Admission Glycaemic Status and Its Correlation with Severity of Acute Cerebral Infarction, Using NIHS Scale in a Tertiary Care Centre, Thodupuzha, Kerala

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ABSTRACT

BACKGROUND

80 % of strokes are due to infarction and uncertainty whether stress hyperglycaemia or chronic dysglycaemia confers poorer outcomes offers a chance for further research to improve clinical practice. Diabetes mellitus, a known independent risk factor is associated with 6-fold risk of stroke, with worse outcome, high morbidity, recurrence, and decreased survival after stroke, with 20 % dying from stroke.

METHODS

The correlation between admission glycaemic status to clinical severity and infarct size was investigated in 60 newly diagnosed computed tomography (CT) - proven cases of acute cerebral infarction. Based on their admission blood glucose, HbA1C, and diabetes history, the patients were categorized into 3 groups: euglycaemia, stress hyperglycaemia, and diabetic. Based on CT, the infarcts were classified into three sizes: small, medium, and big. The National Institute of Health Stroke Scale (NIHSS) scale was used to measure neurological function on admission and day 10 of the illness.

RESULTS

The average age was 53.9 + 12.9 years, with a male to female ratio of 1.73 : 1. The 50-60-year age group had the most cases (58.3 %). The prevalence of hyperglycaemia was 75 %, with admission blood glucose levels ranging from 100 to 512 mg/dL. There were 43.33 % of patients with diabetes, 31.67 % with stress hyperglycaemia, and 25 % with euglycemia. Severe presentation and high NIHSS scores were associated with higher admission glucose levels. High NIHSS score was seen in diabetes with small and medium sized infarcts, and stress hyperglycaemia with large infarcts ($p < 0.05$). Stress hyperglycaemic patients had poor recovery, irrespective of the infarct size ($p < 0.001$)

CONCLUSIONS

High blood glucose levels at admission correlated with infarct size and clinical severity. NIHSS scores assessed over time in stress hyperglycaemia are linked to increased severity and poor recovery. Admission glucose and HbA1C both correlated well with infarct size in diabetes.

KEY WORDS

Stress Hyperglycaemia, Diabetes, Cerebral Infarction, NIHSS, Stroke

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BACKGROUND

Stroke is among the leading cause of death and disability in the world, with 80 % due to infarction.[1] Diabetes mellitus, a known independent risk factor is associated with 6 fold risk of stroke, with worse outcome, high morbidity, recurrence and decreased survival after stroke, with 20 % dying from stroke.[2] The incidence increases with age and is common in males,[3] and believed to due be accelerated atherosclerosis, affect vessels in many distributions, including small and large vessels.[4] Admission random blood sugar (RBS) may not reflect true glycaemia prior to the stroke, HbA1C along with RBS offers a new perspective of the glycaemic status, correlated with average intracellular blood glucose level and with glycaemic levels over the previous 6 - 10 weeks.[5] There is debate whether stress hyperglycaemia confers poorer outcomes[6,7] or chronic dysglycemia[8,9] is responsible for pathological processes in stroke. This uncertainty offers a chance for further research and improve clinical practice.

Objectives

The aim and objective of this study was to correlate glycaemic status with infarct size, severity at presentation and recovery at 10th day of illness in newly diagnosed CT proven cases of acute cerebral infarction.

METHODS

This one-year observation study took place in the tertiary care centre at Al Azhar Medical College in Thodupuzha between January 2019 and December 2020.

Inclusion Criteria

Age > 18 years, CT proven newly diagnosed cases of acute cerebral infarction.

Exclusion Criteria

Intracerebral haemorrhage, traumatic stroke, cerebellar infarction, brainstem infarction, transient ischemic attacks, and previous history of stroke, space occupying lesions and cerebral venous thrombosis were excluded from study.

During the study period, 60 patients with age above 18 years presenting with CT (emergency non contrast) proven cases of acute cerebral infarction were studied for their glycaemic status using the random blood glucose (RBS) and HbA1c at admission.

After receiving written consent and ethical approval, the patients were recruited in the study and after a thorough history and physical examination, the severity of the stroke was determined using the NIHSS score.

The National Institutes of Health Stoke Scale is point based graded neurologic examination for evaluation and quantifying neurological deficits. The points for level of functioning in motor function, visual fields, ataxia, speech, language, cognition, and motor and sensory impairments are combined for total score, which is valid, reliable and easily reproducible. The total score correlates with clinical presentation, greater the score, more severe is the neurological deficit.

