limits or stops blood flow, including extra-cranial or intracranial thrombotic embolism, thrombosis in situ or relative hypo-perfusion. Affected regions with cerebral blood flow of lower than 10 mL/100 gm of tissue/min form the infarct core, and these cells are presumed to die within minutes of stroke onset. Zones of decreased or marginal perfusion (cerebral blood flow <25 mL/100g of tissue/min) are collectively called the ischemic penumbra. Tissue in the penumbra can remain viable for several hours because of marginal tissue perfusion; however, it is often consumed by progressive insults, and coalesces with the infarcted core, often within hours of the onset of the stroke.[2]

On the cellular level, the ischemic neuron becomes depolarized as ATP is depleted and membrane ion-transport systems fail. Disruption of cellular metabolism also impairs normal sodium-potassium plasma membrane pumps, producing an intracellular increase in sodium, which in turns increases intracellular water content. This cellular swelling is referred to as cytotoxic oedema and occurs very early in cerebral ischemia.[3]

Ischemia also directly results in dysfunction of the cerebral vasculature, with breakdown of the blood-brain barrier occurring within 4-6 hours after infarction. Following the barrier's breakdown, proteins and water flood into the extracellular space, leading to vasogenic oedema. This produces greater levels of brain swelling and mass affects that peak at 3-5 days and resolve over the next several weeks with resorption of water and proteins.[4]

Large-artery occlusion typically results from embolization of atherosclerotic debris originating from the common or internal carotid arteries or from a cardiac source. A smaller number of large-artery occlusions may arise from plaque ulceration and in situ thrombosis. Large-vessel ischemic strokes more commonly affect the MCA territory, with the ACA territory and other vessels affected less frequently.[5]

A variety of risk factors influenced by socio-economic, cultural, political and environmental determinants have been identified and associated with the occurrence of ischemic stroke. Some of these risk factors include Dyslipidemia, glycemic control, hypertension, tobacco use and others. In this study authors investigate the influence and correlation of Dyslipidemia and glycemic control in patients with ischemic stroke.[6]

Dyslipidemia is defined as elevated level of total cholesterol (TC) or low-density lipoprotein (LDL), or low level of high-density lipoprotein (HDL). It has been shown to be an independent risk factor for cerebrovascular disease. Type 2 diabetes mellitus (T2DM) is a disorder of insulin secretion and glucose utilization, resulting in a variety of metabolic and vascular complications including Dyslipidemia and stroke. The occurrence of stroke in patients with T2DM may thus be due to independent effect of hyperglycemia or Dyslipidemia, or it may be a combined effect of Dyslipidemia and poor glycemic control.[7]

METHODS

Study design

This is a cross sectional study Carried out in patients presenting with ischemic stroke to the Medicine Emergency Unit of the LLRH Hospital(tertiary center) during January 2018 to October 2019. Patient was randomly assigned to case and control group. This study receives approval from ethical committee of this institute. By calculating minimal sample size, 450 Participants included in the study. 235 were cases and 215 were control.

Inclusion criteria

- Age group 40-80 years
- Patients with ischemic stroke

Exclusion criteria

- Patients with cardio-embolic stroke, with prior history of MI and of non valvular-atrial fibrillation
- Patients with a neurologic deficit attributable to neoplasm, trauma, or subdural or epidural hematoma,
- Transient Ischemic Attack(TIA)
- Patients with hepatic diseases, renal diseases and
- Those who were on lipid lowering medications or on steroids prior to the onset of stroke were also excluded.
- The subjects in the present study were 450 patients comprised of 235 cases with ischemic stroke of age group of 40-80 years and 215 healthy controls of age group of 40-80 years.

Clinical and biochemical assessment

- Interviewer administered questionnaires were used to capture the following data; age, sex, occupation, history of diabetes mellitus (taking OHA), and Dyslipidemia (taking Statins).
- The biochemical parameters that were evaluated within 48 hours of admission included plasma glycosylated hemoglobin (HbA1c), fasting total serum cholesterol, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL).
- A confirmed value of HbA1c at or above 48 mmol/mol (6.5%) is used as diagnostic for diabetes mellitus as recommended by the American Diabetes Association.

The diagnosis of stroke was made clinically and with the aid of computed tomographic (CT) scans and magnetic resonance imaging (MRI) for some patients.

