A STUDY ON THE CLINICAL CORRELATION OF THE GLYCAEMIC STATUS AND STROKE EVENTS AMONG STROKE PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND AND OBJECTIVES

Stroke is a common cause of chronic debilitating disease as a result of the vascular related effect of certain part of the brain. Also the mortality due to the nature of stroke either Intracerebral Haemorrhage (ICH) or Cerebral Infarction (Ischaemic stroke) vary, the earlier causing more fatality. The risk factors of the ICH or the Ischaemic stroke vary to certain degree. Glycaemic state of stroke patients affects the outcome of them. It is of importance to establish clinical correlation of the glycaemic status of the stroke patients with the type and extent of the lesion documented by Computerised Tomography (CT) scan of brain for development of preventive measures and clinical management of such patients for better outcome. Hence, this study was conducted among stroke patients who were admitted in Medicine wards, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Porompat, Manipur.

DATA AND METHODS

A study of stroke cases was undertaken in patients who were admitted to Medicine wards, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Porompat, Manipur from January 2011 till December 2014. All the patients were investigated with CT scan brain, Blood sugar along with Glycosylated Haemoglobin (HbA_{1C}) besides other routine tests and recorded.

RESULT

Out of the 200 stroke patients registered in 48 months, 120 patients were having hyperglycaemia. All the patients with stress hyperglycaemia were haemorrhagic. 85.71% of the cases among known diabetes were also haemorrhagic.

CONCLUSION

Glycaemic state of patients presented in stroke gives a picture of clinical difference. The size of the lesion measured by CT scan of brain also varies among different types of hyperglycaemia and the prognosis of the patients and showed that those patients with higher glucose level had haemorrhagic lesions with bigger size and had higher mortality rate. The deteriorating glucose tolerance with age also contributes to the increased incidence of stroke with age. The newly diagnosed diabetics also had higher mortality rate and it indicates the importance of early detection of diabetes and stress hyperglycaemia and suggested the needful timely management of the glycaemic state of the patient to prevent or reduce the incidence of hyperglycaemia and related stroke.

KEYWORDS

Stress Hyperglycaemia, Infarct, Haemorrhagic Stroke, Glycosylated Haemoglobin.

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INTRODUCTION: The definition of stroke in clinical setting has been known as, "a stroke or cerebrovascular accident is defined as the abrupt onset of neurological deficit which is attributable to a focal vascular cause", the laboratory studies including brain imaging are used to support the diagnosis.[1] 11.3% cases of stroke gave the history of diabetes when studied in cases of stroke population.[2] There is increased risk of stroke in diabetes and increased prevalence rate of stroke in diabetes as compared to several populations.[3] Patients with stress hyperglycaemia as well as diabetes have severe stroke with poor prognosis. The mortality rate of stroke in diabetics is twice that of the general population.[4] Glucose tolerance also deteriorates with age.[5] Blood glucose is a significant predictor of death as predicted by multivariate study.[6]

Among the macrovascular complications due to diabetes, stroke is the most common one and causes morbidity and mortality among people with diabetes.[7] Stress hyperglycaemia after acute stroke is a stress responsive hyperglycaemia found in non-diabetics. Hyperglycaemia found among non-diabetic patients reflects more severe neurological damage.[8]

Hence, the present study has been designed to objectively assess the glycaemic status of the patients and clinical correlation of the glycaemic states of the patients with the type and size of the stroke lesion.

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Even mild hyperglycaemia (6.6 mmol/L) may result in increased brain damage and delayed recovery. Insulin improved the functional recovery from the brain ischaemia probably because of its effect on the glucose and lactate level (a study in rats).[9]

MATERIALS AND METHODS: A total of 200 stroke cases in the age of 30-75 years during a period from January 2011 to December 2014, admitted in Medicine wards of JNIMS Hospital, Impala East, underwent thorough clinical examination. CT scan was performed in all the cases within 3 days of onset of symptoms to confirm the diagnosis and ascertain the type of stroke (ischaemic/haemorrhagic) and size of stroke (small, medium or large). The small-sized stroke was defined as 5 mm in diameter and not visible in more than two adjacent slices; large-sized stroke was defined as 10 mm in diameter or involving one complete vascular territory. The medium was in between small and large.

