

To Determine the Frequency of Hypomagnesemia among patients with Acute Ischemic Stroke and to Study the Correlation of Serum Magnesium with Modified Rankin Scale After Acute Ischemic Stroke

KHALID MAHMUD KHAN, FAIZA NAEEM, RASHID IQBAL*, ZAHID HUSSAIN SHAH, RASHID ALI, NOOMAN GILANI

ABSTRACT

Aim: The objective of this study is. "To determine the frequency of hypomagnesemia among patients with acute ischemic stroke and to study the correlation of serum magnesium with Modified Rankin Scale after acute ischemic stroke."

Study design: It is a cross sectional study.

Setting: Indoor patients, departments of Medicine, Mayo Hospital, Lahore

Duration of study: Six months from "15th May 2014 to 15th November 2014"

Methodology: 200 patients with acute ischemic stroke fulfilling the inclusion criteria were selected. 2ml venous sample for serum magnesium level was taken 1st 6 hour of stroke. Presence or absence of hypomagnesemia in patients after acute ischemic stroke was recorded during hospital stay of patients, receiving standard management protocol of ischemic stroke. The correlation co-efficient of serum magnesium level with Modified Rankin Scale was calculated through SPSS-17 as Pearson Correlation. $P < 0.05$ was taken as significant.

Results: The mean age of patients was 52.65 ± 10.66 years. There were 134(67%) male while 66(33%) were females. The male:female ratio was 2.03:1. The mean magnesium level in all the patients was measured as 1.71 ± 0.51 mg/dl. Hypomagnesemia was found in 32% of patients. The mean MRS score in all the patients was measured as 3.22 ± 1.27 . In this study, the correlation coefficient between magnesium level and MRS score was found as $r = -0.674$ which showed negative relationship between magnesium and MRS.

Conclusion: It was concluded through the results of this study that low levels of magnesium in the body can cause more severe stroke as relationship is strong between low magnesium level and severity of stroke.

Keywords: Stroke, serum magnesium, Hypomagnesemia, Modified Rankin scale.

INTRODUCTION

World Health Organization defines stroke as event caused by the interruption of the blood supply to the brain, usually due to bursting of a blood vessel or its blockage by a clot¹. A local study conducted in Kohat, reported that 64% of strokes are due to cerebral infarction and 36% due to bleed². Stroke is one of the leading causes of mortality and morbidity worldwide and the third most common cause of death in developed world³. The National Health Survey of Pakistan, conducted by Pakistan Medical Research Council, reported that estimated annual incidence of stroke in Pakistan is 25/100,000, projecting an estimate of 350,000 new cases every year^{4,5}.

Common modifiable risk factors for stroke in Pakistan are hypertension (73%), diabetes mellitus (42.5%), coronary artery disease (38%), smoking

(29%), obesity (27%), atrial fibrillation (22%), dyslipidemias (11.8%)⁶. During the last fifteen years, many researchers have identified hypomagnesaemia as an etiological factor for Ischemic stroke. Hypomagnesemia is reported to be found in 24% patients of acute ischemic stroke⁷. Westermaier et al, have studied the role of magnesium therapy in improving the neurological outcome in patients after stroke⁸. Odom et al, from Vanderbilt University, USA have reported 10 RCTs conducted between 2002-2013 proving a role of Hypomagnesemia in the causation and treatment of Stroke⁹.

Hypomagnesemia causes cellular injury and consequently can influence prognosis of ischemic stroke because lower serum magnesium causes greater neurological disability. Magnesium infusion could improve cerebral blood flow through arteriolar vasodilation¹⁰.

Department of Medicine, SIMS*, Mayo Hospital/K E MU, Lahore
Correspondence to Dr. Khalid Mahmud Akhan, Associate
Professor Email: drkm71@yahoo.com Cell: 0300-4167291

Ohira et al followed 14,221 men and women aged 46-64 years for 15 years. During 15-year follow up, 577 ischemic strokes occurred. Serum magnesium was inversely associated with ischemic stroke incidence¹¹.