Statistical analysis

- Statistical analysis was performed using chi-square for qualitative variables and students t-test for quantitative data.
- p value of 0.05 or less was considered as the level of significance.
- A bivariate analysis correlating the biological aspects with biochemical data was also carried out
- The analyses were performed using SPSS 16.0 software.

RESULTS

Total 450 patients were selected in our study. 235 were cases and 215 were control. Study period was January 2018 to October 2019. The total numbers are similar and were chosen to identify the correlation between glycemic control and Dyslipidemia in the normal population as well as patients of ischemic stroke.

The majority of patients in both groups are between 50-70 years of age, accounting for about two thirds of the

study population. The mean age was 59.6±9 years in cases and 58.8±9 years in controls. The number of subject in both groups was similar in each decade of life. The gender distribution is similar in both populations.

Table 1: Demographic profile, baseline characteristics and risk factors.

Age in years	Case	Control
40-50	42(17.88%)	37(17.20%)
50-60	117(49.79%)	110(51.26%)
60-70	51(21.70%)	47(21.82%)
70-80	25(10.63%)	21(9.72%)
Gender	**Case**	**Control**
Male	132(56.55%)	125(58.11%)
Female	103(43.45%)	90(41.89%)
Risk factor	Case	Control
Diabetes mellitus	119(50.63%)	91(42.33%)

The majority of patients in both groups are between 50-70 years of age, accounting for about two thirds of the study population. The mean age was 59.6±9 years in cases and 58.8±9 years in controls. The number of subject in both groups was similar in each decade of life.

The gender distribution is similar in both populations (Table1).

Figure 1 shows the distribution of glycemic status in patients with ischemic stroke, and control. About one half of these patients had diabetic range in cases as compared to control population, as evidenced by HbA1c level, suggesting that diabetes was an independent variable influencing ischemic stroke risk, and it has significant effect on the incidence of ischemic stroke (p value 0.003018).

The mean value of HbA1c in cases was 6.30% ±16.02 and in control group was 5.80% ±14.04.
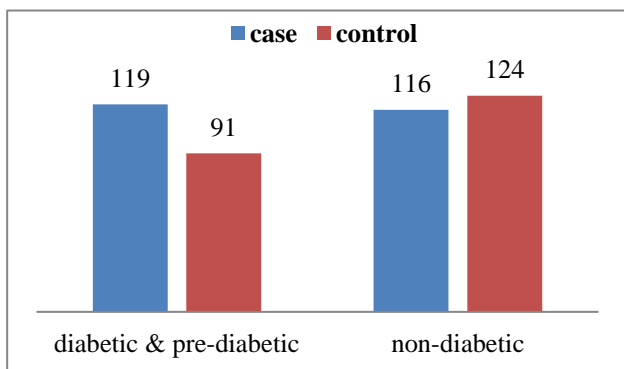
Figure 1: The mean value of HbA1c in case and control group.

Figure 2 shows that the observed value of LDL cholesterol was higher in those patients who had HbA1c level more than 6.5% means diabetic patients, 32 patients

in case group diabetic and 11 patients in control group non-diabetic were with high level of LDL cholesterol.
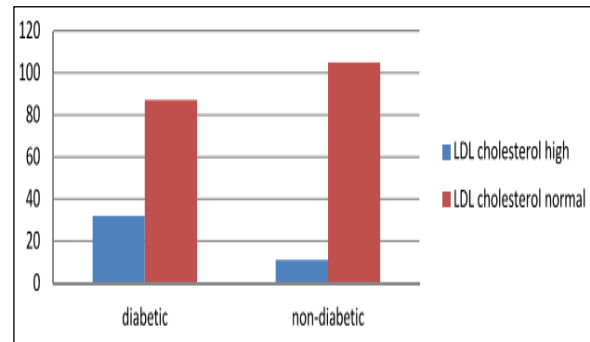
Figure 2: LDL cholesterol in diabetic and non-diabetic patients.

Table 2: Comparison of LDL cholesterol (LDL-C) in ischemic stroke cases and control group.