Inclusion Criteria: All patients were admitted within 72 hours after onset of stroke.

Exclusion Criteria:

1. The other causes that present with stroke like syndromes i.e., subdural haematoma, epilepsy, sub-arachnoid haemorrhage.
2. Any prior neurological disability from previous stroke or other diseases.

The plasma venous glucose level was taken within 24 hours after admission for every patient. Glycosylated haemoglobin (HbA_{1C}) was done to ascertain whether it was stress diabetes or newly diagnosed diabetes.

The patient with raised blood glucose on admission and normal HbA_{1C} without any prior history of diabetes was considered as having stress hyperglycaemia. The patients were divided into 4 groups: Euglycaemic, patient with no history of diabetes and having normal blood glucose and normal HbA_{1C}; patients with stress hyperglycaemia (no history of diabetes with normal HbA_{1C} but raised blood sugar at admission); newly diagnosed diabetic (no history of diabetes, HbA_{1C} greater than normal) and lastly, known diabetic patients.

Glycosylated Haemoglobin (HbA_{1C}) micro-column determination.

Interpretation of HbA_{1C} level	Degree of Glucose Control
>10	Poor
9-10%	Fair
8-9%	Good
7-8%	Excellent
6-7%	Near-normal glycaemia
<6%	Non-diabetic

RESULTS: Out of the 200 patients, 70 cases (35%) of stroke occurred in the age group of 51-60 years; another 58 cases (29%) occurred in the age group of 61-70 years (Table 1). This shows that the commonest age group is in the age group 50–60 years as detected by our study.

There were 80 cases of stroke with euglycaemia, 120 cases of stroke with hyperglycaemia including stress hyperglycaemia, newly detected diabetes and known diabetes. Out of these patients with hyperglycaemia, 56 cases (28%) of all stroke cases occurred in known diabetes patients, 44 (22%) occurred in new diabetes patients and 20 (10%) occurred in stress hyperglycaemia. This shows that stroke occurs mostly in known diabetes (table 2).

Seventy-five percent (75%) of cases of strokes in the euglycaemic group presented as ischaemia (60 out of 80) and twenty cases in the same group occurred as haemorrhage (20 out of 60). All strokes with stress hyperglycaemia were haemorrhagic (100%), and also all the strokes occurred in the newly diagnosed diabetic group were haemorrhagic (100%). 85.71% of strokes in the known diabetic group were haemorrhagic (48 out of 56). This shows that haemorrhagic strokes occurred among the hyperglycaemic patients, maximum being among the stress hyperglycaemia and newly detected diabetes (Table–3).

Age Groups in Years	No. of Patients
Up to 40	12(6%)
41 – 50	30(15%)
51 – 60	70(35%)
61 – 70	58(29%)
Above 70	30(15%)
Total cases	**200(100%)**

Table 1: Age wise Distribution of Patients

Glycaemic status	No. of cases	Percentage
Euglycaemic	80	40%
Stress Hyperglycaemic	20	10%
New diabetic	44	22%
Known diabetic	56	28%
Total	**200**	**100%**

Table 2: Classification of Patients according to Glycaemic Status

Glycaemic status	Ischaemia No.	%	Haemorrhage No.	%
Euglycaemic	60	75%	20	25%
Stress Hyperglycaemic	0	0%	20	100%
New diabetic	0	0%	44	100%
Known diabetic	8	14.28%	48	85.71%
Total	68		132	

Table 3: Types of Stroke in different Glycaemic States

Table 4. shows the relation of the size of stroke and glycaemic status of the patients. Large-sized stroke (> 10 mm) occurred in only in known diabetics (85.71%), newly detected diabetic (100%) and stress hyperglycaemia (100%). Small-sized strokes (0 to 5 mm) occur only in euglycaemic patients (50%), medium-sized stroke (>5 to 10 mm) occurs in euglycaemic (50%) and known diabetics (14.28%). This table shows that large-sized strokes (>10 mm) is common only in hyperglycaemic patients, maximum (100%) being in hyperglycaemia and known diabetes.

