SHORT REPORT

Correlation of serum calcium with severity of acute ischaemic stroke

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Abstract

Stroke results in the death of around 6.5 million people annually with a majority of these occurring in developing countries. Serum calcium has been hypothesised to play a significant role in causing ischaemic stroke. This retrospective observational study was conducted to determine the correlation, if any, between serum calcium and the severity of acute ischaemic stroke in our population. Two hundred and seventy-nine patients admitted with acute ischaemic stroke were enrolled in the study. Of the 279 patients 162 (58%) were male and mean age was 62.4 ± 3.8 years. Characteristics of stroke patients were compared with stroke severity. Mean albumin corrected serum calcium and Scandinavian stroke severity score was 9.1 (± 5.6) and 33.67 (± 15.2), respectively. Hypertension and mean GCS on admission were significantly associated with increased stroke severity score. However, no correlation was observed between serum calcium and severity of acute ischaemic stroke.

Keywords: Stroke, Serum calcium, Scandinavian stroke severity scale, Cerebral ischaemia.

DOI: https://doi.org/10.47391/JPMA.04-593

Introduction

Stroke is categorised as the number one cause of disability and the third most common cause of mortality worldwide. Literature reports that an estimated 6.5 million people lose their lives due to stroke every year, out of which 75% deaths occur in developing countries.[1] The majority of strokes in Pakistan are a result of cerebral ischaemia, with the most common type being lacunar stroke.[2] TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification of stroke has classified the causes of ischaemic stroke into: large artery atherosclerosis, cardio-embolism, small vessel disease, other determined aetiologies and undetermined causes.[3] Multiple variables have an impact on the prognosis and outcome of stroke, such as age, comorbidities, cause of stroke, location and severity of stroke, level of consciousness and blood glucose.[3]

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Calcium is known to play a significant role in the pathogenesis of ischaemic stroke, since cerebral ischaemia causes an increase in intracellular calcium resulting in activation of cytotoxic enzymes leading to cell death.[4] The present study was conducted to determine the correlation, if any, between serum calcium and severity of acute ischaemic stroke, and to establish the local perspective as there is a paucity of local data even though we are burdened with a large number of people presenting with acute ischaemic stroke.

Patients/Methods and Results

A retrospective observational study was conducted at the Department of Medicine, Aga Khan University Hospital, Karachi, from January 2018 to December 2018, after taking ethical approval from the Ethical Review Committee (2018-0267-153). All patients presenting acutely within 24 hours of suffering stroke with CT scan at the time of admission showing a hypodense area, plus any two or more of the following symptoms inability to move one or more limb, aphasia, imbalance and GCS <15, were labelled as acute ischaemic stroke. Severity of the stroke was measured according to the Scandinavian stroke scale (SSS). Patients with a history of mania, bipolar effective disorder or post-traumatic stress, history of thyroid and parathyroid disorders, history of blood transfusion within one week, history of CNS disease (e.g. head trauma, multiple sclerosis), and with history of congestive heart failure, chronic renal failure, chronic obstructive pulmonary disease and chronic liver disease, were excluded. A score of less than 43 was classified as mild stroke, 26-43 as moderate, and less than 26 as severe stroke.[5]

We compared patients' characteristics as mild, moderate, and severe stroke by using Student t-test or Wilcoxon rank-sum test for continuous variables and chi square test or Fisher exact test for categorical variables based on cell counts. Spearman rank correlation test was performed to investigate the relationship between calcium quartiles and stroke severity and p-value of ≤ 0.05 was taken as significant.

A total of 730 patients were reviewed out of which 279 fulfilled the inclusion criteria. Of the 279 patients, 162 (58%) were male, while 117 (42%) were female. The mean age of the sample population was 62.4±13.8 with age

Table-1: Characteristics of stroke patients (N=279).

Characteristics	Overall (N = 279)
Mean age (years)	62.4±13.8
Gender	
Male	162 (58%)
Female	117 (42%)
Comorbid conditions	
Diabetes	152 (54.5%)
Hypertension	211 (75.6%)
Smoking	33 (11.8%)
Hospitalisation factors	
Mean duration of symptoms (hours)	32.9 ± 36.1
Mean systolic BP on admission (mm Hg)	150.1 ± 36.0
Mean diastolic BP on admission (mm Hg)	83.2 ± 18.6
Mean GCS on admission	12.7 ± 3.2
Mean Haemoglobin on admission (Gm/dl)	13.8 ± 10.8
Mean Total Cholesterol (mg/dl)	146.6 ± 62.7
Mean Triglycerides (mg/dl)	125.2 ± 79.3
Mean HDL (mg/dl)	35.65 ± 16.7
Mean LDL (mg/dl)	90.27 ± 45.8
Mean Serum Calcium (mg/dl)	9.1 ± 5.6
Mean Stroke severity score	33.67 ± 15.2
Stroke Severity	
Mild	90 (32.3%)
Moderate	96 (34.4%)
Severe	93 (33.3%)

BP: Blood pressure, GCS: Glasgow coma score, HDL: High density lipoprotein, LDL: Low density lipoprotein.

range between 19 and 94 years. A total of 211 (75.6%) patients were hypertensive with a mean systolic BP of 150.1± 36.0 mmHg and diastolic BP of 83.2 ± 18.6 mm Hg. Mean GCS on admission to the hospital was found to be 12.7± 3.2. Mean serum calcium level at admission (adjusted for albumin) and mean Scandinavian stroke scale severity score were 9.1±5.6 and 33.67±15.2, respectively. The rest of the baseline characteristics have been summarised in Table-1.

