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ACUTE ISCHEMIC STROKE;

CORRELATION BETWEEN SERUM CALCIUM LEVELS AND SEVERITY OF INFARCT IN PATIENTS.

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ABSTRACT… Objectives: Objective of this study is to assess the correlation between severity of ischemic stroke on NIHSS and calcium level in patients presented with acute ischemic stroke. **Study Design:** Descriptive case series and non-probability purposive sampling technique was used in this study. **Setting:** South Medical ward& East Medical Ward, Department of Medicine, Mayo hospital, Lahore. **Period:** One year from 5th January 2015 to 4th January 2016. **Material & Methods:** Informed consent was taken from all the patients. Patients of both genders between 35-70 years of age were included in this study. Demographic record (name, age, sex, contact) were also obtained. Then patients were admitted in ward and were followed up there. Meanwhile no calcium supplement was advised. Then after 72 hours of admission, blood sample were drawn by using 5cc BD syringe and were sent to the laboratory of the hospital to assess serum calcium level. NIHSS score after 72 hours of admission were assessed and noted. Pearson correlation coefficient was calculated to measure the correlation between calcium level and NIHSS score. P-value≤0.05 were considered as significant. **Results:** In this present study the mean age of the patients was noted as 51.47±9.653 years, the male patients were 76% whereas female patients were 24%. The mean serum calcium level after 72 hours of the patients was noted as 7.26±1.41 mg/dl, while the man NIHSS was noted as 23.01±10.38.There was negative and Significant correlation was found between the serum calcium level (mg/dl) after 72 hours and NIHSS after 72 hours of the patients i.e. r=-0.899 (P<0.05). **Conclusion:** Our study results showed the negative correlation between the serum calcium level and NIHSS of ischemic stroke patients which showed that more decrease in calcium level will lead to more severe condition of stroke.

Key words: Acute Ischemic Stroke, Calcium level, Correlation, NIHSS, Severity.

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INTRODUCTION

Cerebrovascular accident (CVA) or stroke is the prompt loss of brain function, this conditions occurs because of disturbance in blood supply. Ischemia or hemorrhage may cause this situation.[1] Resultantly, affected brain area become dysfunction.[2] Thrombosis or embolism cause acute ischemic stroke. This type of stroke is more common as compared to haemorrhagic type of stroke. Previous study recorded haemorrhagic stroke within the range of 8-18%.[3]

The role of calcium is important in intra and extracellular metabolism. It controls various processes including muscle contraction, nerve conduction, regulation of enzyme and electrolytes, releasing hormones, coagulation and pathogenesis of ischemic cell damage. Accumulation of intracellular calcium may cause neuronal damage through triggering the process of cytotoxic events, however, the association of ischemic injury and calcium levels are not clear.[4]

In a study done at University of Toronto by Buck et al it was found that hypocalcemia at the time of admission is negatively correlated with severe cerebral infarct in cases presenting with acute ischemic stroke. Considering these findings, serum calcium levels can be used a prognostic tool and can be used as a useful parameter for improvement of outcome in stroke cases.[5]

Ovbiagele B et al, evaluated the impact of Calcium levels on clinical outcomes from acute ischemic

stroke through (NIHSS) score(r=-0.30, p=0.000). They concluded that serum $Ca^{(2+)}$ appear to be prognostic significance.[6]

Rationale of this study is to assess the correlation between severity of ischemic stroke and calcium level in patients presented with acute ischemic stroke. Acute ischemic stroke is an important cause of mortality and morbidity and the functional outcome is related to severity of the disease which in turn depends on infarct size, which can be predicted by measuring serum calcium which is cost effective test and by this way we can predict the morbidity and mortality of patients at time of admission.

Literature is also evident that low calcium level can cause more severe level of stroke. But not much literature is present which showed the correlation between calcium level and stroke severity using NIHSS criteria except one. Local estimates are also missing and on the basis of that often physicians do not recommend calcium assessment which may predict the prognosis of stroke patients. So we want planned this study to assess the correlation between calcium level and stroke severity so that we may gain local magnitudes which can be reliable. This may help physicians to improve practice and guidelines for management of stroke patients even during hospital stay.

MATERIAL & METHODS

This descriptive case series study was conducted in South Medical and East Medical Ward of Mayo hospital, Lahore from 5th January 2015 to 4th January 2016. Sample size of 100 cases was calculated with 5% type I error, 10% type II error and taking magnitude of correlation coefficient i.e. r=-0.3 0 between calcium level and NIHSS score in cases presenting with acute ischemic stroke.