These patients were separated into three groups according on their admission RBS, HbA1C, and diabetes history: euglycaemia, stress hyperglycaemia (RBS > 140mg percent and normal HbA1C), and diabetes.

Based on the CT (Emergency non contrast 32 slice PHILIPS) findings, the infarct size was divided into three categories: small, medium, and big. The small infarcts (A) were < 3 cms2, extending 2CT slices (1slice = 10mm), medium-sized infarcts (B) were > 3 cms2, but 5 cms2 and > 2CT slices, and big-sized infarcts (C) were > 5cms2, including substantial vascular area, and were independently confirmed by two radiologists.

Where the initial CT scan was normal, a second CT scan of the brain was scheduled after 72 hours. On day 10 of the illness, the NIHSS was used to conduct another evaluation. The patients were followed up on until they were discharged from hospital.

Statistical Analysis

The statistical tests used in the study were 't' test and Pearson's co-efficient.

RESULTS

The study comprised sixty patients with cerebral infarction who were hospitalised to Al Azhar Medical College Hospital and satisfied the inclusion criteria. The fifth and sixth decades had the highest number of cases (58.3 percent). The study group's average age was 53.9 + 2.9 years. The ratio of males to females was 1.73 : 1.

Glycaemic Group	Admission RBS	Number of Case and %	Male	Female
Euglycaemia	100 - 140 mg%	15 (25 %)	12 (31.58 %)	3 (13.64 %)
Stress hyperglycaemia	141 - 300 mg%	19 (31.67 %)	9 (23.68 %)	10 (45.45 %)
Diabetes	100 - 512 mg%	26 (43.33 %)	17 (44.74 %)	9 (40.91 %)

Table 1. Glycaemic Groups and Admission RBS

The study group's blood glucose at admission levels ranged from 100 through 512 mg/dL.

The prevalence of hyperglycaemia (admission glucose > 140 mg) was 75 %, with 43.33 percent having diabetes, 31.67 percent having stress hyperglycaemia, and 25 % having euglycaemia. 44 % of male patients had diabetes, whereas 45 % of female patients had stress hyperglycaemia.

Class	Infarct Size	Number and Percentage	Baseline NIHSS Score ± SD	Euglycaemia	Stress Hyperglycaemia	Diabetes
A	Small	19 (31.67 %)	15.95 ± 6.05	10 (67 %)	2 (10.53 %)	7 (27 %)
B	Medium	22 (36.66 %)	20.73 ± 6.63	5 (33 %)	11 (57.89 %)	6 (23 %)
C	Large	19 (31.67 %)	31.63 ± 3.64	0	6 (31.58 %)	13 (50 %)

Table 2. Infarct Sizes in Various Glycaemic Groups

The medium-sized infarcts (B), defined as those > 3 cm2 but < 5 cm2 and visible on more than two CT slices, accounted for 36 % of all infarcts, while small (A) and large-sized infarcts (C) accounted for 32 % each.

Smaller infarcts were more prevalent in the euglycaemia group, medium-sized infarcts in the stress hyperglycaemic group (57 %) and large-sized infarcts (50 %) in the diabetic group.

Baseline NIHSS score corresponded to infarct size in all the three study groups. The mean NIHSS score was 15.95 ± 6.05 with small sized infarcts, 20.73 ± 6.63 with medium sized infarcts and 31.63 ± 3.64 with large infarcts.

Glycaemic Group	Admission RBS	Baseline NIHSS Score ±SD	Pearson's Co Efficient
Euglycaemia	122.47 ± 10.80	12.47 ± 3.62	0.5696
Stress hyperglycaemia	188.35 ± 46.87	23.53 ± 7.82	0.419
Diabetes	267.96 ± 93.21	27.92 ± 5.34	0.5138

Table 3. Admission RBS, Baseline NIHSS Score and Pearson's Co Efficient in Various Glycaemic Groups

Glycaemic Group	Baseline NIHSS Score ± SD Day 0	Baseline NIHSS Score ± SD Day 10	Change in Score
Euglycaemia	12.47 ± 3.62	7.53 ± 0.99	4.93 ± 3.08
Stress hyperglycaemia	23.53 ± 7.82	15.84 ± 7.65	7.68 ± 0.89**
Diabetes	27.92 ± 5.34*	19.46 ± 4.56	8.73 ± 1.73

Table 4. Progression of NIHSS Scores from Day 1 to 10 in Various Glycaemic Groups

*p>0.05 **p<0.020

NIHSS score at presentation was highest for diabetes with small and medium sized infarcts, and in stress hyperglycaemia group for the large infarcts ($p < 0.05$). In each glycaemic group, the NIHSS score rose as the size of the infarct increased. As the glycaemic state moved from euglycaemia to diabetes, a gradual rise in the NIHSS score was found across all groups, regardless of infarct size.