The modified Rankin Scale is commonly used to measure the degree of disability in daily activities of patients after stroke. This scale runs from 0-6, "0" depicting perfect health and "6" signifying death¹². Studies conducted in Iran has suggested reciprocal statistical correlation between serum magnesium and modified Rankin scale in first 72hrs (P=0.000, r=0.73) and in one week (p=0.002, r=0.693) after an acute ischemic stroke¹³. On the contrary, a study conducted in Lublin showed no statistical relationship between hypomagnesaemia and neurological outcome after an acute ischemic stroke (r=0.04, p>0.1)¹⁰.

Previously most of the studies were done to determine hypomagnesaemia as a risk factor for stroke^{9,11}. Frequency of Hypomagnesaemia and its correlation with Modified Rankin Scale after acute ischemic stroke has not been studied in the Pakistani Population as yet. And because of discrepancies in the results of other previous studies conducted elsewhere, we want to undertake this study to evaluate role of Hypomagnesemia in stroke in Pakistani milieu by studying its frequency and correlation with Modified Rankin Scale to develop a better management protocol for ischemic stroke.

MATERIAL AND METHODS

It is a cross sectional study conducted on the indoor patients of the Departments of Medicine, Mayo Hospital, Lahore for a period of 6 month from "15th, May 2014 to 15th November 2014".The sample size was calculated 200 cases using 95% confidence level, 6% margin of error taking an expected percentage of hypomagnesemia as 24%¹⁴. In patients after acute ischemic stroke and correlation of hypomagnesemia with modified Rankin scale at 72hr after an acute ischemic stroke r=0.73¹⁷. Non probability purposive sampling technique was used. Both male and female patients of 35 year of age and above with acute ischemic stroke (as per operational definition) presenting in first 6 hours of attack.

Exclusion criteria:

- Old cerebral infarct (diagnosed on history and computed tomography of brain)
- Hemorrhagic infarct (diagnosed on history and computed tomography of brain)
- Other neurological disorders (e.g. epilepsy, neurodegenerative or demyelinating disease etc., diagnose on history, examination, electroenceplogram, nerve conduction studies, CT-brain, MRI-brain etc).

- Psychiatric diseases (diagnosed on history and drug history)
- Medical disorders: Renal diseases, liver diseases, thyroid disorder, malignant diseases (diagnosed on history, examination, complete blood count, renal function, liver function, abdominal ultrasonography, urine complete examination).

After obtaining approval from Hospital Ethical Committee, 200 patients with acute ischemic stroke fulfilling the inclusion criteria were selected from indoor of departments of medicine, Mayo Hospital Lahore. The purpose of the study was explained to each patient or attendant and informed consent was obtained. The demographic history and detailed examination and laboratory parameters of ischemic stroke were entered in a predesigned Performa. 2ml venous sample for serum magnesium level was taken in 1st 6 hour of stroke. Presence or absence of hypomagnesaemia in patients after acute ischemic stroke was recorded. Modified Rankin Scale at 72 hours after ischemic stroke was recorded during hospital stay of patients, receiving standard management protocol of ischemic stroke.

All the data was analyzed by SPSS version 17 and the quantitative variables of the study like age, serum magnesium and score on Modified Rankin scale were presented as mean and standard deviation. The qualitative variables like gender and hypomagnesaemia were presented as frequency and percentages. The correlation co-efficient of serum magnesium level with Modified Rankin Scale was calculated through SPSS-17 as Pearson Correlation. P< 0.05 was taken as significant.

RESULTS

In this study we included 200 cases of acute ischemic stroke There were 134 (67%) male while 66 (33%) were females. The male-to-female ratio was 2.03:1. The minimum age of patients was 36 years and maximum age of patients was 70 years with the mean age of 52.65± 10.66 years.The mean age of male patients was 53.52±10.65 years (range 36-70 years) and the mean age of female patients was 50.88±10.54 years (range 36-70 years) as shown in table-1.

Table1:Descriptive statistics of age (years) both genders

Age (years)	Male	Female
N	134	66
Mean	53.52	50.88
SD	10.65	10.54
Minimum	36	36
Maximum	70	70

The mean magnesium level in all the patients was measured as 1.71±0.51mg/dl. The minimum magnesium level was 0.5mg/dl and maximum magnesium level was 2.3mg/dl. The mean magnesium level of male patients was measured as 1.71±0.52mg/dl (range 0.5-2.3) and the mean magnesium level of female patients was measured as 1.72±0.51mg/dl (range 0.5-2.3). There was insignificant difference observed between both genders (P>0.05). Out of 200 patients, there were 64(32%) patients who developed hypomagnesaemia while 136(68%) patients did not have hypomagnesaemia. Among 134 male patients, 43(32.1%) developed hypomagnesemia while 91(67.1%) had normal magnesium level. Among 66 female patients, 21(31.8%) developed hypomagnesemia while 45(68.2%) had normal magnesium level. There was insignificant difference observed between both genders for presence of hypomagnesaemia.