Sampling technique was of non-probability, and purposive type. Patients of either gender of age 30-70 years of age with acute ischemic stroke (as per operational definition) presenting in emergency within 24 hours of the onset of symptoms were included. All patients with history of hemorrhagic stroke, patients with history of previous ischemic stroke, patient already taking calcium supplements (through medical record) and patients taking drugs that can effect serum calcium levels e.g. phenytoin, diuretics etc. (through medical record) were excluded.

100 patients who fulfill the inclusion criteria were identified and included in the study from emergency department of Medicine, Mayo hospital, Lahore. Informed consent was obtained from attendants of patients. Demographic record (name, age, sex, contact) were also obtained. Then patients were admitted in ward and were followed up there. Meanwhile no calcium supplement was advised. Then after 72 hours of admission, blood sample were drawn and were sent to the laboratory of the hospital to assess serum calcium level. NIHSS score after 72 hours of admission were assessed and noted (as per operational definition). All this information was recorded on proforma (attached).

Statistical analysis was carried out by using SPSS version 16. Quantitative variables like age, calcium level and NIHSS score was calculated as mean and standard deviation. Qualitative variables like gender were calculated as frequency and percentage. Pearson correlation coefficient was calculated to measure the correlation between calcium level and NIHSS score. P-value≤0.05was considered as significant.

RESULTS

Total 100 patients were enrolled in this study with the mean age of 51.47±9.653 years with minimum and maximum ages of 12 and 67 years respectively. Table-I

Age (years)	N	100
	Mean	51.47
	SD	9.65
	Minimum	35
	Maximum	67

Table-I. Descriptive statistics of age in years

The study results showed that 76% patients were males whereas 24% patients were females. Figure-1

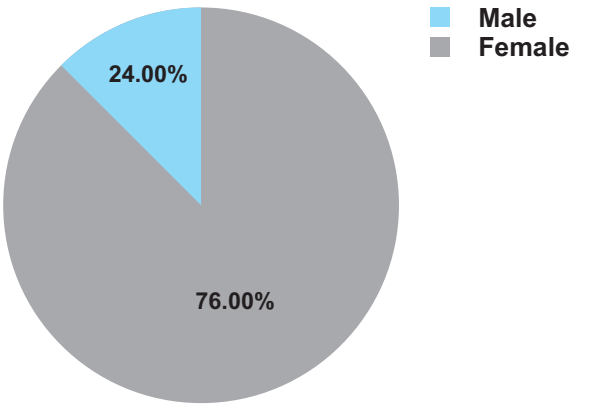

Figure-1. Distribution about gender of the patients

In this study the mean serum calcium level after 72 hours of the patients was noted as 7.26±1.41 mg/dl with minimum and maximum values of 5 & 10 mg/dl respectively. Table-II

Serum Calcium level (mg/dl)	N	100
	Mean	7.26
	SD	1.41
	Minimum	5
	Maximum	10

Table-II. Descriptive statistics of serum calcium level after 72 hours

In this study the mean NIHSS after 72 hours of the patients was noted as 23.01±10.38 with minimum and maximum values of 11 & 45 respectively. Table-III

NIHSS after 72 hours	N	100
	Mean	23.01
	SD	10.38
	Minimum	11
	Maximum	45

Table-III. Descriptive statistics of NIHSS after 72 hours

Our study results showed the negative and significant correlation between the serum calcium level (mg/dl) after 72 hours and NIHSS after 72 hours of the patients i.e. r=-0.899, p=0.000. Figure-2

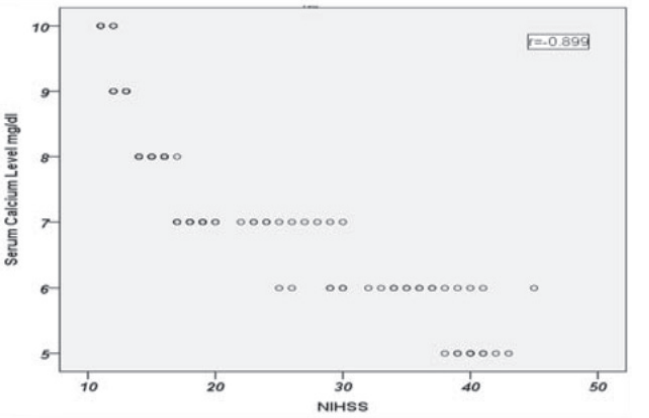

Figure-2. Correlation between serum calcium level and NIHSS

DISCUSSION

This present study was conducted at South Medical ward & East Medical Ward Department of Medicine, Mayo hospital, Lahore to assess the correlation between severity of ischemic stroke on NIHSS and calcium level in patients presented with acute ischemic stroke.