When compared to the diabetes group, the stress hyperglycaemia group showed slower NIHS score development from baseline (p - 0.020). On day 10 of hospitalisation, this slower shift in the scores implied sluggish or delayed recovery. In stress hyperglycaemia, all infarct sizes showed slower score development.

Among the glycaemic groups, the diabetes group has a higher baseline score ($p > 0.05$). For small-sized infarcts, the diabetes group had a higher baseline NIHSS score than the normoglycaemic group ($p< 0.001$). The diabetic group's higher baseline scores suggested clinically severe stroke for even small infarcts, as evidenced by an increase in baseline NIHSS.

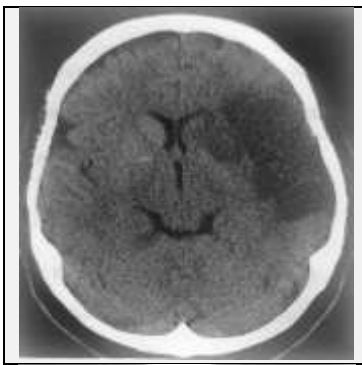

Figure 1.
Lt MCA Territory Infarct

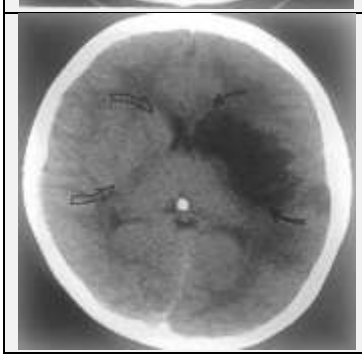

Figure 2.
Left Basal Ganglia Infarct

Glycaemic Status with Infarct Size	No. of Cases	Admission RBS	HbA1c	Day 0 Mean NIHSS Score ± SD	Day 10 Mean NIHSS Score ± SD	Day10 Change in Mean NIHSS Score ± SD
Euglycaemia	15	100 - 140 mg%	< 6.5	12.47 ± 3.62	7.53 ± 0.99	4.93 ± 3.08
Small infarct	10			11.50 ± 2.99	7.40 ± 1.17	4.10 ± 2.23
Medium infarct	5			14.40 ± 4.34	7.80 ± 0.45	6.60 ± 4.10
Large Infarct	0			0	0	0
Stress hyperglycaemia	19	141 - 300 mg	< 6.5	23.53 ± 7.82	15.84 ± 7.65	7.68± 0.89 $^{p<0.020}$
Small infarct	2			15	7	8
Medium infarct	11			19.91 ± 3.96	12.09 ± 3.33	7.82 ± 0.87 $^{p<0.035}$
Large Infarct	6			33.00 ± 4.77	25.50 ± 4.14	7.50 ± 1.05 $^{p<0.029}$
Diabetes Mellitus	26	301 to 531 mg%	> 6.5	27.92 ± 5.34 $^{p>0.05}$	19.46 ± 4.56	8.73 ± 1.73
Small infarct	7	191.43 ± 34.2 $^{*p<0.05}$		22.57 ± 3.41 $^{p<0.001}$	15.43 ± 2.64	7.14 ± 1.46
Medium infarct	6	235.5 ± 36.36 $^{p<0.05}$		27.50 ± 6.47 $^{p<0.08}$	18.17 ± 5.91	9.93 ± 1.86
Large Infarct	13	324.15 ± 97.98 $^{p<0.002}$		31.00 ± 3.00 $^{p=.027}$	22.23 ± 2.59	8.77 ± 1.09

Table 5. Admission RBS, Infarct Size and Progression of NIHSS Scores from Day 1 to 10 in Various Glycaemic Groups

When NIHSS scores were compared over time, stress hyperglycaemia was accompanied by increasing severity and poor recovery. The stress hyperglycaemic patients had statistically significant slow progression in NIHSS scores for all age groups, irrespective of the infarct size ($p < 0.001$).

