A Cross-Sectional Study of Prognostic Importance of Lipid Profile, Plasma Glucose Level, and HbA1C Levels in Patients with Acute Ischemic Stroke

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ABSTRACT

BACKGROUND

In India, stroke is a serious medical condition that frequently results in emergency admissions. People who have a stroke frequently experience higher rates of morbidity, mortality, & reduced quality of life. Among the risk factors for stroke are metabolic disorders like DM (diabetes mellitus) & dyslipidaemia. Acute stroke stress can manifest as hyperglycaemia, which in people without DM history might indicate undiagnosed DM or stress hyperglycaemia.

METHODOLOGY

This cross-sectional study was performed in a teaching hospital over the course of a year. Acute stroke patients who were hospitalized within three days of the stroke episode & who satisfied additional study inclusion requirements were progressively enrolled. Biochemical evaluations & clinically pertinent data were recorded within 3 days of hospitalization. Blood glucose, glycosylated haemoglobin (HbA1c), as well as lipid profile tests were performed at presentation. An irregular lipid profile, stress hyperglycaemia, undiagnosed DM, & a prior history of DM were observed. The statistical tests employed were Chi square as well as Student's t test.

RESULTS

Of the 130 stroke patients who were enrolled, 76 percent satisfied the requirements for ischaemic stroke. Mean age & age range of Study subjects had been 54.4yrs. According to their glycaemic status, the study participants were divided into four groups: stress hyperglycaemia, euglycaemia, DM, & previously undiagnosed diabetes mellitus. In 5th decade of life, stress hyperglycaemia was

common & equally prevalent in people who had haemorrhagic as well as cerebral stroke. Low HDL & increased LDL-C were the most frequent lipid abnormalities.

CONCLUSIONS

Upon detection of an abnormal metabolic environment, there exists a critical opportunity for assertive intervention, which will enhance outcomes for stroke patients. Using blood glucose as well as glycosylated haemoglobin tests, routine screening for hyperglycaemia in stroke patients may reveal previously undetected DM.

KEYWORDS: Cerebrovascular Diseases, Glycosylated Haemoglobin, Stroke, Aneurysms.

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INTRODUCTION

Stroke, often known as cerebrovascular diseases, encompasses a range of prevalent and severe conditions, including ischemic stroke, haemorrhagic stroke, as well as cerebrovascular abnormalities encompassing arteriovenous malformations (AVMs) & intracranial aneurysms. The majority of cerebrovascular disorders present with a sudden occurrence of a localized neurological impairment, as if the patient was unexpectedly affected by a divine force. GHO (Global Health Observatory)[1] reports that stroke is becoming more common and has become second leading cause of death in last ten years.

CVA (cerebrovascular accident), commonly referred to as a stroke, is specified by the abrupt onset of neurological impairment brought on by a localized vascular problem.[2] Definition of stroke is determined by clinical evaluation, with additional evidence provided by laboratory investigations such as brain imaging. The primary vascular incident can encompass cerebral infarction, ICH (intra-cerebral haemorrhage), as well as SAH (subarachnoid haemorrhage).[3]

Stroke is the most common & serious illness affecting the central nervous system. Each year, almost 20 million individuals experience a stroke; out of these, 5 million don't survive.[4] Stroke's annual incidence of in India reported to be 13 per 100,000 & 33 per 100,000 people in previous population-based studies.[5,6] Approximately 20 percent of neurological cases, 4.5 percent of medical cases, & 1 percent of hospital admissions are caused by strokes.[7]

Untreated metabolic disorders can significantly impact the results of individuals who have experienced an acute stroke. Dyslipidemia and hyperglycemia are common metabolic abnormalities observed in stroke patients. Non-diabetic people who have experienced an ischemic stroke often experience hyperglycemia, which can be temporary and caused by the body's rapid stress reaction or may indicate underlying abnormal glucose metabolism. Several studies have shown that individuals who do not survive a stroke tend to have higher average levels of glucose upon admission compared to those who do survive. This highlights the need of screening stroke patients for this significant metabolic abnormality. The findings are supported by references.[8-10] Studies have suggested that acute hyperglycemia is a liable indicator of higher chances of death during hospitalization for ischemic stroke. It also increases the likelihood of stroke survivors experiencing poor functional recovery.[11]

The relationship between hyperglycemia, poor glycaemic control, and dyslipidemia in stroke patients hasn't been extensively evaluated. Therefore, this investigation aimed to assess impact of increased FBS (fasting blood sugar), HbA1c (glycated hemoglobin), & lipid profile on severity & prognosis of patients with cerebral infarction while they are hospitalized.

