Relationship between serum calcium level and severity of acute ischaemic stroke

SAJJAD ALI1, MUHAMMAD ADNAN KHALIQ2, SABEEN FATIMA RIZVI3

ABSTRACT

Background: Stroke is amongst the leading causes of mortality and morbidity worldwide. Nearly 350,000 new cases of stroke per year are seen in Pakistan. The prognosis of patient depends mainly on the severity of the stroke. In this study we evaluated serum calcium as a marker of severity of ischemic stroke

Study design: Cross-sectional study.

Setting: Department of Medicine, Chaudhary Rehmat Ali Memorial Trust Hospital, Lahore.


Data collection: 132 patients of acute ischaemic stroke presented within 72 hours were included. Stroke was diagnosed as new onset focal neurologic deficit and plain computed tomography showing ischemic infarct. Severity of stroke was assessed using NIHSS. Patients’ serum calcium, albumin and renal function tests were recorded in the study proforma. SPSS version 22 was used for data analysis. Correlation between serum calcium level and stroke severity was determined by calculating Pearson correlation coefficient.

Results: The mean calcium level was 8.74±0.58mg/dl. About 40(30.3%) patients had serum calcium level <8.7 mg/dl, 35 (26.5%) had calcium=8.7-9.00mg/dl, 25 (18.9%) had calcium=9.01-9.30mg/dl and calcium >9.30mg/dl in 32 (24.2%) patients. Pearson Correlation coefficient was calculated to be r = -0.318.

Conclusion: Low calcium levels has very weak correlation with severity of ischaemic stroke as determined via NIHSS score.

Keywords: National institute health stroke score (NIHSS), Ischemic stroke, Albumin corrected serum calcium level

INTRODUCTION

Stroke is defined by WHO as: clinical disease typified by fast emerging symptoms of crucial or overall disruption in cerebral functions, prolonged >24hours or cause death, with no obvious causes other than vascular origin.1 Stroke is one of the main cause of mortality and morbidity worldwide. Its incidence is expected to double in coming years in our part of the world2.

Risk factors include hypertension, diabetes mellitus, dyslipidemia, smoking, family history of stroke and past episode of transient ischemic attack (TIA) or stroke. Pakistan is a developing country recently having major economic and demographic alterations, causing a standard shift from poverty-related infectious & nutritious deficiency diseases toward lifestyle-related cardiovascular & cerebrovascular diseases. So there is a need for reliable prognostic markers in order to assess the severity of stroke considering the economic burden it poses due to the disability associated with stroke. Precise data, regarding epidemiology of stroke in Pakistan, is not available, however, since associated factors for stroke are readily present, the burden is assumed to be high.

Calcium (Ca) plays a pivotal role in the development of ischemic stroke4. Cerebral hypoxia leads to build up of calcium inside cells resulting in a cascade which eventually activates cytotoxic enzyme leading to cell death.5 It has also been reported that high dietary intake of Calcium has been associated with reduced risk of stroke6.

Chung et al., reported that higher albumin modified serum calcium concentrations were associated with short-term adverse outcome and higher risk of long-term mortality after stroke.7 However, Ovbiagele et al., found high calcium concentrations to be linked with reduced severity of ischemic stroke. This was in concordance with the findings of a local study conducted recently by Ishfaq et al.8 Moreover, another study conducted in Canada showed that patients with high calcium concentrations had minor cerebral infarct size.5 Considering these contradictory findings we felt prompted to conduct this study evaluating the association between calcium level and grading of acute ischemic stroke. The results of this study will further add to the evidence regarding the part of calcium as a predictive marker of acute ischemic stroke. It will also help us understand whether altering calcium intake in candidates at increased risk for stroke will help in lowering the chances and severity of ischemic stroke.

MATERIALS & METHODS

This cross-sectional survey was carried out in outdoor patients Department (OPD) and Indoor Department of Medicine, Chaudhary Rehmat Ali Memorial Trust Hospital, Lahore from 1st March 2017 to 31st August 2017. The Sample size of 132 cases was calculated by using correlation coefficient i.e. r = -0.2379 with 95% power of test and 5% significance level. Non-probability, consecutive sampling was employed to recruit patients.

Inclusion criteria: Patients aged above 18 years of either gender with acute ischemic stroke(diagnosed as focal neurologic deficit and ischemic infarction computed tomography scan) presenting within 72 hours.

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Exclusion criteria: Patients with recurrent stroke, renal failure, malignancy, aspiration pneumonia.

Detailed history & clinical examination was done for each case. Severity of stroke was determined using national institute of health stroke severity score (NIHSS). Serum calcium levels, albumin and renal function tests were done on day 0 and day 3. Other routine BLIs such as CXR, ECG, LFTs and S/E were also done.

Patient’s demographics and labs were recorded in a predesigned proforma. SPSS version 22 was used for analysing the data. The mean ± SD was calculated for calcium level and NIHSS score. Frequencies and percentages were calculated for categorical variables like gender. Pearson’s correlation coefficient was calculated between serum calcium and severity of stroke (NIHSS category).