A poor clinical recovery was more evident in medium and large infarcts among the stress hyperglycaemia, compared to diabetes ($p < 0.001$)

For medium-sized infarcts, the diabetic group has a higher baseline NIHSS score than the stress hyperglycaemic and euglycaemia groups (p = 0.008).

In the diabetic group, both admission blood glucose and HbA1c correlated well with infarct size and clinical severity. Lower HbA1C and admission glucose were associated with smaller infarct sizes, whereas poorly managed patients experienced a severe stroke with a bigger infarct size (p < 0.002).

Presentation	Euglycaemia (n = 15)	Stress Hyperglycaemia (n = 19)	Diabetes (n = 22)	Total (n = 60)
Hemiplegia	8	16	14	28
Monoparesis	2	2	5	9
Sensory dysfunction	5	6	4	15
Altered sensorium	1	8	12	21
Language disturbances	3	7	10	20
Gait unsteadiness	1	3	0	4
Cranial nerve dysfunction	5	9	9	23

Table 6. Clinical Presentation of the Study Group

Severe symptoms and signs at presentation were noted in hyperglycaemic groups. Hemiplegia, cranial nerve dysfunction mainly VII CN, altered sensorium, language disturbances, and sensory symptoms were common.

Complications	Euglycaemia N = 19	Stress Hyperglycaemia N = 19	Diabetes n=22	Total N = 60
Pneumonia	2	4	5	11
UTI	1	3	3	7
Seizures	0	2	4	6
Upper GI bleed	1	3	2	6
Renal failure	0	0	1	1
Cardiac failure	0	1	1	2
AMI	2	2	0	4
AF	2	2	0	2
Hemorrhagic transformation on CT	0	2	2	4

Table 7. Complications in Various Glycaemic Groups

The complications such as pneumonia, urinary tract infection (UTI), seizures, upper GI bleed, myocardial infarction, cardiac failure, renal dysfunction and hemorrhagic transformation of infarct were highest in the hyperglycaemic groups (stress and diabetes).

DISCUSSION

The mean age of the study group was 53.9 $\pm$ 12.9 years, the maximum distributions of cases were in the fifth and sixth decade. (58.3 %) and male preponderance with male : female ratio 1.73 : 1 is comparable to many studies.[3,8,10] Advancing age and male sex were an important risk factor for stroke.[3,8,10] The incidence of hyperglycaemia (admission glucose > 140 mg) in this study was 73.33 % and 43.33 % diabetes prevalence in this study was comparable to other studies.[3,8,10]

The categorization of infarcts was similar to study done by Yadav et al.[11] In our study, hyperglycaemic patients had medium to large sized infarcts. In the stress hyperglycaemia and diabetes groups, the percentage of large infarcts was 31.58 percent and 50 %, respectively. The diabetes group had a larger percentage of small and big infarcts, whereas the stress hyperglycaemia group had a higher percentage of medium-sized infarcts, and the infarct size increased with increasing glycaemic status deterioration. Our findings are consistent with R Chen et al.[9,12] who reported increased infarct size in hyperglycaemia.

The National Institute of Health Stroke Scale was used to evaluate the clinical severity of the stroke, which was monitored throughout the hospitalisation. The NIHSS score increased with increase in the size of infarct.[13] The admission glucose correlated well with NIHSS score in all three glycaemic groups. These findings are comparable to Johnston et al. where infarct volume was a significant predictor of NIHSS score.[14]

A rise in admission glucose on presentation was associated with a higher NIHSS score, indicating that the stroke was severe clinically (Pearson's co-efficient: 0.5696 for normoglycaemia, 0.419 for stress hyperglycaemia and 0.5138 for diabetes group). Our findings are comparable to study by. Kiers et al. that found severe stroke and higher mortality rates in patients with stress hyperglycaemia, with mortality increasing independently with admission blood glucose. The increased mortality rate was not attributable to any stroke type or location.[15,16] Our findings show that admission hyperglycaemia is a poor prognostic predictor. Many studies have demonstrated the ill effects of admission hyperglycemia.[15,16,17]

As the glycaemic state transitioned from euglycaemia to diabetes, the NIHSS score increased in all groups, regardless of the extent of the infarct. The score in each glycaemic group increased as the infarct size grew larger. The score for each infarct size rose when the glycaemic spectrum changed from normoglycaemia to diabetes. This was observed for both small and medium-sized infarcts, where diabetes had the highest NIHSS score at presentation, however the stress hyperglycaemia group had a higher baseline score for large-sized infarcts compared to the diabetes group (p < 0.05).

