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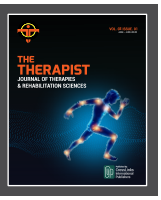

Original Article

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Correlation of Serum Calcium with the Severity of Acute Ischemic Stroke Patients Presenting at Tertiary Care Hospital, Karachi

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ABSTRACT

Stroke is a significant chronic illness, death and disability in both developed and developing nations. The interrelation between the level of serum calcium and the processes of ischemic injury is not clear. **Objectives:** To identify the relationship between the level of serum calcium and the extent of acute ischemic stroke behavior in patients who reported to a tertiary care hospital in Karachi. **Methods:** The cross-sectional analytic study was done in the Neurology Department of Civil Hospital, Karachi. A total of 138 patients diagnosed with acute ischemic stroke, fulfilling the diagnostic criteria, were included after obtaining verbal consent. Serum calcium levels were measured within 24 hours of admission. Simple descriptive statistics (mean ± SD) were used for quantitative data, while qualitative variables were given in terms of frequencies and percentages. A p-value of less than 0.05 was taken as statistically significant. **Results:** Among 138 patients, the mean age was 51.14 ± 4.49 years, and the mean calcium level was 10.7 ± 1.32 mg/dl. Based on calcium quartiles, 28 (20.3%), 35 (25.4%), 54 (39.1%), and 21 (15.2%) patients fell into quartiles 1, 2, 3, and 4, respectively. Stroke severity (based on NIHSS scores) distribution was: mild (15.2%), moderate (29.7%), moderate to severe (20.3%), and severe (34.8%). Higher calcium levels were positively correlated with increased stroke severity ($p \leq 0.05$). **Conclusions:** Serum calcium levels measured within 24–48 hours of admission showed a strong correlation with both stroke severity and functional outcome. Therefore, calcium levels may serve as an indicator of disease severity in acute ischemic stroke patients.

INTRODUCTION

Stroke ranks third in developed nations and is the second most common cause of mortality worldwide [1]. It is the most common cause of disabilities among adults in the USA [2]. One stroke happens in the United Kingdom every three minutes and twenty-seven seconds. Asia is experiencing a rise in the prevalence of strokes, which is severely impacting individuals, family members, and the medical community in addition to causing a significant financial burden [3]. Every year, 16.3 million new instances of stroke are reported globally. The World Health Organization (WHO) predicts that between thirteen percent and twenty percent of acute ischemic stroke patients experience neurocognitive consequences [4]. The first week post-stroke is when individuals are particularly at risk of dying. Patients suffering a stroke are most vulnerable in the first few weeks after the event; in the initial thirty days, between twenty percent and fifty percent of patients pass away. Even for those who do make it through, there may still be mild, moderate, or severe disabilities, and substantial natural recovery may not occur for up to six months [5]. On

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the contrary hand, individuals who previously suffered a fatal stroke have a ten percent first-year chance and a five percent second-year probability of having a second stroke [6]. Sixty-five to eighty-three percent of stroke survivors are self-sufficient in their care after a year. One year following a stroke, between sixty percent and eighty-three percent of patients are independent in their ability to take care of themselves [7]. Cerebrovascular disorders remain a leading cause of death, according to cause-of-death statistics from the 1990s. It was projected that cardiovascular disorders, including stroke, would cause an estimated 5.5 million fatalities worldwide, or 9.6% of global deaths [8]. One of the major health problems in the UK is stroke. It was the cause of more than fifty-six thousand deaths in 1999, or eleven percent of total fatalities in the United Kingdom and Wales [9]. Out of the 135 diseases considered in the worldwide burden of disease research, ischemic stroke was one of the largest factors in mortality; cerebrovascular illnesses came in second [10]. Both the total number of stroke-related fatalities and the worldwide cost of stroke are high and rising [11]. According to Ashraf et al. there are no gender differences in the frequency of hemorrhagic strokes, while men are more likely to get ischemic strokes. Men have a twenty-five percent greater chance of suffering a stroke than women do, particularly if they are young [12]. Despite the extensive global research on stroke prevalence, mortality, and risk factors, there remains a limited understanding of the biochemical predictors that influence stroke severity, particularly serum calcium levels, in South Asian populations. Most existing studies have been conducted in Western countries, and regional variations in diet, genetics, and comorbidities may influence this association.