Aim

To evaluate the effect of glycemic status & lipid profile in patients admitted with acute ischemic stroke & its impact on stroke outcome.

MATERIALS AND METHODS

Study Area

A Prospective, observational, clinical

investigation was performed on patient's age from 30 years to 70 years of both sexes diagnosed with acute ischemic stroke at Department of Medicine, Raipur Institute of Medical Sciences, Raipur, Chhattisgarh for 2 years (May 2022 to May 2024) with a sample size of 130.

Sample size was evaluated employing given formulae:

$n= (Z\alpha/2)^2 * (PQ)/ E^2$

n- Sample size

$Z\alpha/2$–Z value at 5% error (1.96) P – Taken as 44% [107]

Q-1-P

E–Absolute error (taken as 20%)

$$\frac{n – (1.96)^2 * (0.44*0.56)}{(0.2)^2}$$

n- 130 (approx.)

Inclusion Criteria

CT diagnosed patients of age 30 to 70 years, both sexes of cerebral infarction admitted in Raipur Institute of Medical Sciences with parameters.

Exclusion Criteria

1. Traumatic Stroke
2. Intracerebral Haemorrhage
3. Space-occupying lesions present on CT
4. Not consenting patients
5. Previous history of CVA
6. Chronic debilitating disease

Methodology

Study began after approval from Institutional ethical committee. Patients were chosen according to inclusion & exclusion criteria along with provided informed consent. A comprehensive history obtained from all patients, was accompanied through a comprehensive clinical evaluation.

RBS was assessed at time of admission. The patient's FBS level, HbA1c, as well as fasting lipid profile were subsequently assessed. Severity of a stroke is assessed employing NIHSS (National Institute of Health Stroke Scale) upon admission & at discharge. Outcome was observed as survived or died. Association among subsequent variables was assessed:

1. Patient's diabetic status, stroke severity, & Outcome
2. HbA1c; stroke severity& Outcome
3. Lipid profile; stroke severity &Outcome

RESULTS

Nearly one-third (36.9 percent) of the population was over 60, & mean age of stroke cases was 54.34 years. Proportion of individuals under 40 was mere 16.9%.

Stroke cases were found to be more common in men (54.6 percent) than women (45.4 percent).

NIHSS Score at Admission	**N**	**%**
Mild (1-4)	17	13.1%
Mod (5-15)	75	57.7%
Severe (16-20)	18	13.8%
Very Severe (>20)	20	15.4%
Total	130	100.0%
Table 1: Distribution of study groups as per severity of stroke		

According to the NIHSS Score, upon admission, 13.1 percent of patients had mild stroke, 71.5 percent had moderate to severe stroke, & 15.4 percent had severe stroke.

Outcome	**N**	**%**
Survived	119	91.5%
Died	11	8.5%
Total	130	100.0%
Table 2: Distribution of study groups as per outcome		

Mortality rate observed in ischemic stroke cases in present study was 8.5%.

NIHSS Score at Discharge	N	%
Mild(1-4)	36	33.0%
Mod(5-15)	83	69.7%
Severe(16-20)	0	0.0%
Very Severe(>20)	0	0.0%
Total	120	100.0%

Table 3: Distribution of study groups as per NIHSS score at discharge

At discharge, the severity of symptoms was mild in 33% of the survived cases while it was moderate in remaining 69.7% cases.

Blood Sugar Indices	Outcome	N	Mean	SD	p-value
RBS (mg %)	Survived	119	156.31	28.50	<0.01
	Died	11	189.73	46.26	
FBS (mg %)	Survived	119	128.30	25.89	0.79
	Died	11	128.64	33.78	
HbA1c (%)	Survived	119	6.25	1.26	0.024
	Died	11	7.11	1.04	

Table 4: Comparison of blood sugar indices between survivors and non-survivors

Mean random blood sugar (189.73 vs 156.31; p<0.01) and HbA1c values (7.11 vs 6.25%;p-0.024) were significantly higher among non-survivors in comparison to survivors.

