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A Clinical Profile In Acute Ischemic Stroke With Special Reference To Vitamin D Level And Glycaemic Status And Their Impact On The Outcome

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Abstract

Introduction: Vitamin D deficiency leads to systemic hypertension, which may increase stroke risk. Admission hyperglycaemia usually correlates with increased infarct size on admission and poor clinical outcome. This study was performed to assess the clinical profile of patients in acute ischaemic stroke with special reference to Vitamin D levels and glycaemic status and their impact on the outcome.

Material and Methods: An observational study was conducted in a tertiary care centre where 60 patients aged 18 and above with symptoms of ischaemic stroke were enrolled. Capillary blood glucose levels and neuroimaging findings at admission were noted. Further imaging was done between the 3rd and 7th days. Analysis was done using SPSS version 19.

Results: Most of the patients were in the aged between 46 to 65. Hypertension was the most common comorbidity (88%), followed by Diabetes Mellitus (31%). Most patients presented with a facial weakness (33.3%) and an altered sensorium (23%). Left hemiparesis was the most common motor weakness (38.3%). On MRI Brain, the anterior territory was most involved (58%). The most common etiology of stroke was large artery atherosclerosis (38%). Vitamin D levels were insufficient in 18.3% of the study population and deficient in 10%. With respect to neuroimaging, the euglycemic patients on admission had a mean change in infarct volume of 10.6 cm^3. In contrast, the hyperglycaemic patients on admission had a mean change in infarct volume of 15.4 cm^3.

Conclusion: Hyperglycaemia is associated with a poorer prognosis as compared to normoglycemia on admission. Vitamin D deficiency has an independent correlation with ischaemic stroke.

Keywords: Ischaemic stroke, vitamin D levels, hyperglycemia, hypertension

Introduction

A stroke, or cerebrovascular accident, is an abrupt onset of a neurologic deficit attributable to a focal vascular cause. Stroke remains one of the leading causes of mortality worldwide, even though diagnostic tools have improved vastly. Cerebrovascular and cardiovascular disease constitutes a large proportion of such cases. Hypertension is one of the significant risk factors for stroke. Other risk factors include smoking, diabetes mellitus, obesity, dyslipidemia, history of stroke, TIA, or atrial fibrillation[1]. Acute ischaemic stroke (AIS) is defined as an episode of neurological dysfunction caused by focal cell death of the brain, spine, or retina due to ischemia based on: (a) pathologic, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or (b) clinical evidence of cerebral, spinal cord, or retinal focal ischaemic injury based on symptoms persisting for 24 or more hours or until death, and other causes excluded[2]. Vitamin D plays a crucial role in maintaining homeostasis in the body. Other functions of Vitamin D include decreasing renin-angiotensin-aldosterone, anti-inflammatory, anti-atherosclerotic activity, and reducing vascular calcification. Another part includes decreasing the protein excretion in urine. It also seems to have neuro-protection activity, like insulin-like growth factor-1 synthesis.Vitamin D deficiency leads to systemic hypertension, which may lead to an increased risk of stroke. Acute hyperglycaemic response to stress has been recognized since Claude Bernard's observations more than a century ago. Stress hyperglycaemia or in-hospital hyperglycaemia is any blood glucose value above 140 mg/dl. Stroke, a form of stress, causes stimulation of the HPA axis, leading to stress hyperglycaemia. Hyperglycaemia following ischaemic stroke is common, irrespective of the diabetic status and regardless of the period between stroke and glucose estimation. Admission hyperglycaemia usually correlates with increased infarct size on admission and poor clinical outcome. This study was to study the clinical profile in ischaemic stroke patients with respect to clinical presentation, risk factors, comorbidities, classification based on circulation involved, area of involvement, diet, personal history. We also wanted to assess the vitamin D levels in patients admitted for ischemic stroke and to find a correlation between glycaemic status and the extent of stroke from the time of admission to the (3-7th day) of hospital stay by using Multimodal CT/MRI Brain Scans.

Material and methods

This observational study was conducted in the Department of Medicine, Gauhati Medical College and Hospital, Assam, between June 2020 and May 2021. After obtaining approval from the institutional ethics committee, patients fulfilling the inclusion criteria were enrolled.