HbA1c>6.5%	High	Normal	Total
Present	32	87	119
Absent	11	105	116
Total	43	192	235

Table 2 shows the LDL levels were normal in 192 patients and elevated in 43 patients based on measured blood levels. Authors correlated the HbA1c with LDL levels 235 patients of which 32 had diabetes and dyslipidemia, 87 had diabetes only and 11 had dyslipidemia only, while 105 had neither diabetes nor Dyslipidemia. This correlation was statistically highly significant (P<0.0001) suggesting that patients with high HbA1c and LDL levels were more likely to have a stroke. These findings resonate with guidelines which recommend treating diabetes and dyslipidemia to goal to achieve favourable clinical outcomes.

DISCUSSION

Acute ischemic stroke accounts for the largest subgroup of stroke patients in our hospitals. Similar proportions of ischemic stroke ranging as high as 80%, have been reported in literature from other centres and countries as well.[8]

Several risk factors have been identified as being associated with the occurrence of ischemic stork. These include modifiable and non-modifiable factors, with the former including hypertension, hyperglycemia, Dyslipidemia, tobacco and alcohol use and obesity. Non-modifiable risk factors include family history of vascular events, age, gender and personal history of vascular events in other parts of the body.[9]

Authors conducted a study in 235 confirmed ischemic stroke patients using standard clinical criteria laid and confirmed by radiological evidence on CT scan head or

MRI brain. Authors then attempted to investigate the correlation between two modifiable risk factors found together frequently, and which are also known to be independent variables in the occurrence of ischemic stroke. These include Dyslipidemia and hyperglycemia, and authors studied their correlation through two tiers of investigation. First authors elicited a history of medication for anti-diabetic or lipid lowering agents at the time of presentation of the stroke patient. Second, authors measured their glycemic and lipid control through glycosylated hemoglobin and lipid profile measurements. Then authors correlated these two variables and compared the levels and correlation with a control population to ascertain their combined influence on the occurrence of stroke. LDL levels were normal in 192 patients and elevated in 43 patients based on measured blood levels.

Authors correlated the HbA1c with LDL levels 235 patients of which 32 had diabetes and Dyslipidemia, 87 had diabetes only and 11 had Dyslipidemia only, while 105 had neither diabetes nor Dyslipidemia. This correlation was statistically highly significant ($P<0.0001$) suggesting that patients with high HbA1c and LDL levels were more likely to have a stroke.[10]

REFERENCES

1. Fauci J, Longo K. Harrison's principles of internal medicine. 20th ed. 472;2.
2. Smith WS, Johnston SC; J. Claude Hemphill Harrison's principles of internal medicine. 20th ed. 472;3.
3. Kouna NP, Millogo A, Siemefe KF, Assengone ZY. Epidemiological and progressive aspects of stroke at the Hospital Center of Libreville. African J Neurol Scien. 2007;26:12-7.
4. Hollander M, Koudstaal PJ, ML Bots, Grobbee D, Hofman A, Breteler M. Incidence, risk and case fatality of ever stroke in the elder population. The rotterdamstudy. J neurolneurosurg Psychiatry. 2003 Mar; 74 (3):317-21.
5. Collins R, Peto R, macmahon S, Hebert P, Fiebach NH, Eberlein KA, et al. Blood pressure, stroke and coronary heart disease - Part 2: Short-term reductions in bloodpressure: overview of randomized drug trials in their epidemiological context. Lancet. 1990 Apr; 335(8693):827-38.
6. Chan S, Ros S, You KY, Nhem S, Room JY, Dudognon P, et al. Management of Stroke in Phnom Penh, Cambodia. Bull Soc Patholexot. 2006 Feb; 100(1):32-5.
7. Sweileh WM, Sawalha AF, Al-Aqad SM, SH Zyoud, Al-Jabi SW. The Epidemiology of Stroke in Northern Palestine: A 1 year, Hospital-Based Study. J strokecerebrovasc Dis. 2008;17(6):406-11.
8. Sène DF, Bass AM, Ndao AK, Ndiaye M, Toure K, Thiam A, et al. Functional prognosis of cerebrovascular accidents in developing countries: Senegal. Ann Readaptmed Phys. 2006 Apr; 49(3):100-4.
9. Pellerin C, Mauget Y, Bouju A, Chavot D, Berges S, Rumbach L. Stroke. Emerg Med. 2003:107-17.
10. Ducluzeau R, Busseuil C, Bedock B, Schir S. Management of stroke at reception and emergency services. Resuscitation Emerg. 1997;6:500-3.