Lipid Profile	Group	N	Mean	SD	p-value
TG (mg %)	Survived	119	128.98	66.78	0.217
	Died	11	154.37	33.68	
TC (mg %)	Survived	119	157.75	35.43	<0.01
	Died	11	188.98	38.74	
HDL (mg %)	Survived	119	47.39	9.80	0.039
	Died	11	41.02	7.72	
LDL (mg %)	Survived	119	85.30	27.46	0.187
	Died	11	96.81	26.69	
VLDL (mg %)	Survived	119	28.79	9.32	<0.01
	Died	11	41.53	15.76	
HDL/ LDL	Survived	119	0.63	0.29	0.049
	Died	11	0.46	0.17	

Table 5: Comparison of lipid profile between survivors and non-survivors

Among lipid profile, mean total cholesterol (188.98 vs 157.75 mg%;p<0.01) & VLDL levels (41.53 vs 28.79;p<0.01) were significantly higher while mean HDL levels (41.02 vs 47.39; p-0.039) were significantly lower among non-survivors.

Pearson co-relation		
NIHSS Score(admission)	**r- value**	**p-value**
RBS	0.24	<0.01
FBS	0.04	0.65
HbA1c	0.26	<0.01

TG	0.05	0.56
TC	0.21	0.02
HDL	-0.34	<0.01
LDL	0.09	0.31
VLDL	0.29	<0.01
HDL/ LDL	-0.21	0.02

Table 6: Correlation analysis of NIHSS score with blood sugar indices and lipid profile

Stroke severity as determined by the NIHSS score had been positively correlated with RBS, HbA1c, total cholesterol, VLDL, & HDL/LDL, but inversely correlated with HDL levels($p<0.05$).

Logistic Regression: Mortality (Y/N)								
Variables	**B**	**S.E.**	**Wald**	**df**	**p- value**	**Odds Ratio**	**95% C.I. for EXP (B)**	
							Lower	**Upper**
RBS	0.028	0.011	5.882	1	0.02	1.028	1.005	1.051
HbA1c	-0.232	0.344	0.453	1	0.501	0.793	0.404	1.556
TC	0.016	0.012	3.766	1	0.04	1.017	1.031	1.042
HDL	-0.035	0.046	0.578	1	0.447	0.965	0.881	1.057
VLDL	0.064	0.038	2.919	1	0.088	1.066	0.991	1.148

Table 7: Regression analysis for predictors of mortality

On multi-variate regression analysis, random blood sugar and total cholesterol levels at admission were observed to be significant predictors of poor outcome among ischemic stroke cases ($p<0.05$).

Area Under the Curve					
Test Result Variable (s)	**Area**	**SE**	**p-value**	**Asymptotic 95% Confidence Interval**	
				Lower Bound	**Upper Bound**
RBS	0.707	0.11	**0.02**	0.492	0.922
TC	0.735	0.083	**0.01**	0.572	0.897

Ideal Cut-off	**Sensitivity**	**Specificity**
RBS >160 mg%	72.7%	60.6%
TC>170 mg%	81.8%	67.9%

Table 8: ROC Curve analysis for predictors of mortality and optimal cut-off values

For RBS levels, the ideal cut-off was >160 mg% with a sensitivity & specificity of 72.7 percent & 60.6 percent, according to ROC analysis. For TC levels, ideal cut-off was >170mg% with sensitivity & specificity of 81.8% & 67.9%, respectively.

DISCUSSION

This investigation is a prospective observational study that was performed in a hospital facility. Its goal is to evaluate how a patient's lipid profile and glycemic state affect their outcome after suffering an acute ischemic stroke. Study comprised of 130 individuals, ranging in age from 30-70years, of both genders, who were diagnosed with acute ischemic stroke. RBS had been assessed at admission. Subsequently, the patient's FBS Level, Fasting lipid profile, & HbA1c were measured. Severity of a stroke is assessed employing NIHSS during admission and at time of discharge.

Upon admission, NIHSS Score indicated that 13.1% of cases exhibited mild severity, 71.5% of cases showed moderate to severe grade stroke, and 15.4% of cases displayed severe stroke. The study found that the mortality rate among instances of ischemic stroke was 8.5%.

Harthi HA et al.[12] identified a death

rate of 7.7% in patients with ischemic stroke in their research. Vaidya CV et al. reported a death rate of 5.6% for cases of ischemic stroke, whereas Bhutta MI et al,[13] found that the mortality rate during hospital stay was 5.3%, and the post-discharge mortality rate recorded 3.4%. The overall mortality rate recorded 8.5%.

Non-survivors had substantially higher mean random blood sugar levels (189.73 vs 156.31; p<0.01) & HbA1c values (7.11 vs 6.25%;p-0.024) compared to survivors. An important and positive relationship was seen between severity of Stroke, as evaluated by NIHSS score, and levels of RBS and HbA1c (p<0.05). In the study of multi-variate regression, it was shown that random blood sugar levels were significant predictors of poor outcome in instances of ischemic stroke (p<0.05). During the ROC analysis, it was determined that the ideal threshold for RBS levels was more than 160 mg% with sensitivity of 72.7% & specificity of 60.6%.

