**ABSTRACT**

**Objectives:** To estimate the occurrence of hyperglycemia in patients with cerebrovascular accident (ischemic) to compare the frequency of mortality among the patients with and without hyperglycemia presenting with acute CVA.

**Study Design:** Descriptive cross-sectional study.

**Place and Duration of Study:** Department of General Medicine, Combined Military Hospital Quetta Pakistan, from May 2018 to May 2019

**Methodology:** A total of 347 patients of both genders diagnosed with acute stroke were included. Blood glucose levels were evaluated and hyperglycemic and normo-glycemic patients were identified. CT scan was performed. Standard treatment was provided to the patients according to the type of stroke (ischemic or hemorrhagic). These patients were discharged.

**Results:** Patients in this study were having age range of 20 to 70 years. SO mean age of 53.76 ± 9.08 years. Many patients 283 (81.56%) were 45-71 years of age. 183 (52.74%) were of male gender and 164 (47.26%) were females. We have found hyperglycemia in 96 (27.67%) patients. There was no hyperglycemia observed in 251 (72.33%) patients. Frequency of hyperglycemia was 12.97%. Frequency of mortality was 30.21% in hyperglycemic patients vs. 6.37% in normo-glycemic patients (p=0.0001).

**Conclusion:** Frequency of hyperglycemia with acute stroke is high with high mortality among the patients presenting with acute stroke as compared to normo-glycemic.

**Keywords:** Acute stroke, Hyperglycemia, Mortality.


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**INTRODUCTION**

In countries with stable economic conditions, stroke (CVA) has been acknowledged 3rd commonestiology of death after cardiovascular diseases and tumors. Those who have survived, stroke remained common cause of death and physical deficits. Only fewer patients (about 20%) need admission for prolonged periods and rehabilitation therapy in coming months after disease episode (CVA). 1, 2

Stroke has been declared prominent neurological reason for death and physical disability throughout the world. It is has been declared 3rd foremost reason of death among entire countries. Evaluation of various risks as etiology in patients is supportive for recognition for early disease management. All this strategy will contribute for health professionals for managing target population. Ischemic stroke is world wide disease contributing in mortality. 3 A research article at international level has calculated a figure of 15 million individuals sustain nonfatal stroke yearly. Among these people, 33% developed disability for whole life. 4 In lower and middle-income countries only 80% of all stroke deaths are registered. A projected annual occurrence of CVA in Pakistan is 250/100,000. Pakistan has annual occurrence of about 350,000 new cases. 5

Stroke not only causes but also aggravates the pre-existing dementia. Stroke also leads to cognitive impairment especially in elderly individuals. 5 Due to non-availability of central registry and inadequate data availability in Pakistan on this subject, there is insufficient research work on risk factors of stroke in Pakistani population. A study conducted in 2014 showed a high incidence of modifiable risk factors. Among these risk factors, Hypertension and dyslipi-demias were contributory factors in Pakistani population. The same study showed that atherosclerosis as the most common culprit in elderly patients. Elderly patients have a higher risk adjusted mortality rate. Elderly population also have higher rate of complications and require longer periods for hospitalization. 6 Strokes can be divided into two main categories i.e., hemorrhagic and non-
hemorrhagic. Intracranial bleed-includes 10% to 15% of all CVA cases. ICB has higher death rate as compared to ischemic stroke entity. About 50 out of 100 patients with diagnosis of intra-cranial bleed during first 30 days of illness.\textsuperscript{7}

Different prognostic markers were assessed to predict the outcome and to evaluate the association with ischemic stroke. These biomarkers include brain natriuretic peptide, highly sensitive C-reactive protein. In addition, the markers like homocysteine and insulin like growth factor have also been studied at different intervals. Serum blood glucose level and throm-bomodulin also have prognostic value in stroke patients.\textsuperscript{8}

Al-Weshahy et al, a study of the patients coming with acute stroke. The frequency of hyperglycemia among these patients was 34.4% while the frequency of mortality was 85.7% in hyperglycemic patients vs. 5% in normoglycemic patients; \( p=0.00 \).\textsuperscript{9}

The results of our established that hyperglycemia is one of the most reliable markers in defining the outcome of the stroke in relation to mortality. Being a good predictor, there is a need to conduct further studies on local population so that its relationship with the outcome of the stroke could be determined in local population. This would help us in creation of local guidelines for admitting and giving intensive care to patients. This would help to opt early interventional radiological measures which would help in dealing with the pathology (ischemia or intracranial bleeding). This would also help in reducing mortality rate in these patients.

**METHODOLOGY**

This Descriptive cross sectional study was conducted at department of medicine Combined Military Hospital Quetta, from May 2018 to May 2019. Sample size of 347 cases was calculated with 95% confidence level. 5% margin of error was kept while taking predictable frequency of hyperglycemia to be 34.4% among the patients presenting with acute stroke.\textsuperscript{9} Non-probability, Consecutive sampling technique was adopted.