The sample patient population was almost equally divided into three categories of stroke severity scale (Mild = 90, Moderate = 96, and Severe = 93). Mean serum calcium level at the time of admission was not significantly related to stroke severity. However, baseline comorbid and mean GCS on admission were both significantly related to stroke severity (p value < 0.05). Table-2 shows the characteristics of stroke patients according to stroke severity score.

Discussion

Stroke is one of the foremost causes of mortality and morbidity throughout the world, whether it is in the developing or developed country.[1] Calcium ions are known to be involved in the pathophysiology of cerebral ischaemia as hypoxia/ischaemia results in transfer of calcium ions from extracellular to intracellular cerebral tissue spaces.[4] Our study, however, showed no significant correlation between serum calcium and

Table-2: Characteristics of stroke patients according to stroke severity score (N=279).

Characteristics	Overall (N = 279)	Mild (N = 90)	Moderate (N = 96)	Severe (N = 93)	P-value
Mean age (years)	62.4±13.8	59.9±14.3	64.9±12.6	62.19±14.3	0.547
Gender					0.268
Male	162(58%)	58	55	49	
Female	117(42%)	32	41	44	
Comorbid conditions					
Diabetes	152(54.5%)	41	55	56	0.109
Hypertension	211(75.6%)	58	79	74	0.010
Smoking	33(11.8%)	9	12	12	0.805
Hospitalisation factors					
Mean duration of symptoms (hours)	32.9 ±36.1	33.24± 35.9	32.47± 36.7	33.12± 36.1	0.595
Mean systolic BP on admission(mm Hg)	150.1±36.0	152.57 ± 50.0	154.16±27.6	143.37±25.4	0.181
Mean diastolic BP on admission(mm Hg)	83.2± 18.6	83.3± 17.3	84.01± 18.1	82.42± 20.5	0.637
Mean GCS on admission	12.7± 3.2	14.5± 1.8	13.6± 2.0	10.0± 3.5	<0.001
Mean Haemoglobin on admission	13.8±10.8	13.0± 2.4	13.8±12.4	14.5±13.7	<0.001
Mean Total Cholesterol(mg/dl)	146.6±62.7	152.6± 56.3	151.0± 57.5	136.1±72.4	0.657
Mean Triglycerides(mg/dl)	125.2±79.3	137.9± 85.9	122.4± 66.2	115.8±84.4	0.614
Mean HDL(mg/dl)	35.65±16.7	36.2±14.5	37.1±19.1	33.6±19.1	0.463
Mean LDL(mg/dl)	90.27±45.8	94.2± 40.7	93.5±44.8	83.1±50.8	0.766
Mean Serum Calcium	9.1± 5.6	8.8± 0.5	9.7± 9.4	8.8±1.0	0.756

BP: Blood pressure, GCS: Glasgow coma score, HDL: High density lipoprotein, LDL: Low density lipoprotein.

acute ischaemic stroke severity.

Review of literature, both global as well as regional has shown conflicting results. Some studies have found serum calcium to be low in transient ischaemic attack and further low calcium has been hypothesised to occur in ischaemic cerebral infarction.[6] Some meta-analyses have even reported an inverse association between dietary calcium intake and risk of ischaemic stroke.[7] However, some studies have reported that there is no significant association between serum calcium and stroke severity or serum calcium and risk of ischaemic stroke.[8,9] One study has even suggested that higher levels of serum calcium are associated with more severe artery stenosis lesions.[10] These arguments have led us to believe that serum calcium is not a reliable marker for accurate prediction of severity of stroke or its prevalence.

The study is limited by its design (retrospective study) and the timing of calcium samples could also not be accurately ascertained. However, it is important to note that all patients had a serum calcium sent at admission as part of initial baseline workup, from the emergency. Furthermore, since a majority of the patients presenting to our tertiary hospital have either been previously admitted elsewhere or are from far flung areas, true serum calcium values can neither be found nor can it be judged, if the value of serum calcium will be classified as early or late even if the study was done prospectively. Another problem with retrospective data collection was the quality of the data in the file and variability in the examination done by the physicians. Nonetheless, this study has offered new local information to clinicians which can influence clinical practice. Previous studies on this topic have used the modified NIHSS scale. Our study is unique as it uses the Scandinavian stroke severity scale, which has been found to be equal to the NIHSS and is easy to apply in the acute clinical setting.[5]

Conclusion

In conclusion, our results did not show any correlation between serum calcium levels at the time of admission and ischaemic stroke severity. However, further studies in South Asian population are warranted to properly quantify the correlation between serum calcium and stroke severity and to assess the importance of serum calcium as a prognostic marker of stroke outcome.

Disclaimer: None.

Conflict of Interest: The authors declare they have no conflict of interest.

Funding Disclosure: None.

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