Original article:

Glycosylated haemoglobin in Ischemic stroke and Transient Ischaemic Attacks (TIA) - A cross sectional study

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Abstract
Introduction: Diabetes Mellitus may increase the risk of stroke/TIA by affecting auto-regulation of Cerebral Blood Flow (CBF) and causing endothelial dysfunction.

Methods: 100 consecutively selected patients with stroke/TIA selected were tested for their RBS and HbA1c levels. Data was analyzed using descriptive statistics.

Results: 74, 16 and 10 patients had HbA1c levels >6.5 g/dl, 6-6.4 g/dl and 4-6 g/dl respectively. Only 28 had RBS >200 mg/dl whereas 74 had HbA1c >6.5g/dl.

Conclusion: Three fourths of Stroke/TIA patients had long term hyperglycemia which may be a risk factor for their disease. HbA1c is more sensitive in detecting hyperglycaemic status compared to random blood sugar (RBS).

Key words: Diabetes Mellitus, Stroke, TIA, HbA1c, RBS

INTRODUCTION
Diabetes mellitus is frequently encountered co-morbidity in cerebrovascular disease- ischaemic stroke/transient ischemic attacks (TIA). Impaired auto regulation of Cerebral Blood Flow (CBF) has been demonstrated in diabetes and is thought to contribute to the pathogenesis of diabetic cerebrovascular disorders. Endothelial dysfunction due to hyperglycemia may also contribute to the risk. Epidemiologic data show an increased risk of stroke associated with hyperglycemia. For example, in the Framingham Study the incidence of thrombotic stroke was 2.5 times higher in diabetic men and 3.6 times higher in diabetic women than in those without diabetes. However, the prevalence of hyperglycemia preceding cerebrovascular events is poorly defined, so the relative importance of hyperglycemia as a risk factor is unclear. In particular, the importance of mild hyperglycemia, as opposed to symptomatic diabetes, as a precursor of stroke is unclear. Measurement of glycosylated hemoglobin (GHB), which reflects glycaemic levels for the preceding 1-3 months in patients with recent stroke or TIA may allow us to address this question.

AIM OF THE STUDY
1) To study the association between glycated hemoglobin levels and ischemic stroke/ TIA.
2) To investigate the usefulness of glycated hemoglobin in accurately assessing the glycaemic control in stroke and TIA patients as compared to capillary glucose levels.
MATERIALS AND METHODS

Source of Data:
Patients admitted in the Department of Medicine, Hassan Institute of Medical Sciences.

One hundred consecutive patients admitted from July 2017 till August 2018 with proven ischaemic stroke and TIA who match the inclusion and exclusion criteria were enrolled in the study.

Inclusion Criteria:

Adult patients of either sex with ischemic stroke and TIA irrespective of their previous

a. Glycaemic status.
b. Smoking history.
c. Hypertension and use of anti hypertensives.
d. Cholesterol levels and use of hypolipidaemics.
e. History of similar complaints.

Exclusion Criteria:

A. Hemorrhagic stroke
B. Stroke mimickers- unusual manifestations of nonvascular conditions that may resemble acute stroke syndrome

➢ Metabolic derangements
  • Hypoglycemia
  • Hyperglycemia
  • Hepatic encephalopathy
➢ CNS disorders
  • Seizure / postictal
  • hemiplegic migraine
  • subdural hematoma
  • abscess
➢ Intracranial tumors
➢ Hypertensive encephalopathy
➢ Multiple sclerosis
➢ Psychiatric problems
➢ Factitious disorders

Demographic data, complete medical history, physical examination findings, relevant investigation results were recorded for every enrolled patient.

Following investigations were done:

1. Complete hemogram
2. Capillary Random blood glucose
3. Fasting lipid profile
4. Blood urea and serum creatinine
5. Glycated hemoglobin level
6. CT of Brain

RESULTS

Graph 1: Age Wise distribution (in years)

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>8</td>
</tr>
<tr>
<td>41-50</td>
<td>10</td>
</tr>
<tr>
<td>51-60</td>
<td>26</td>
</tr>
<tr>
<td>&gt;60</td>
<td>56</td>
</tr>
</tbody>
</table>

Graph 2: Sex Wise distribution

- Male: 62
- Female: 38
Graph 3: Distribution of patients based on type of stroke
Out of 100 patients studied, 26 were found to have TIA and 74 were found to have ischemic stroke.