This study aimed to determine the correlation between serum calcium levels and the severity of acute ischemic stroke in patients.

METHODS

The analytical study was carried out as a cross-sectional study at the Neurology Department of Civil Hospital Karachi during the period of six months, that is, between 14 January and 14 July 2019, following the permission granted by the College of Physicians and Surgeons, Pakistan, and the local ethical review committee. The non-probability consecutive sampling was used to enroll 138 patients; the size of the sample was calculated based on the Pearson correlation coefficient ($r = -0.3$), 95% power, and 5% level of significance. The patients of the study were newly diagnosed patients who had their first stroke, of a non-contrast CT scan with the time frame not exceeding 24 hours after their symptoms began, aged between 30 and 60 years, and of either gender, and presenting with a clinical presentation of focal neurological deficits. Hemodynamically stable patients who could undergo serum calcium testing were included, while those with conditions such as thyroid or parathyroid disorders, SLE, CCF, chronic liver, renal, or lung diseases, neurological disorders, recent blood transfusions, or psychiatric illnesses were excluded. Verbal consent was obtained from all the participants. At the time of admission, demographic and clinical information were gathered, and ischemic stroke was diagnosed by a radiologist with more than five years' experience. The estimation of serum calcium was performed with the help of a 5 mL venous blood sample, and laboratory testing was carried out in a standard facility. The SPSS version 23.0 was used to analyze the data, and quantitative variables (age, calcium, lipid profile) were analyzed as the mean and SD, whereas the qualitative variables (gender, hypertension, diabetes, smoking, anemia) were analyzed as frequencies and percentages. Pearson correlation was used to establish a relationship between serum calcium levels and stroke severity (NIHSS score), whereas Chi-square tests were used to determine the relationship between categorical variables. The p-value was taken to be statistically significant when it was less than 0.05.

RESULTS

The age of the patients ranged from 38 to 60 years, with a mean age of 51.14 ± 4.49 years. The mean age of the 138 patients was 38 years old, while the highest age was 60 years old. In our study, the average age was 51.14 years, with an SD of ± 4.49. In the present investigation, the average length of symptoms, height, weight, cholesterol, triglyceride, bad cholesterol (LDL), good cholesterol (HDL), SBP, DBP, calcium, and hemoglobin were 22 ± 7.21 hours, 161 ± 6.78 centimeters, 85.2 ± 8.54 kilograms, respectively (Table 1).

Table 1: Baseline Characteristics of Study Participants (n=138)

Variables	Mean ± SD	Min-Max
Age (Years)	51.14 ± 4.49	38-60
Duration of Symptoms (Hours)	22 ± 7.21	12-42
Height (cm)	161 ± 6.78	148-168
Weight (Kg)	85.2 ± 8.54	68-115
Cholesterol (mg/dl)	196.7 ± 12.88	180-225
Triglycerides (mg/dl)	144.7 ± 10.43	130-168
LDL (mg/dl)	123.8 ± 9.06	110-140
HDL (mg/dl)	41.61 ± 4.03	34-47
SBP (mmHg)	141 ± 9.81	138-178
DBP (mmHg)	92 ± 7.22	78-105
Calcium (mg/dl)	10.71 ± 1.32	9-12
Hemoglobin (mg/dl)	11.57 ± 2.88	9-13

According to stratification for the calcium quartile based on acute stroke severity, individuals in calcium quartile 1 reported moderate, mild, moderate-severe, and severe

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NIHS scores; accordingly, for 0 (0 percent), 14 (23.1%), 00 (00%), and 14 (29.5%) of the patients. A p-value (r = 0.05) was 0.17. On the other hand, the NIHS scores for patients in the calcium quartile 2 were 07 (33.3%), 21 (51.2%), 00 (00%), and 07 (14.6%), respectively. The p-value (r = 0.14) was 0.00. Additionally, among patients in the calcium quartile 3, 14 (66.7%), 06 (14.6%), 14 (50%), and 20 (41.6%) had moderate, mild, moderately-severe, and serious NIHS scores, respectively. 0.95 (r = 0.00) was the p-value. Lastly, the NIHS scores for those in the calcium quartile 4 were 0 (0%), 00 (00%), 14 (50%), and 07 (14.6%), respectively. These individuals had moderate, mild, moderate-severe, and severe scores. 0.01 was the 0-value (r = 0.08) (Table 2).