**Included Criteria:** Patients of both gender groups with ages in the range of 20-70 years suffering from acute stroke as defined in operational definition, were included. Patients who signed written informed consent to join in the study were also included.

**Exclusion Criteria:** Patients who were excluded include patients with diabetes who had fasting blood glucose level ≥120mg/dl). In addition, patients with history of neurological deficits that reverts within 24 hours after onset (transit ischemic attack) were also excluded. Patients with history of head trauma having biconvex, concave or intraparenchymal white area on plan CT scan were excluded. Patients with space occupying lesion on CT scan and patients with serum creatinine >2mg/dl, serum sodium <120 mmol/l or have liver cirrhosis along with as citese were also excluded from the study.

SPSS-22 used for data analysis. Data collected, entered in SPSS and study variables i.e. age, glycemic levels, blood pressure level, basal metabolic index values and hospital stay days were calculated. \( p \)-values were calculated for mortality in normoglycemic and hyperglycemic patients presenting with acute ischemic stroke.

### RESULTS

Total 347 patients were selected and their age range was from twenty to seventy years. While calculated mean age found to be 53.76 ± 9.08 years. Many of participants of study 283 (81.56%) were between 46 to 70 years of age.

Out of 183 (52.74%) were male and 164 (47.26%) were females. Distribution of patients having various variables affecting mortality are mentioned below in Table-I. Mean hospital admission was 10.24 ± 3.20 days. Mean estimated BMI was 28.56 ± 2.99 kg/m\(^2\).

#### Table-I: variables affecting mortality among stroke patients (n=347).

<table>
<thead>
<tr>
<th>Variables Affecting Mortality</th>
<th>Frequency(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Stays (Days)</td>
<td></td>
</tr>
<tr>
<td>≤10</td>
<td>136 (39.19%)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>211 (60.80%)</td>
</tr>
<tr>
<td>Basal Metabolic Index (kg/m(^2))</td>
<td></td>
</tr>
<tr>
<td>≤27</td>
<td>127 (36.60%)</td>
</tr>
<tr>
<td>&gt;27</td>
<td>220 (63.40%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>233 (67.15%)</td>
</tr>
<tr>
<td>No</td>
<td>114 (32.85%)</td>
</tr>
</tbody>
</table>

#### Table-II: Comparison of frequency of mortality among the patients with and without hyperglycemia presenting with acute stroke (n=347).

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Hyperglycemic n=96 (26.67%)</th>
<th>Normoglycemic n=251(73.33%)</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Patients %Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>29 (30.21%)</td>
<td>16 (6.37%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>No</td>
<td>67 (69.79%)</td>
<td>235 (93.63%)</td>
<td></td>
</tr>
</tbody>
</table>

Hyperglycemia was observed in 96 (27.67%) patients. There was no incidence of hyperglycemia in 25 1(72.33%) patients. Frequency of mortality was 29 (30.21%) in hyperglycemic patients vs. 16 (6.37%) in
Hyperglycemia

normoglycemic patients; \( p=0.0001 \) as shown in Table-II.

Percentages of occurrence of hyperglycemia was distributed on different age groups. Results revealed that no significant difference between different age groups found. While hyperglycemia frequency with respect to gender also didn’t revealed significant differences between both genders. Table-I have shown the data with respect to hospital stay, BMI & hypertension respectively. Association of hyperglycemia with respect to hospital also showed positive link with longer hospital stay.

<table>
<thead>
<tr>
<th>Table-III: Association of Hyperglycemia with respect to gender, Basal metabolic index and hyper tension.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
</tbody>
</table>

DISCUSSION

Acute stroke patients showed already existent of hyperglycemia found in our patients. Occurrence was about 20-50% among stroke patients.20-30% of patients were found to be hyperglycemic in various studies using thrombolytic therapy as treatment measure. Hyperglycemia creates worst outcome in acute stroke patients. 30-day mortality was three-fold more in patients who were found to be hyperglycemic with previous normo-glycemic history. While patients with past history of diabetes only have 2-fold 30-day mortality.10 Hy perglycemia has been declared as independent risk in various studies using thrombolytic and anticoagulation therapy.11 While hyperglycemia has also been declared to be worst factor causing hemorrhage in ischemic area.

This research work conducted to estimate the occurrence of hyperglycemia in individuals presenting with acute ischemic stroke. Also, to compare the incidence of mortality in patients with and without hyperglycemia developing acute stroke. Age range found in between 20 to 70 years. Mean age of 53.76 ± 9.08 years. Most of the patients 283 (81.56%) fell in age range of 46 to 70 years. Among 347 patients, 183 (52.74%) were male and 164 (47.26%) were females with male to female ratio of 1.1.1. In this study, hyperglycemia observed in 96 (27.67%) patients. There was no hyperglycemia in 251 (72.33%) patients. Frequency of hyperglycemia between these patients was 12.97%. The frequency of mortality was 30.21% in hyperglycemic patients vs. 6.37% in normoglycemic patients; \( p=0.0001 \).