Inclusion criteria

1. Age of 18 years and above
2. Patients getting admitted within 24 hours of the onset of symptoms of ischaemic stroke.
3. Patients willing to participate in the study

Exclusion criteria

1. Patients with hemorrhagic stroke, tumors, abscesses, subarachnoid hemorrhage
2. Patients selected for thrombolytic therapy
3. History of previous ischemic stroke or Transient ischemic attack in the past
4. Cortical venous thrombosis

A total of 60 patients were enrolled. History and clinical examination findings were recorded in a structured proforma. NIHSS scale assessment was done at admission. The patient's glycemic status was assessed by measuring the capillary blood glucose (CBG) levels at admission, irrespective of the prior meal status. The fasting and post-prandial blood sugar levels were measured after the hospital stay. During admission, patients with ischemic stroke on initial CT Scan and without evidence of hemorrhage were subjected to MRI Brain/MR Angiography/MR Venography within 24 hours of the onset of the neurological deficit. Then a repeat MRI Brain/MR Angiography/MR Venography was done between 3-7th day. The ischemic stroke volume was assessed using Diffusion-weighted imaging (DWI). The volume was calculated by using the product of "a," b," and" c" divided by 2, where "a" stands for the maximum length of the infarct, "b" stands for the maximum breadth of the infarct, "c" stands for the height of infarct seen in Diffusion-weighted images. The volume of the infarct on day one, and the volume of the infarct on days 3-7 are calculated, and the difference between these two volumes measures the rise in the volume of the infarct. These three infarct volumes were correlated with the capillary blood glucose (CBG) obtained during the admission. Vitamin D levels were assessed using the Competitive immunoassay technique during the period of stay in the hospital. Then the patients were classified based on vitamin D levels into normal (30-100 ng/ml), insufficiency (10-30 ng/ml), and the deficiency (< 10 ng/ml). Statistical analysis was carried out using SPSS version 19.0 (IBM SPSS, US). Results on continuous measurements are summarized as mean and Standard deviation (min-max), and results on categorical measurements are presented in numbers (%). Significance is assessed at a 5 % level of significance.

Results

The age and gender distribution showed males were highest in the age group of 46 to 65 years that is 62.8%. Females were also highest in the same group with 56% population in the age group of 46 to 65 yrs.

Lowest percentage of population was in the age group above 75 years. **The mean age of the study population is 57.57±12.08 years.** Hypertension was seen in majority (88.30 %) of the study population, followed by Diabetes mellitus (31.70%). CAD was seen in 8.30%. Renal disease was seen in 3.30%. **(Table 1).**

Table 1: Various comorbidities and risk factors in study population (n=60)

Comorbidity	**No. of patients**
Diabetes Mellitus	**19(31.7%)**
Hypertension	**53(88.3%)**
Heart Disease	**5 (8.3%)**
Renal Disease	**2(3.30%)**
Other Causes	**1(1.70%)**

In the study population, 30% of patients were smokers, and 26.7% had a history of alcohol dependence. A large portion of the patients was non-vegetarians/mixed (61.70%). 38.30% of patients were vegetarian. The mean BMI of the study population was 24.65 ± 1.74 kg/m2. 33.3% of the study population was overweight. The blood pressure of all patients was recorded during their initial hospitalization. The mean SBP was 145.33 ± 12.18 mm of Hg, and the mean DBP was 92.97± 10.27mm of Hg. The SBP was higher than baseline in 86.7%, while DBP was higher in 88.3% of the patients. More than half of the patients were alert 48.30% (29), 28.30% were confused, and 23.30% (14) were comatose. Around 33% of the study population presented with facial weakness, followed by altered sensorium in 23.30%. Headache, seizures, speech and language, and vomiting were seen in 10% of the study population. The clinical presentation recorded was the primary presentation with which the patient presented to the hospital. **(Table 2)**

Table 2: Clinical presentation in the study population

Clinical Manifestation	**No. of patients**
Altered sensorium	**14(23.3%)**
Facial weakness	**14(23.3%)**
Headache	**10(16.7%)**
Seizures	**9(15%)**
Speech and language	**7(11.7%)**
Vomiting	**6(10%)**
Total	**60**

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Motor weakness

The pattern of motor weakness in our study population was documented. 38.30% of patients had left-sided hemiparesis, 13.30% presented with complete left-sided hemiplegia while 20% of patients had right hemiparesis, and 6.7% had right-sided hemiplegia. The motor weakness which was documented was based on the presenting weakness.

Infarct region

In our study 32 patients had Cortical (53.30%) involvement, 21 patients had Subcortical (35%) involvement and 7 patients had lacunar Infarct on MRI Brain.