Table 2: Distribution of Acute Ischemic Stroke Severity Across Different Age Groups (n=138)

Age (Years)	Acute Ischemic Stroke				Total	Correlation Coeff (p-Value)
	Mild	Moderate	Moderate-Severe	Stress		
30-45	10 (47.6%)	14 (34.1%)	15 (53.6%)	22 (45.8%)	61 (44.2%)	0.496 (<0.0001)
46-60	11 (52.4%)	27 (65.9%)	13 (46.4%)	26 (54.2%)	77 (55.8%)	0.485 (<0.0001)
Total	21 (100%)	41 (100%)	28 (100%)	48 (100%)	138 (100%)	-

Stratification by comorbidities revealed distinct associations with stroke severity.

Hypertension and dyslipidemia showed statistically significant associations with higher NIHSS scores (p<0.0001 for both). For instance, over 90% of patients with mild stroke had hypertension, underscoring its role as a major risk factor. In contrast, the presence of Type 2 Diabetes Mellitus, smoking status, or anemia did not show a significant association with initial stroke severity in this cohort (p>0.05) (Table 3).

Table 2: Ischemic Stroke Severity with Hypertension, Diabetes Mellitus Type-II, Dyslipidemia, Smoking, and Anemia Status (n=138)

Variables	Acute Ischemic Stroke				Total	Correlation Coeff (p-Value)
	Mild	Moderate	Moderate-Severe	Stress		
Hypertension						
Yes	19 (90.5%)	28 (68.3%)	21 (75%)	33 (38.8%)	101 (73.2%)	0.39 (<0.0001)
No	02 (9.5%)	13 (31.7%)	07 (25%)	15 (31.2%)	37 (26.8%)	0.02 (0.18)
Total	21 (100%)	41 (100%)	28 (100%)	48 (100%)	138 (100%)	–
Diabetes Mellitus Type II Status						
Yes	07 (33.1%)	14 (34.10%)	11 (39.30%)	24 (50%)	56 (40.60%)	0.485 (<0.0001)
No	14 (66.7%)	27 (65.90%)	17 (60.70%)	24 (50%)	82 (59.40%)	0.031(0.81)
Total	21 (100%)	41 (100%)	28 (100%)	48 (100%)	138 (100%)	–
Dyslipidemia						
Yes	10 (47.6%)	17 (41.5%)	13 (46.4%)	21 (43.8%)	61 (44.2%)	0.49 (<0.0001)
No	11 (52.4%)	24 (58.5%)	15 (53.6%)	27 (56.2%)	77 (55.8%)	0.32 (0.05)
Total	21 (100%)	41 (100%)	28 (100%)	48 (100%)	138 (100%)	–
Smoking Status						
Yes	07 (33.3%)	21 (51.2%)	07 (25%)	21 (43.8%)	56 (40.6%)	0.37 (<0.001)
No	14 (66.7%)	20 (48.8%)	21 (75%)	27 (56.2%)	82 (59.4%)	-0.0036 (0.92)
Total	21 (100%)	41 (100%)	28 (100%)	48 (100%)	138 (100%)	–
Anemia Status						
Yes	04 (19%)	10 (24.4%)	06 (21.4%)	10 (20.8%)	30 (21.7%)	-0.0036 (0.92)
No	17 (81%)	31 (75.6%)	22 (78.6%)	38 (79.2%)	108 (78.3%)	-0.004 (0.91)
Total	21 (100%)	41 (100%)	28 (100%)	48 (100%)	138 (100%)	–