Table 2: Distribution of hypomagnesemia in both genders

Hypomagne-saemia	Male	Female	Total
Yes	43 (32.1%)	21(31.8%)	64(32%)
No	91 (67.1%)	45(68.2%)	136 (68%)

Chi-square = 0.001, p-value = 0.969 (insignificant)

The mean MRS score in all the patients was measured as 3.22±1.27. The minimum MRS score was 1 and maximum MRS score was 6. The mean MRS score of male patients was measured as 3.22±1.32 (range 1-6) and the mean MRS score of female patients was measured as 3.24±1.18 (range 1-5). There was insignificant difference observed between both genders (P>0.05). There were 9(4.5%) patients who had MRS 1, 62(31%) had MRS 2, 54(27%) had MRS 3, 30(15%) had MRS 4, 40(20%) had MRS 5 and 5(2.5%) had MRS 6. In this study, the correlation coefficient between magnesium level and MRS score was found as r=0.674 which showed negative relationship between magnesium and MRS. The magnesium level has significant effect on MRS score of stroke patients.

DISCUSSION

Cerebral thrombosis is the most common type of stroke, and hemiplegia is most common somato-neurological presentation encountered clinically¹⁴. Lower plasma magnesium levels may be associated with higher blood pressure and endothelial dysfunction, but sparse prospective data are available for stroke. It has been proved through few studies that low plasma magnesium levels may contribute to higher risk of ischemic stroke¹⁵.

It has been also reported that men are at higher risk for stroke than women; white men have a stroke incidence of 62.8 per 100,000, with death being the final outcome in 26.3% of cases, while women have a stroke incidence of 59 per 100,000 and a death rate of 39.2%^{16,17}. In our study, there were 134(67%) male while 66(33%) were females. The male-to-female ratio was 2.03:1. In our study, the presentation of male cases was more as compared to females.

Serum magnesium is an indispensable element for man. It is indispensable activator of over 300 enzymes in human. Hypomagnesaemia leads to neuromuscular hyperirritability, tremors, increases vascular resistance, coronary vasospasm and hypertension. Magnesium deficiency triggers vasoconstriction, enhances vascular endothelial injury and hence leads to atherosclerosis¹⁸.

Romero et al., found that Hypomagnesemia is found in 24% patients of ischemic stroke¹⁴. Kaur et al., reported mean magnesium level in stroke patients was 2.07±0.47mg/dl¹².

Studies conducted in Iran has suggested reciprocal statistical correlation between Serum magnesium and modified Rankin scale in first 72hrs (P=0.000, r=0.73) and modified Rankin scale in one week (p=0.002, r=0.693) after an acute ischemic stroke¹³.

On the contrary, a study conducted in Lublin showed no statistical relationship between hypomagnesaemia and neurological outcome after and acute ischemic stroke (r=0.04, p>0.1)¹⁰. Ohira et al followed 14,221 men and women aged 46-64 years for 15 years. During 15- year follow up, 577 ischemic strokes occurred. Serum magnesium was inversely associated with ischemic stroke incidence.¹¹ In our study the mean magnesium level in all the patients was measured as 1.71±0.51mg/dl and 64(32%) patients had hypomagnesaemia while 136 (68%) patients had normal magnesium level. The mean MRS score in all the patients was measured as 3.22±1.27. There were 9(4.5%) patients who had MRS 1, 62(31%) had MRS 2, 54(27%) had MRS 3, 30(15%) had MRS 4, 40(20%) had MRS 5 and 5(2.5%) had MRS 6.

In our study, we also calculated the correlation coefficient between magnesium level and MRS score as r=0.674 which showed negative relationship between magnesium and MRS. The magnesium level has significant effect on MRS score of stroke patients. This showed that if magnesium level decreases in the body, then stroke will be more severe.