Arterial territory

Arterial territory showed anterior territory involvement in half of the patients (58.3%), followed by posterior territory (30%) while 11.6% had multiple territory involvement on MRI Brain

TOAST classification of ischaemic stroke

The most common etiology of stroke according to TOAST classification was large artery atherosclerosis which included 38.3% of the study population while cardio-embolism was seen in 8.30% of the study population. **(Table 3)**

Table 3: Etiological profile of ischaemic stroke according to TOAST classification

Etiology	**No. of patients**
Cardio-embolism	**5(8.3%)**
Large artery atherosclerosis	**23(38.3%)**
Small vessel occlusion	**9(15%)**
Stroke of undetermined Etiology	**14(23.3%)**
Stroke of other determined Etiology	**9(15%)**
Total	**60**

Vitamin D levels

Around 72% of patients in the study were found to have the vitamin D in the normal range. About 18% were found to have insufficiency and 10% had deficiency. **(Table 4)**

Table 4: Vitamin D levels in the study population

Vitamin D3 Levels	**No. of patients**

Deficiency <10 ng/ml	**6(10%)**
Insufficiency 10-30 ng/ml	**11(18.3%)**
Normal 30-100 ng/ml	**43(71.6%)**
Total	**60**

CBG status on admission

On admission, the CBG of the study population was measured in which 58.33% of patients had CBG <140, 57.14% were male, and 42.26% were female. 41.77% of patients had CBG >=140, of which 60% were male and 40% female. In the study population, the mean NIHSS Score among patients with euglycemia on admission was 11.49, whereas 19.72 was among patients with hyperglycaemia on admission. T-test was used to establish a relation between the CBG status on admission and the NIHSS Score on admission. The p-value came out to be 0.0001, which is highly significant, indicating that patients with higher CBG levels on admission had a higher NIHSS Score, thus having a poorer prognosis compared to their euglycemic counterparts. **(Table 5)**

Table 5: Comparison of on admission CBG with NIHSS Score on admission

CBG on admission (mg/dl)	No. of Patients	Mean NIHSS Score	Standard Deviation	t test value of equality of means	p value
<140	35	11.49	2.89392	-9.589	0.0001 (Highly significant)
>=140	25	19.72	3.75855		

Infarct volume on day 1 in comparison with CBG on admission

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In the study population, patients with euglycemic status on admission had a mean infarct volume of 13.77 cm3 (<24hrs), whereas patients with hyperglycaemic status on admission had a mean infarct volume of 21.28 cm3 (<24hrs).

Infarct volume on days 3 to 7 in comparison to CBG status on admission

In the study population, patients with euglycemic status on admission had a mean infarct volume of 24.06 cm3 (3 to 7 days). In contrast, patients with hyperglycaemic status on admission had a mean infarct volume of 36.04 cm3 (3 to 7 days).

Change in infarct volume in comparison with CBG status on admission

In the study population, the euglycemic patients on admission had a mean change in infarct volume between day 1 and day 3 to 7 of 10.6 cm3. In contrast, hyperglycaemic patients on admission had a mean change in infarct volume between the same period of 15.4 cm3. **In the study population comparison of the change in infarct volume between day 1 and day 3 to 7 in patients who had euglycemia and hyperglycaemia** on admission showed a higher risk of progression of the stroke in patients with hyperglycaemia on admission as compared to their euglycemic counterparts with a t-test value of -3.177 and p-value of 0.002 which suggests that there is a significant relation between on admission hyperglycaemia and subsequent progression of stroke. **(Table 6).**

Table 6: Comparison of change in infarct volume with CBG status on admission

CBG (in mg/dl)	No. of Patients	Mean Infarct Volume (cm^3)	Standard Deviation	t test for equality of means	p value
<140	**35**	**10.6**	**5.0944**	**-3.177**	**0.002**
>=140	**25**	**15.4**	**6.60808**		

Discussion

In our study, 33.3% presented with facial weakness, 23.3% presented with altered sensorium, and 13.3% presented with headache. Seizures, headaches, and speech and language abnormalities were seen in 10% of patients each. In a similar study by Sylaja et al., 7% had convulsions, and 63% had a facial weakness[3]. The pattern of motor weakness in our study population showed that 38.3% had left hemiparesis, 13.3% had left-sided hemiplegia while 20% had right-side hemiparesis, and 5% had right-sided hemiplegia. Sylaja et al showed 42% had right-sided weakness and 46% had a left-side weakness. In a study by Vaidya C.V. et al, altered sensorium was present in 13.1% of cases. The speech was involved in 25.1% of cases[4]. A study by Khuraijam T. et al., showed middle cerebral artery involvement in 68% of the study population[5]. A study by Chung J.W. et al, on “vascular territory of ischemic stroke lesions diagnosed by diffusion-weighted imaging” where the middle cerebral artery territory was involved in 65% of cases[6].