The investigation conducted by El-Gendy, H.A et al,[14] demonstrated that patients having elevated RBS (random blood sugar) upon admission exhibit notably higher values for median NIHSS score as well as median duration of hospital stay. Strong connections among stress-induced high blood sugar levels and the likelihood of dying within 30 days (p<0.001), as well as the requirement for mechanical breathing (p<0.001) as well as vasopressors (p<0.001) were there. 24-hour RBS levels, with a cut-off greater than 145 mg/dl, demonstrated a high level of accuracy in predicting 30-day mortality, as shown by an area under the curve of 0.809. Lee KJ et al,[15] examined a cohort of 2595 individuals diagnosed with acute ischemic stroke. After accounting for variables, fasting blood sugar (FBS) showed significant association with severity of the first stroke (P<0.001), while glycated haemoglobin (HbA1c) did not show a significant association (P=0.16). Nevertheless, a significant correlation was seen between FBS and HbA1c in relation to the severity of the first stroke (P<0.001). Huang ZX et al,[16] sought to see whether correlation among blood glucose levels & unfavourable outcomes in individuals with ischemic stroke was there. The multivariate regression analysis revealed a substantial independent association among admission blood glucose level & poor outcome (P<0.001). With a 100 percent sensitivity & 53 percent specificity, an entrance blood glucose level >107.1mg/dL considered a strong predictor for poor outcome. Roquer J et al,[17] sought to assess the impact of both HbA1c & first glucose test values on predicting death during a three-month period. Diabetic patients with good glycemic control had an unadjusted relative risk of 3-month mortality of 6.10, those with poor glycemic control of 1.44, & those without diabetes had an unadjusted relative risk of 3.76 for those with glucose level of 200mg/dl or higher. Glycemia cut-offs that showed the strongest correlation with mortality rose when the PGC (Pancreatic Glucose Control) dropped. Specifically, the cut-off was 107mg/dl for non-diabetic patients, 152mg/dl for diabetic patients with excellent PGC, and 229mg/dl for diabetic patients with poor PGC. The level of glucose in the blood was connected to severity of stroke in individuals without diabetes & diabetic patients who had good glucose control. However, this correlation was not observed in diabetic patients having poor glucose control. The study found that combining the measurement of HbA1c with the first recorded glucose value is a viable method for categorizing the risk of death. Hu GC et al. sought to assess the correlation between early glucose levels & mortality among individuals facing acute ischemic stroke. Individuals in highest quartile of initial glucose level exhibited substantial relation with all-cause mortality (hazard ratio [HR], 2.18; 95percent CI[confidence interval], 1.36-3.48) as well as cardiovascular mortality (HR, 1.91; 95percent CI, 1.01-3.61) when compared to those in the lowest quartile. Study investigated by Wang H et al. observed that 30.9% of the patients had intermediate HbA1c levels, whereas 31.6% had high HbA1c levels. After controlling for potential confounding factors, both patients in the high HbA1c level group (P = .013) and intermediate HbA1c level group (P = .048) exhibited substantially greater rates of poor neurological outcomes

compared to the group in the low HbA1c level.

In summary, there was a significant correlation seen between unfavorable prognosis in stroke patients and elevated glucose levels at admission, inadequate management of blood sugar levels, & lipid indicators high-density lipoprotein cholesterol, encompassing total cholesterol, as well as very low-density lipoprotein cholesterol. However, after analyzing the data using a multivariate model, it was determined that admission hyperglycemia and high total cholesterol levels were the only factors that significantly predicted death. Consequently, the study determined that elevated total cholesterol (TC) levels above 170 mg% and stress-induced high blood sugar levels beyond 160 mg% at admission had a significant part in predicting acute stroke patient's outcome and were linked to less favorable results.

CONCLUSION

Present study observed that high admission glucose levels, poor glycemic control and lipid parameters like TC, HDL and VLDL were significantly associated with poor outcome in stroke patients. On multi-variate analysis, however admission glucose and high TC levels were observed as only significant predictors of mortality. Study thus concludes that high TC (>170 mg%) and stress hyper glycaemia (>160 mg%) at admission serve as prognostic role & associate with less-favorable outcomes of individuals facing acute stroke.

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