



Original Article

Serum Magnesium Level among the Patients Admitted with Acute Stroke in a Tertiary care Hospital

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Abstract

Magnesium deficiency was shown to trigger vasoconstriction and enhance vascular endothelial injury, thus promoting the development and progression of atherosclerosis. We hereby intended to investigate serum magnesium in the early stage of acute stroke and to evaluate the relationship between serum magnesium concentration and the development of neurological deficits. This is a descriptive type of cross sectional study was carried out in department of medicine, Comilla Medical College Hospital from June 2013 to December 2013. Fifty admitted acute stroke patients were randomly chosen for this study who fulfills inclusion criteria. The serum magnesium concentrations were measured by photometric colorimetric end point method on admission. Out of 50 acute stroke patients 30 (60%) were male and 20 (40%) were female. The mean age is 66.44 (SD \pm 14.8) years with male predominance. Most of the patients 30 (60%) belongs to above 60 years and 36 (72%) patients had hypomagnesaemia and 14 (28%) had normal serum magnesium level. Serum magnesium level more low in ischemic stroke (56%) . The mean serum magnesium level was 1.59 (SD \pm 0.37) mg/dl in all stroke patient and 1.47 (SD \pm 0.32) mg/dl in ischemic stroke patient was and was 1.83 (SD \pm 0.34) mg/dl in hemorrhagic stroke patients. Among 33 ischemic stroke patients mostly 17 (34%) patients had serum magnesium level between 1.0-1.4 mg/dl and in hemorrhagic stroke patients maximum 05 (10%) serum magnesium level was in between 1.5-1.8 mg/dl (P-value 0.0017 HS). In our study most of the patients with acute stroke were improved with marked residual disability were [19 (38.0%)], improved with minimal residual disability were [08 (16%)], improved without residual disability [04 (08%)] and death [03 (6%)] having hypomagnesaemia compared to the patients who have normal serum magnesium level with maximum improvement with minimal residual disability were [10 (20.0%)], improved without residual disability were [06 (12%)], improved with marked residual disability and death were [0 (0%)]. Gross clinical outcome disability of acute stroke patients was worse who had hypomagnesaemia (P-value 0.001 significant). Magnesium levels are significantly decreased in acute stroke; both in ischemic stroke patients as well as in patients of hemorrhagic. Patients with low serum magnesium level in acute stroke associated with worse clinical outcome.

Key word: Serum magnesium, acute stroke

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Introduction

Stroke is a major cause of morbidity and mortality.¹ It is one of the most common

neurological disorder and third most common cause of death in the developed world after heart disease and cancer, after the age of 40.^{2,3} About

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one fifth of patient with stroke will die within a month of event and half of those who survive will be left with physical disability.⁴ Stroke is the predominant vascular disease in many parts of Asia.⁵ The World Health Organization (WHO) estimates that by 2030, 80% of strokes will occur in people living in low and middle income countries, and stroke will account for 7.9% of all mortality in low income countries, coming a close third after ischemic heart disease and HIV/AIDS. The world wide incidence of stroke has been quoted as 2/1000 population/annum; about 4/1000 in people aged 45-84 years.^{6,7} A WHO study, in 1990 quoted incidence of mortality due to stroke in India to be 73/100,000 per year.⁸ Magnesium is a natural calcium antagonist and modulates vasomotor tone, blood pressure, and peripheral blood flow. In the brain magnesium is predominantly complexed with adenosine triphosphate(ATP).⁹ Magnesium deficiency was shown to trigger vasoconstriction and enhance vascular endothelial injury, thus promoting the development and progression of atherosclerosis.¹⁰ Magnesium prevent the development of atherosclerosis by inhibiting lipid accumulation in the aortic wall.¹¹ Diabetes mellitus is usually associated with hypomagnesia¹² and therefore may be accompanied by atherogenic alteration in the blood lipid composition¹³ and increased morbidity from cardiovascular diseases.¹⁴ In the Atherosclerotic Risk in Communities [ARIC] study, serum magnesium levels were inversely related with the incidence of hypertension and stroke but dietary magnesium levels were not.^{15,16} During a stroke, the massive amount of glutamate released produces a flood of calcium inside brain cells which in turn causes them to die prematurely. Magnesium is thought to have the ability to prevent glutamate from causing this flood calcium in the cells, thus protecting them from premature death.¹⁷ Physiological extracellular Mg²⁺ level (up to 1 mmol/l) inhibit glutamate release and specifically antagonize NMDA receptors.¹⁸ Magnesium, an important cofactor in metabolism and protein synthesis, joins into a complex with adenosine triphosphate acting as a noncompetitive NMDA receptor blocker; it inhibits the release of excitatory neurotransmitters at the presynaptic level and blocks voltage-gated calcium channels¹⁹ Prophylactic use of magnesium can inhibit the