Only few studies evaluated prognostic significance of serum calcium levels in cases with acute stroke. Stroke is associate with a tremendous burden of cost to the society. Most strokes are ischemic, but about 15% of strokes are caused by intra-cerebral or subarachnoid hemorrhage.[7-9]

Previous data reveal that higher levels of serum calcium at 72-96 hrs of ischemic stroke are associated with higher three months functional independence scores. However, elevated serum calcium levels recorded on interval of 72 to 96 hrs, the index stroke was found with better functional activity at 3 months, but the relationship could not recorded with significant difference. Previously, two single center studies revealed that clinical outcome is better with elevated serum calcium levels.[8-10]

In this study, mean NIHSS after 72 hours of the patients was 23.01±10.38with range of 11-45and serum calcium level after 72 hours of the patients was noted as 7.26±1.41 mg/dl. Sharma V et al revealed that higher levels of serum calcium are associated with less severity of acute ischemic stroke and also recorded a favorable outcome

in these cases at 7 days.[11] In our study, there is negative correlation found between the calcium level and NIHSS of the patients i.e. r = -0.899.

Bruce Ovbiagele et al correlation analyses showed early Ca2+ correlated weakly with baseline NIHSS score (r=−0.05, P=0.21); 72- to 96-hour NIHSS score (r=−0.10, P=0.01); NIHSS (72- to 96-hour NIHSS score–baseline NIHSS score, r=−0.09, P=0.04); and 72- to 96-hour Barthel Index score (r=0.11, P=0.008). Delayed Ca2+ showed stronger correlations with baseline NIHSS score (r=−0.2, P=0.0001); 72- to 96-hour NIHSS score (r=−0.3, P<0.0001).[6] They were also of the view that calcium levels recorded at early stage of stroke i.e. <5 hours have no prognostic association but higher levels at 72-96 hrs of stroke are significantly associated with good clinical outcome during 3rd month of stroke.[7]

Brian H et al are of the view that elevated serum calcium levels recorded at the time of admission are associated with smaller volume of cerebral infarction cases presenting with acute ischemic stroke.[5]

Few of the epidemiological trials linked higher dietary calcium intake to reduce mortality in ischemic and hemorrhagic stroke cases.[12-13]

Guven H et al showed that NIHSS scores were recorded higher in those cases which consist of lower Ca levels when compared to others (p value was < 0.05 and< 0.001 respectively), and they were found to be higher in group 2 than group 3 (p = 0.029). mRS scores at discharge showed no differences between groups.[4]

Further, two studies evaluated prognostic significance of calcium levels in ischemic stroke cases and recorded a better functional outcomes in those cases having elevated levels Ca2 at the time of admission while significantly higher rate of mortality in those with lower levels of Ca^2 during hospitalization as compared to the survivors.[8-10] Peuler J Det al, in an experimental study, a significant lower histological damage due to ischemia and mortality was recorded in rats administered with calcium infusion.[14] Cerebral ischemia causes at least temporary depletion of extracellular Ca because of Ca influx and intracellular Ca accumulation.[15-16] However, it is still to be clear that whether the rate of this decrease is adequate to account for the decreased calcium levels recorded in cases with infarction.[17]

Buck BH et al showed the mean age of the patients 70.3 years with range of 24 to 100 years and the median National Institutes of Health Stroke Scale score, 4 [range, 0-38]), and The median DWI infarct volumes for the serum calcium level quartiles (lowest to highest quartile) were 9.42, 2.11, 1.03, and 3.68 mL.[17]

CONCLUSION

Our study results showed the negative correlation between the serum calcium level and NIHSS of ischemic stroke patients which showed that more decrease in calcium level will lead to more severe condition of stroke. Moreover, we have got local magnitude. Now it will help us to predict the prognosis of such critical cases.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Lal Badshah	Review of literature	
2	Asim Khan	Data collection	
3	Shahida Malik	Data analysis	