Graph 5: Distribution of patients based on HbA1c and RBS levels
Graph 6: Status of diabetes mellitus in the study group
Out of 100 patients 40 were known diabetics on treatment and 60 did not know their glycaemic status

![Diabetic status of the patients](image)

Table 1: HbA1c levels in Stroke patients

<table>
<thead>
<tr>
<th>Stroke</th>
<th>Ischemic Stroke</th>
<th>Number</th>
<th>HbA1cGr</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>4-6%</td>
<td>6-6.4%</td>
<td>6.5%</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Number</td>
<td>8</td>
<td>12</td>
<td>54</td>
</tr>
<tr>
<td>TIA</td>
<td>Number</td>
<td>2</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>Number</td>
<td>10</td>
<td>16</td>
<td>74</td>
</tr>
</tbody>
</table>

Table 2: Glycaemic parameters in diabetics vs non-diabetics

<table>
<thead>
<tr>
<th>Diabetic status</th>
<th>Number</th>
<th>RBS &gt; 200mg/dl</th>
<th>HbA1c &gt;6.5g/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known diabetic</td>
<td>40</td>
<td>22</td>
<td>40</td>
</tr>
<tr>
<td>Status unknown</td>
<td>60</td>
<td>6</td>
<td>30</td>
</tr>
</tbody>
</table>
70 of the patients had HbA1c of ≥ 6.5% whereas only 28 of the patients had RBS > 200 mg/dl, suggesting that many of the patients who had normal RBS had high HbA1c levels in the diabetic range.

**DISCUSSION**

Stroke as an important cause of morbidity is in rising trend. Epidemiologic data show an increased risk of stroke associated with hyperglycemia\(^9\)-\(^{11}\). In large necropsy series an increased incidence of cerebral infarction has been found among diabetics\(^{13}\)-\(^{16}\).

Diabetes is an independent risk factor for atherothrombotic brain infarction at all ages.\(^{17}\) The type and topography of diabetes related cerebral infarction may differ from brain infarcts in non-diabetics. Diabetes may be a risk factor for lacunar infarction\(^{18,19}\). Kane and Aronson found that diabetics had more lacunar lesions, especially in the distribution of parasagittal perforating arteries feeding the Basal ganglias, thalamus, pons and cerebellum\(^13\). Press et al also found that the frequency of these infarcts was greater in diabetics and increased as they aged\(^{14}\). Alex et al found a higher frequency of all types of cerebral infarction in diabetics\(^{15}\). Davis et al\(^{20}\) reported that recent onset of hyperglycemia was a more important risk factor for stroke than long standing diabetes and that there is short median time between the onset of diabetes and stroke. Pulcinelli et al\(^{21}\) reported that both diabetics and non diabetics who were hyperglycaemic at the time of stroke as measured by admission blood glucose did worse.

Out of 100 stroke patients 74 had HbA1c ≥ 6.5% which clearly indicates that, they had impaired glucose tolerance even before the insult occurred. We also noted that 40 out of 100 patients were diabetics who were on treatment (either with OHA or insulin). 38 (95%) of them had HbA1c ≥ 6.5% and among these 32 (80%) had HbA1c > 7% indicating their glycaemic target was unachieved.

Even in 60 non-diabetics 32 (53.3%) had HbA1c ≥ 6.5%. 20 (33.3%) of the 30 had HbA1c in pre-diabetes (5.7-6.4) range and 4 (6.7%) had HbA1c < 5.7%. The proportion of glycaemic abnormality detected in our study roughly matches two other studies: Gertler et al\(^{22-23}\) found 70% whereas Riddle MC et al found 62% glycaemic abnormality in Stroke/TIA patients not diagnosed with DM.\(^{24}\)

In our study we also noted that, RBS was ≥ 200 in only 22 out of 40 (55%) patients whose diabetic status was known and were on treatment. All these patients (100%) had HbA1C ≥ 6.5% suggesting the high sensitivity of HbA1c. Among the patients with the diabetic status unknown 54 of 60 patients (90%) had RBS in normal range out of which 30 (55.5%) had HbA1c in the diabetic range (≥ 6.5%) suggesting the poor sensitivity of RBS in detecting glycaemic status. 6 out of 60 patients (10%) had RBS > 200 and all of them had HbA1c ≥ 6.5%.

**CONCLUSION**

- Hyperglycemia recognized or unrecognized is a major risk factor for stroke.
- HbA1c may be a better indicator of glycaemic status than RBS in stroke.
- Achieving HbA1c target to less than 7% in diabetic patients may be useful in preventing stroke.
BIBLIOGRAPHY