Al-Weshahy et al, in 20017 performed study in which patients presenting with acute stroke, the frequency of hyperglycemia was 34.4%. However, the frequency of mortality was 85.7% in hyperglycemic patients vs. 5% in normoglycemic patients; \( p=0.00 \).9

Under diagnosed diabetes mellitus cases (6-42%) have been found in acute stroke cases.12 Diabetes mellitus was found in 24.8% of study participants with supratentorial strokes. 36.3% of patients showed temporary rise in blood sugar levels.13 Zahra et al,14 has demonstrated that 20% stroke patients were having high blood sugar levels who were previously normoglycemic. Zafar A et al,15 in one study declared results that patients with normal blood glucose levels 29 (58.0%) suffered ischemic stroke and 21 (42.0%) suffered intracranial bleed.

Glycemia in Acute Stroke (GLIAS), study tried to find the level of blood sugar levels after which worst outcome in patients can be estimated. Minimum level found to 155 mg/dl. Further increase in blood sugar levels during first 48 hrs above this limit showed added worst outcome and mortality.16 In a post hoc scrutiny of same study, it is observed that 40% of the patients with hyperglycemia kept values of >155 mg/dl in spite of the hypoglycemia treatment.

Lindsberg et al,17 found that raised glucose levels is common phenomenon in early few hour of stroke diagnosis. 2/3 of all patients with ischemic stroke showed high sugar levels during admission in health care facility. A common phenomenon that has been observed that stress hyperglycemia was found in 27.67% of patients showed similar results as found by Melamed et al,18(35%).

Hyperglycemia on admission has direct correlation with stroke outcome. However, no correlation has been observed between catecholamine and glycemic levels.19 Tuomilehto et al,20 found a mortality figures of 16% in males and 33% in females participants of study. These figures were directly proportional to diabetes.
Hyperglycemia and stroke outcome correlation differs between different stroke subtypes. Correlation between hyperglycemia and poor stroke mortality has been observed in few studies in patients who sustained cortical stroke. However, lacunar stroke didn’t contribute to excess mortality. Many studies completed the correlation between raised glucose levels and clinical outcome before giving therapeutic trial of thrombolytic therapy and has been declared standard approach in stroke patients. However, in ongoing studies important factor has been observed that increased sugar levels at hospital admission also resulted in worst outcome in patients treated with thrombolytic therapy.

In the Capes et al., results showed that those patients not having diabetes mellitus, stress related hyperglycemia was linked with a three-fold more risk of mortality. This rate of mortality was calculated after stroke (pooled relative risk, 3.07; 95% CI, 2.50–3.79). Those patients who have no evidence of diabetes it was found that stress hyperglycemia was not linked with increased risk of short-term mortality after occurrence of stroke (pooled relative risk, 1.30; 95% CI, 0.49–3.43).

Exact mechanism through which high serum glucose levels results in worst outcome who received anticoagulants or thrombolytics is not clear yet. In target vessels, high glucose level cause glycosylation which deranges protein and enzyme function. Vasodilation and cellular adhesion within the vasculature downregulate production of normal molecules in vascular bed. Hyperglycemia damages endothelial surfaces through glycosylation. Free radicals’ production further damages vessels.

Hyperglycemia increases death rate of mortality from ischemic stroke. Few methods have been postulated which describe wrong influence of high serum glucose levels in blood. First mechanism proposes that vessel damage occurs due to poor reperfusion. This results in downregulation of nitric oxide dependent mechanism which results in decrease vessels tone. Second mechanism proposes that increase lactic acid production causes vessel injury leading to increase stroke occurrence. Experimental data has supported above two hypotheses.

**CONCLUSION**

As per our research it is obvious that occurrence of hyperglycemia in individuals representing with ischemic stroke is high. It also estimates the high incidence of mortality between the patients with hyperglycemias presenting with acute stroke as compared to patients coming with normoglycemia. So, we suggest those patients presenting with cerebrovascular accidents (ischemic), hyperglycemia is necessary to be determined in these individuals. So prompt diagnosis and evaluation is necessary to minimize death among these patients for better outcome.

**Conflict of Interest:** None.

**Author’s Contribution**

MR: Conception of design, collection of data, ALK: Proof reading and editing of manuscript, MKAK: Data analysis and collection, RIK: Writing of manuscript, SKHSB: Overall supervision of the study project, references, FM: Discussions and data analysis.

**REFERENCES**