RESULTS

Mean age of patients (n = 132) was 57.98 ± 8.3 years. There were 60 males and 72 females. The mean NIHSS score was 18.24 ± 5.86. The mean calcium= 8.74±0.58mg/dl. About 40(30.3%) patients had serum calcium level <8.74, 35(26.5%) had calcium=8.71-9.00mg/dl, 25(18.9%) had calcium=9.01-9.30mg/dl and calcium >9.30mg/dl in 32 (24.2%) patients. The mean NIHSS of these calcium groups was 21.56, 15.63, 18.56 & 16.25 respectively. Pearson Correlation coefficient was r = -0.318.

Table 1: Clinical details of patients

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>57.98±8.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (m:f)</td>
<td>60:72</td>
</tr>
<tr>
<td>Hypertension</td>
<td>72 (54.5%)</td>
</tr>
<tr>
<td>Previous stroke / TIA</td>
<td>36 (27.3%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>52 (39.4%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>66 (50%)</td>
</tr>
<tr>
<td>High Cholesterol</td>
<td>50 (37.9%)</td>
</tr>
</tbody>
</table>

Table 2: Level of Calcium and mean NIHSS distribution

<table>
<thead>
<tr>
<th>Level of Calcium (mg/dl)</th>
<th>n</th>
<th>Mean NIHSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 8.71</td>
<td>40 (30.3%)</td>
<td>21.56</td>
</tr>
<tr>
<td>8.71 - 9.00</td>
<td>35 (26.5%)</td>
<td>16.25</td>
</tr>
<tr>
<td>9.01 – 9.30</td>
<td>25 (18.9%)</td>
<td>15.63</td>
</tr>
<tr>
<td>&gt; 9.30</td>
<td>32 (24.2%)</td>
<td>16.25</td>
</tr>
<tr>
<td>Total</td>
<td>132 (100%)</td>
<td>18.24</td>
</tr>
</tbody>
</table>

DISCUSSION

Stroke is the commonest preventable cause of debility worldwide. Projected incidence of stroke in Pakistan is 250/100,000 rendering to 350,000 new cases per year. Ischemic stroke occurs when blood flow to a certain part of brain drops below critical level leading to hypoxic insult. The resulting cellular hypoxia leads to calcium influx into the cells. Serum calcium levels have a significant role in the molecular pathways of ischemic neuronal death and damage. The prognosis of patient depends mainly on the severity of the stroke. Various methods can be used to assess the severity e.g. infarct volume on CT, clinical assessment of severity and certain biochemical parameters like C reactive protein etc. In this study we embarked upon to assess serum calcium as a marker of severity of ischemic stroke.

The average age of our study population was 57.98 years close to 61.09 years as reported by Ishfaq et al in a recent local study whereas Guven et al., reported a mean age of 67 years and Appel et al., found out average age of 70.7 years. The difference was probably due to fact that major stroke inhibition strategies are not implemented fully and the average life expectancy is lower than developed nations as noted by Ishfaq et al. The female to male ratio was 1.20:1 demonstrating a female preponderance in line with the findings of Ishfaq et al and Guven H et al.

In our study, the mean calcium level was 8.74±0.58mg/dl, which was quite similar to that of Ishfaq et al; however, it was considerably lower as compared to 9.2±0.5 mg/dl as reported by Appel SA et al. Nutritional deficiency due to poor socioeconomic status of our population could be a potential reason.

In this study, we found negative correlation between calcium and stroke severity assessed by NIHSS (r= -0.318, p<0.05). Ishfaq et al and Guven et al also reported negative correlation between calcium level and NIHSS score. In our study serum calcium level was measured within 48-72 hours of stroke as most of the people came from far flung areas with considerable delay before presenting to ER since the onset of initial symptoms. This proved useful to our study because the calcium levels that we measured were similar to the “delayed calcium” group of Ovbiagele et al which they found to correlate with lesser severity of stroke and better recovery at 3 months. However albumin adjusted serum calcium did not correlate accordingly with stroke severity; rather, it was total calcium which correlated with severity of stroke as reported previously by Erasmo et al.

The pathophysiological basis for the observed trend probably involves calcium influx via N-methyl-D-aspartate (NMDA) receptors. Low Vitamin D levels offer another possible explanation for the increased severity of stroke seen in setting of low serum calcium levels.
There were certain limitations to our study. The serum calcium and albumin levels were measured on admission, without any fixed time interval from the onset of the stroke. Thus, this may lead to a bias in the analysis due to lack of standardization of the timing of blood sampling. However, as there have been very few studies of correlation between the calcium levels and severity of stroke, this study adds to the evidence and proves calcium levels to be a useful prognostic marker in stroke.

CONCLUSION

Lower calcium concentration is high chances of more severe ischemic stroke, although a very weak relation was determined. So future multicenter surveys are warranted to confirm our findings.

REFERENCES