DISCUSSION

Stroke is a medical condition marked by rapidly increasing symptoms and/or evidence of focal decline in neurological function, sometimes worldwide (for individuals in coma), persisting over twenty-four hours or resulting in death from a cause that isn't of arterial origin [13-15]. Among the most prevalent and fatal conditions are cerebrovascular diseases, which also include cerebral malformations, including intracranial aneurysms and cerebrovascular defects, as well as ischemic and hemorrhaging strokes [16, 17]. Both the total number of predicted scores and the frequency of cerebrovascular illness rise with advancing age. Low haemoglobin levels, tobacco usage, high blood pressure, and diabetes are major contributors to risk. It is also recognized that there is an association with more recent risk factors such as uric acid, C-reactive protein (hs-CRP), homocysteine, and more. The levels of calcium and albumin are two of the more recent ones. An important part of the biochemical pathways leading to ischemic neuronal

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death and injury is played by serum calcium levels [18]. There were 138 individuals with an ischemic stroke diagnosis. In our study, the mean age was 51.14 ± 4.49 years, and the mean calcium level was 10.71 ± 1.32 mg/dl. There were forty-seven (33.3%) male and ninety-two (66.7%) male and female. Comparing people in lower calcium quartiles (Q1, Q2) with the people in higher calcium quartiles (Q3, Q4), Gupta et al. found that people in higher calcium quartiles (Q3, Q4) had much fewer severe strokes over the 24-48-hour period [9]. In particular, no less than 72.73 percent of the patients in Q3 and 42.86 percent of the patients in Q4 scored below the mild range of the NIH scale compared to 7.69 percent of patients in the Q2 range and 0 percent of patients in the Q1 range. Ca significantly correlated with NIHSS, BI, and IS (all patients) and BI, which was reported in solitary and lacunar strokes in all patients and both NIHSS (admission) and BI in lobar, anterior circulation, and bilateral cerebrovascular accidents [19]. CCa was closely related to IS and BI in all individuals, including those with anterior circulatory ischemic attacks. BI and NIHSS (admission) had a significant correlation with IS. High Ca (and CCa in part groups) is related to better survival and recovery after AIS (except in posterior circulatory strokes) and low IS with high Ca and CCa. A previous study on how blood calcium was measured within a period of 78 hours after the stroke had been experienced was tested, and the National Institute of Health Stroke score was used to estimate the extent of a stroke at the same time. Sixty-seven (48.5%) and 71 (51.4%) men out of 138 were cases. The mean age was thirty-four to one hundred years, with a mean of 61.1 ±11.93. Mean National Institute of Health Stroke 17.7/ + 7.73/ 2-35. The serum calcium of each patient was noted and corrected by the quantity of albumin in the patient. The concentration of calcium in the serum was 8.82 + 0.7 mg/dl (mean: 6.84, 10.48). In order to get further information on blood calcium and the National Institute of Health Stroke score, a bivariate correlation was performed [20]. The results of our research, nevertheless, suggest that in stroke patients with acute stroke, lower Ca levels may be associated with more acute stroke symptoms at admission. Moreover, the quartile-based stratification of serum calcium, although convenient in pointing out trends, might simplify the nature of the relationship between calcium levels and the severity of strokes, which is continuous in nature. This also implies that the cut-off values that are determined are also specific to our study population and cannot be generalized directly.

CONCLUSIONS

In conclusion, the researchers have shown that there is a high level of correlation between the level of serum calcium and the severity of acute ischemic stroke. The more calcium in the patients, the more severe the stroke was; this means that serum calcium could be an independent predictor of stroke severity and functional outcome. These results indicate that the amount of calcium may be a possible prognostic factor in the treatment of acute ischemic stroke.

Authors Contribution

Conceptualization: FH
Methodology: FH, MK, SGA, MS, AJ, WA
Formal analysis: FH, MK, SGA, MS, AJ, WA
Writing review and editing: FH, MK, SGA, MS, AJ, WA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

All the authors declare no conflict of interest.

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