The NIHS scale was used for follow-up assessment on the 10th day. The drop in score from baseline showed progress or recovery. Non progression in the scores from the day of admission or slow progression was taken as slow or non-recovery and bad prognostic sign. These findings were comparable to Green et al. Adams et al. who noticed decrease in likelihood of survival by 24 % and excellent outcome at 7 days for additional increase in the baseline score.[17,18]

The patients who were normoglycaemia on admission had good recovery. Gray et al. observed complete functional recovery in patients with normal admission blood glucoselevels.[19]

In contrast, the stress hyperglycaemic patients had statistically significant slow progression in scores for all age groups, irrespective of the infarct size. This change was more evident in medium and large infarcts where the progression was slower, with slow and poor clinical

recovery compared to diabetes ($p < 0.001$) Thus, when the NIHSS scale was used serially, stress hyperglycaemia was related with higher severity and poor recovery. Overall, hyperglycaemia on presentation was associated with larger infarct size and poor recovery compared to the normoglycaemia individuals. This was comparable to studies by Green SR et al. Kamouchi et al. who noticed poor recovery in their patients admitted with hyperglycemia.[16,17] The patients with no history of DM who had an ischemic stroke and moderately elevated glucose levels (stress hyperglycaemia) also had higher risk of short-term mortality and increased risk of poor functional recovery compared with patients with lower glucose levels.[20]

Hemiplegia, cranial nerve dysfunction mainly VII CN, altered sensorium, language disturbances were common presenting symptoms. The complications were highest in the hyperglycaemic groups (stress and diabetes) with four cases of hemorrhagic transformation of infarct on repeat CT in the hyperglycaemic group. This finding is comparable to Yuan et al. who found hemorrhagic transformation of infarct in hyperglycemia.[21] Acute hyperglycaemia affects several coagulation factors and has been associated with hemorrhagic transformation after ischemic infarct.[21] Hyper coagulation in combination with alterations in thrombolysis may, in part, explain the increase in both intracerebral haemorrhage and mortality in hyperglycaemic patients after stroke.[21]

The diabetes group formed 43.33 % of the cases in the study group. Both admission glucose and HbA_1C correlated well with infarct size in the diabetes group.[12] Lower HbA1C was linked to a smaller infarct size, but poorly managed diabetics experienced a severe stroke and greater infarct size ($p < 0.002$). The use of HbA1c to define pre-existing glycaemic status is supported by an increase in vascular risk seen with even modest elevations in glycosylated haemoglobin levels and markedly increased stroke risk in people with $HbA_1C > 7$ %. This finding is more consistent with a threshold relationship between HbA_1C levels and stroke risk and lower neurological recovery.[9,12,16,17,20]

CONCLUSIONS

The clinical severity of stroke was well connected with the admission random blood glucose and NIHSS scores. Regardless of infarct size, individuals with hyperglycaemia at presentation had greater stroke severity and high NIHSS scores at admission. Regardless of their glycaemic condition, those with hyperglycaemia had larger infarcts.

The subjects with stress hyperglycaemia were associated with a high percentage of medium-sized infarcts and poor NIHSS score recovery from baseline for both medium and large-sized infarcts.

High NIHSS score at presentation; large infarct and bad recovery were seen with poorly managed diabetes mellitus, with strong correlation of infarct size to both admission glucose and HbA1c.

Cerebral infarction with hyperglycaemia is not an unusual finding and is related to increased severity, large sized infarct and poor clinical recovery and predicts poor outcome and increased mortality. Early diagnosis and treatment of diabetes, strict normalization of blood glucose with periodic HbA1c monitoring may prevent, reduce the morbidity and mortality.

Limitations of the Study

The study has a small sample size. The study didn't look at whether treating hyperglycaemia would lower the morbidity and mortality linked with the condition. The patients had relatively limited follow-up in the hospital; if they had been followed after discharge, a greater long-term correlation would have been conceivable.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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