CONCLUSION

It was concluded through results of this study that low magnesium level in body can cause more severe stroke as relationship is strong between low magnesium level and severity of stroke. Moreover, we have resolved the discrepancy present in previous literature and found high prevalence of hypomagnesaemia in stroke patients.

REFERENCES

1. Stroke, Cerebrovascular accident-World Health Organization. [Online] 2012 [cited 2013]. Available from: URL:<http://www.who.int/topic/cerebrovascular-accident/>.
2. Kamal A, Aslam S, Khattak S. Frequency of risk factors in stroke patients admitted to DHQ teaching hospital D.I. KHAN. *Gomal J Med Sci* 2010;8(2):200-3.
3. Feigin VL, Laws CM, Bennett PA, Barbercollo SL. Worldwide Stroke incidence and early case fatality reported in 56 population-based studies. *Lancet Neurol* 2009;8:355-69.
4. Khatri IA, Wasay M. Can we stop the stroke epidemic in Pakistan. *J Coll Physician Surg Pak* 2011;21(4):195-6.
5. Farooq MU, Majid A, Reeves MJ, Birbeck GL. The epidemiology of stroke in Pakistan: past, present, and future. *Int J Stroke* 2009;4(5):381-9.
6. Mahmood T, Anjum SM, Iqbal S, Kalsoom N, Manzoor H. Evaluation of risk factors in ischemic stroke. *J Rawal Med Coll* 2013;17(1):138-9.
7. Romero FR, Neto BG, Munhoz GA, Figueiredo EG. Serum magnesium levels and neurological outcome after acute ischemic stroke. *Rev Neurociencia* 2012;20(3):468-72.
8. Westermaier T, Stetter C, Kunze E, Willner N, Raslan F, Vince HG, et al. Magnesium treatment for neuroprotection in ischemic diseases of brain. *Exp Transl Stroke Med* 2013;5(6):1-10.
9. Odom MJ, Zuckerman SL, Mocco J. The Role of Magnesium in the Management of Cerebral Vasospasm. *Neurol Res Int* 2013;2013:943914.
10. Kurzepa J, Bielewicz J, Grabarska A, Stepulak A, Psujek BH, Stelmasiak Z. Magnesium level in serum during acute ischemic stroke the relationship with neurological status and Tau protein serum level. *Ann umcs Lublin* 2009;1(11):69-75.
11. Ohira T, Peacock JM, Iso H, Chambless LE, Rosamond WD, Folsom AR. Serum and dietary magnesium and risk of ischemic stroke; The atherosclerotic risk in community study. *AM J Epidemiol* 2009; 169(12):1437.
12. Modified Rankin Scale [online] 2013 [cited 2013, March 11]. Available from: URL:http://www.en.wikipedia.org/wiki/Modified_Rankin_Scale.
13. Saberi A, Hatamian HR, Smaelizadeh K, Heydarzadeh A. The relationship between magnesium level and first 72 hours Rankin score and Rankin score in one week after an ischemic stroke. *Ir J Neurol* 2011; 10(1-2):26-28.
14. Singh H, Jalodia S, Gupta M, Talapatra P, Gupta V, Singh I. Role of magnesium sulfate in neuroprotection in acute ischemic stroke. *Annals of Indian Academy of Neurology* 2012;15(3):177.
15. Akarolo-Anthony SN, Jimenez MC, Chiuve Se, Spiegelman D, Willett WC, Rexrode KM. Plasma Magnesium and Risk of Ischemic Stroke Among Women. *Stroke* 2014;45(10):2881.
16. Fonarow GC, Saver JL, Smith EE, Broderick JP, Kleindorfer DO, Sacco RL, et al. Relationship of National Institutes of Health Stroke Scale to 30-day mortality in Medicare beneficiaries with acute ischemic stroke. *Journal of the American Heart Association* 2012;1(1):42-50.
17. Schneider AT, Kissela B, Woo D, Kleindorfer D, Alwell K, Miller R, et al. Ischemic stroke subtypes A Population-based study of incidence rates among blacks and whites. *Stroke*. 2004;35(7):155-6.
18. Kaur J, Prabu KM, Thakur LC. Serum Magnesium level in ischemic cerebrovascular disorder-control pilot study in north India population. *J Pharm Biomed Sci* 2012;17(02):1-4.