Size of lesion (CT) at different glycaemic states						
Glycaemic states	**Small 0-5 mm**		**Medium >5-10 mm**		**Large >10 mm**	
Euglycaemia	40	50%	40	50%	Nil	Nil
Stress hyperglycaemia	0	0%	0	0%	20	100%
Newly detected diabetes	0	0%	0	0%	44	100%
Known diabetes	0	0%	8	14.28%	48	85.71%

Table 4: Size of Lesion (by CT) at different Glycaemic States

All the stress hyperglycaemic patients, newly detected diabetics, had large-sized haemorrhagic lesions>10 mm diameter and 83.3% of the known diabetics had large-sized haemorrhagic lesions (>10 mm diameter). The small-sized lesions (up to 5 mm diameter) occurred in only euglycaemic patients (40%).

Medium-sized lesions (>5 mm up to 10 mm) were present only among euglycaemic (40%) and 16.7% of known diabetics (Table 4).

The clinical outcome of the patients is shown in Table 5. A poor clinical outcome was more in stress hyperglycaemic patients, newly detected diabetics and known diabetics. All the stroke patients in the newly detected diabetics expired (100% mortality rate), and 66.7% of all the known diabetics left hospital as their condition deteriorated. Thus, a positive correlation is ultimately established between type, size of stroke and glycaemic state.

Clinical outcome	**Euglycaemic**		**Stress hyperglycaemic**		**Newly detected diabetic**		**Known diabetic**	
Improvement	8	10%	12	60%	40	90.91%	40	42.85%
Death	0	0%	8	40%	4	9.09%	12	21.42%
Left hospital	24	30%	0	0%	0	0%	4	7.14%

Table 5: Clinical Outcome of Patients

DISCUSSION: According to this study, there is higher prevalence of diabetes in patients with acute stroke in the age group of 51-60 years, which is in agreement with the findings of Topic et al.[9] However, Sharma et al reported maximum prevalence among 41-50 years of age group. The majority of the strokes were ischaemic and were mainly in the euglycaemic patients.

The present study shows a high prevalence of known diabetics presenting with acute stroke (24%). Gracy et al found the prevalence of stroke in known diabetics as 8.5%[10] and Keirs et al[11] found it to be 17%. This higher prevalence may be due to lack of health awareness and living pattern, dietary habit of this region.

The study also shows a high prevalence of newly diagnosed diabetics (18%) in patients presenting with acute stroke. Sharma et al[6] reported as 16% and 12% in known diabetics and newly diagnosed diabetics respectively. These are in agreement with the observations in the series of Kiers et al[11] and Sharma et al.[6]

Previous studies have found a range of prevalence of undiagnosed diabetes in acute stroke population from 6% to 42% (Riddle MC et al).[12]

This study revealed higher mortality with stress hyperglycaemia and diabetes (Table 5) which are consistent with other series as reported by some authors.[13,14,15] However, some other studies did not show any significant increase in diabetic stroke deaths in diabetics compared to non-diabetics.[16]

Various pathophysiological mechanisms have been described to explain the effects of blood sugar level on stroke such as impaired auto-regulation of cerebral blood flow in diabetics.[17] Patients of stroke with hyperglycaemia are more prone to develop cerebral oedema,[18] patients with stroke and hyperglycaemia had higher lactate content in their ischaemic brain compared to normoglycaemics.[19] Hyperglycaemia is harmful to calcium recovered during early recirculation period following focal cerebral ischaemia.[20]

Openheimer et al stated that there was increased adhesiveness of erythrocytes in diabetes with stroke.[21] This effect was found to be associated with increased activity of fibrinogen and non-enzymatic glycosylation of Haemoglobin. Further reduced red cell life span has been observed in a few patients with severe microangiopathy.

Recovery of cerebral ATP generation following cerebral ischaemia is impaired when the ischaemia occurs in the setting of hyperglycaemic patients, particularly above blood glucose level of 225 mg/dL.[22]

In general, the brain has been considered as insulin independent organ; however, insulin receptors have been identified in rat brain. Insulin also regulates ornithine decarboxylase activity, which the rate-regulates in the synthesis of polyamines in the brain. Recently, insulin

receptors have been found on the endothelium of cerebral microvessels, on platelets and throughout the brain. Therefore, insulin may exercise beneficial effect on ischaemic stroke by enhancing the survival of neurons in the ischaemic zones.[23]