Vitamin D levels

Selim F.O. et al. found vitamin D deficiency to be an independent risk factor for stroke outcome at levels <17 ng/ml and the best predictor for stroke severity at levels <9ng/ml[7]. In a study by Alfieri D.F. et al, 77.3% of the 168 acute ischemic stroke patients had vitamin D deficiency[8]. In a study by Manouchehri N. et al., mild, moderate, and severe Vitamin D deficiency were observed in 10.8%, 32.4%, 8.1% vs. 34.3%, 31.5%, 9.5% of small vessel and large vessel group, respectively. 21.7% of the controls were Vitamin D deficient. Vitamin D deficiency was significantly associated with higher risk for ischaemic stroke[9].

Hyperglycaemia and stroke

Our study defined stress hyperglycemia as blood glucose levels >=140 mg/dl. In Pan et al., out of the 999 patients followed up for 12 months after acute ischaemic stroke, there were 105 (10.9%) recurrent strokes and 76 (7.6%) death at 12 months[10]. Patients with a higher glucose-to-HbA1c ratio were associated with an elevated risk of stroke recurrence and ended at 12 months. Janghorbani M. et al., noted a stronger association between hyperglycaemia and stroke in women than in men[11]. In this study, 40% had hyperglycaemia on admission, while the remaining 60% were Euglycemic on admission. Of this, 37.93% of males were hyperglycaemic, and 42.85% of females had hyperglycaemia on admission. In Shimoyama T. et al., the hyperglycemia cut-off was 140 mg/dl. Of the 375 patients enrolled in the study[12]. A total of 143 patients (38.1%) were classified into the hyperglycaemic group and 230 patients (61.9%) into the non-hyperglycaemic group. The initial infarct volume measured amongst the hyperglycaemic group was 17.2 ml compared to 12.2 ml amongst the nonhyperglycaemic group. The infarct volume growth in the hyperglycaemic group was 28.2 ml compared to 16.3 ml in the nonhyperglycaemic group. The baseline NIHSS Score was 16 in the hyperglycaemic group and 15 in the nonhyperglycaemic group. 30.1% of patients in the hyperglycaemic group had neurological deterioration compared to 17.2% of patients in the nonhyperglycaemic group. In our study, the initial infarct volume in the hyperglycaemic group was 21.28 cm3, and the initial infarct volume in the euglycaemic group was 13.77 cm3. The infarct volume between days 3 to 7 in the hyperglycaemic group was 36.04cm3, and it was 24.06cm3in the euglycaemic group. The change in infarct volume in the hyperglycaemic group was 15.4cm3 and 10.6cm3 in the euglycaemic group. Statistical analysis comparing the change in infarct volume with the glycaemic status on admission showed a p-value of 0.002, suggesting a significant relation between on-admission hyperglycaemic status and subsequent progression of stroke. In our study, the mean NIHSS Score among patients with hyperglycaemia on admission was 19.72 compared to 11.49 in the euglycaemic group. The relation between on-admission CBG status and NIHSS Score resulted in a p-value of 0.0001, thus suggesting that patients with hyperglycaemia on admission had a higher NIHSS Score and, therefore, a poorer prognosis as compared to their euglycaemic counterparts.

Conclusion

Cerebrovascular accidents are a significant health problem throughout India because of their morbidity and mortality.

Based on the results and the methodology employed, we have concluded that:

1. Hyperglycaemia on admission is associated with greater infarct volume and a more significant increase in the infarct volume in the subsequent days compared to normoglycemia on admission.
2. Hyperglycaemia on admission is associated with a higher NIHSS score and thus associated with a poorer prognosis compared to normoglycemia on admission.
3. Vitamin D deficiency appears to have an independent correlation with ischaemic stroke.

However, the limitations of this study are that the study is small sample-sized and Institutional research carried out in a short time. Hence it is difficult to draw a definite inference. Therefore, prospective, epidemiological, and analytical studies are required to arrive at a definite conclusion. Also, the management of hyperglycaemia and stroke per se was not standardized.

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