Increased blood glucose concentration at or around the time of a brain ischaemic event may worsen outcome; even mild hyperglycaemia (6.6 mmol/L) may result in increased brain damage and delayed recovery. Studies in rat showed that insulin improved functional recovery from brain ischaemia, probably through its effects on glucose and lactate levels, although there is no information on the benefit of this approach. It is of note that one practical implication state by the studies,[24] dextrose should not be provided to patients with acute ischaemic strokes. They indicated that moderate hyperglycaemia can exaggerate ischaemic brain damage by enhancing formation of lactic acid and impairment of normal phosphorous metabolism. However, hypoglycaemia should be avoided.[25]

The main goal of fluid management in the acute phase of stroke is to establish and to maintain normovolaemia. Fluid depletion is best treated with isotonic saline or Ringer's solution. Except for the treatment of hypoglycaemia, no glucose-containing infusions should be used in the early stroke patient. Fever also negatively influences outcomes after stroke. Lowering of elevated body temperature is strongly suggested.[26]

Acute stroke, either ischaemic or haemorrhagic lead to a hypertensive reaction in the first hours and days after stroke. Antihypertensive drugs should be used only in rare exceptions in the early hours following acute ischaemic stroke, i.e., for hypertensive crisis or heart failure. Frequently, it is suggested that in the early hours after stroke, arterial hypertension should only be treated if the systolic BP exceeds 180 mmHg. Drugs recommended for the treatment of such elevated hypertension vary from country to country. In essence, short-acting parenteral drugs that may be titrated over a venous line are to be used to control it best. Oral nifedipine is strongly discouraged.[26]

Between 5 and 10% of patients develop enough cerebral oedema to cause obtundation or brain herniation. Oedema peaks on second or third day but can cause mass effect up to tenth day. Water restriction and intravenous mannitol may be used to raise the serum osmolality but hypovolaemia should be avoided as this may contribute to hypotension and the worsening of infarction.[1]

Neuroprotection is the concept of providing a treatment that prolongs brain's tolerance to ischaemia. Drugs that block the excitatory aminoacid pathways have been shown to protect neurons and glia in animals, but despite multiple clinical trials they have not been proven to be beneficial in humans (Wade S et al).[1.] Serum glucose should be monitored and kept <6.1 mmol/L (110 mg/dL) using an insulin pump if necessary.[27] Blood pressure should be lower if there is malignant hypertension or myocardial ischaemia or if blood pressure >185/110 mm of Hg and thrombolytic therapy is anticipated.[27] It is recommended to keep mean arterial pressure (MAP) <130 mm of Hg in cases of cerebral haemorrhage unless an increased in ICP is expected.[28] For patients with cerebral infarction who are not candidates for thrombolytic therapy one recommended guideline is to initiate antihypertensive therapy only for patients with a systolic blood pressure >220 mmHg or a diastolic blood pressure >130 mmHg. In patients with haemorrhagic stroke, suggested guidelines for initiating antihypertensive therapy are systolic blood pressure>180 mmHg or diastolic blood pressure> 130 mmHg. Cautious reduction of blood pressure is indicated if mean arterial pressure < 130 mmHg.[29]

In the last decade, the incidence of ischaemic stroke and of related in-hospital mortality declined in persons within diabetes, while increasing among diabetic patients of advanced age. Women with diabetes, compared with men had a higher-in-hospital mortality risk.[30]

Diabetes is not only a highly important risk factor for ischaemic stroke at all ages, but is especially so in those less than 65 years of age. Thus, physician caring for patients at risk for stroke should be careful for diabetes, as well as other concurrent stroke risk factor that tend to cluster with diabetes.[31]

The preventive measures include good living habits, such as smoking cessation, limiting alcohol and avoiding high glucose and high fat diet, is an effective way to prevent the stroke. It helps decreasing the morbidity and mortality in stroke patients with DM and improves the patient life quality. Thus, treatment can prevent the development of complications in the blood vessel in DM patients.[32]

LIMITATIONS OF THE STUDY:

1. Exclusion of cases of stroke due to haematological disorders.
2. Exclusion of intracerebral pathology existing from before.

CONCLUSION: The glycaemic status of the patients in diabetics and non-diabetics correlates with the severity of the stroke. Hyperglycaemia in non-diabetic patients after acute stroke is a stress response reflecting more severe neurological damage. Management of hyperglycaemia in patients with diabetes and non-diabetes is an important aspect of the emergency management of stroke.

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