disability in persons that will be involved by ischemic stroke in future and can reduce social emotional and economical loses among them.²⁰ The aim of this study was to know the relationship between serum magnesium level and in patients with acute stroke and also note its association with the outcome.

Material and Methods

This study was a descriptive type of cross sectional study and was conducted in the department of Medicine Comilla Medical College Hospital, Comilla from June 2013 to December 2013. A total 50 adult patients both sex , with acute stroke who were admitted in department of Medicine of Comilla Medical College Hospital who has fulfilled the inclusion criteria were taken in the study. Inclusion criteria was , patients admitted in adult ward of Comilla Medical College Hospital with acute stroke confirmed by clinical finding and CT scan or MRI of brain and who consented to participate, patient having aged 18 years irrespective of gender. Patient not willing to participate in my study,stroke patient having any malignancy, renal impairment, GIT & other endocrine disorder, patient on diuretic therapy were excluded from the study. Purposive non-probability sampling technique was used for data collection. Informed consent was obtained and the data were obtained in a predesigned and pretested questionnaire. All the patients were assessed by taking complete history and clinical examination both general and systemic examination.

Thorough physical examination and CT scan of brain was done in all patients. Blood serum magnesium was measured using photometric colorimetric end point method (Human Gesellschaft furb Biochemica and Diagnostica mbH, Germany).

Results

The outcome of the study was as follows:

The maximum number of patients 30 (60.0%) in this study were above 60 years followed by 12 (24.0%) between the age of 51-60 years, 7 (14.0%) between the age of 41-50 years, 01 (2.0%) between the age of 21-30 years and 0 (0%) between 18-20 years and 31-40 years. The age of

the patients ranged from 21 to 90 years with the mean age of 66.44 (SD \pm 14.8) years. The age of the male patients ranged from 40 to 90 years with the mean age of 66.26 (SD \pm 12.80) years; while the age of the female patients ranged from 21 to 90 years with the mean age of 66.20 (SD \pm 17.90 years). The mean age of the male patients was slightly higher than that of female patients.(Table I)

Table I Age distribution of the patients (n=50)

Study group	Age in years		
	Range	Mean	Standard deviation
Total (n-50)	21-90	66.22	14.8
Male (n-30)	40-90	66.26	12.80
Female (n-20)	21 -90	66.15	17.90

A total of 28 (56%) of the ischemic stroke patients and 08 (16%) hemorrhagic patients had hypomagnesaemia (P-value 0.0009), 05 (10%) ischemic stroke and 09 (18%) hemorrhagic stroke patients had normal serum magnesium level.(Table II)

Table II Serum magnesium levels in different type of stroke

Serum magnesium	Ischemic stroke		Hemorrhagic stroke		P-value
	Number	Percentage	Number	Percentage	
Normal	05	10	09	18	0.285
Hypomagnesaemia	28	56	08	16	0.0009

The serum magnesium level of ischemic and hemorrhagic stroke patients were categorized into four categories. Out of 50 patients among 33 ischemic stroke 17 (34%) patients serum magnesium level were between 1.0-1.4 mg/dl followed by 11 (22%) were in between 1.5-1.8 mg/dl, 04 (08%) were between 1.9-2.0 mg/dl and 01 (02%) were of $>$ 2.0 mg/dl level. Among 17 hemorrhagic stroke , 03 (06%) patients serum magnesium level were between 1.0-1.4 mg/dl followed by 05 (10%) were in between 1.5-1.8 mg/dl, 03 (06%) were between 1.9-2.0 mg/dl and 06 (12%) were of $>$ 2.0 mg/dl level. (P-value were significant).(Table III)

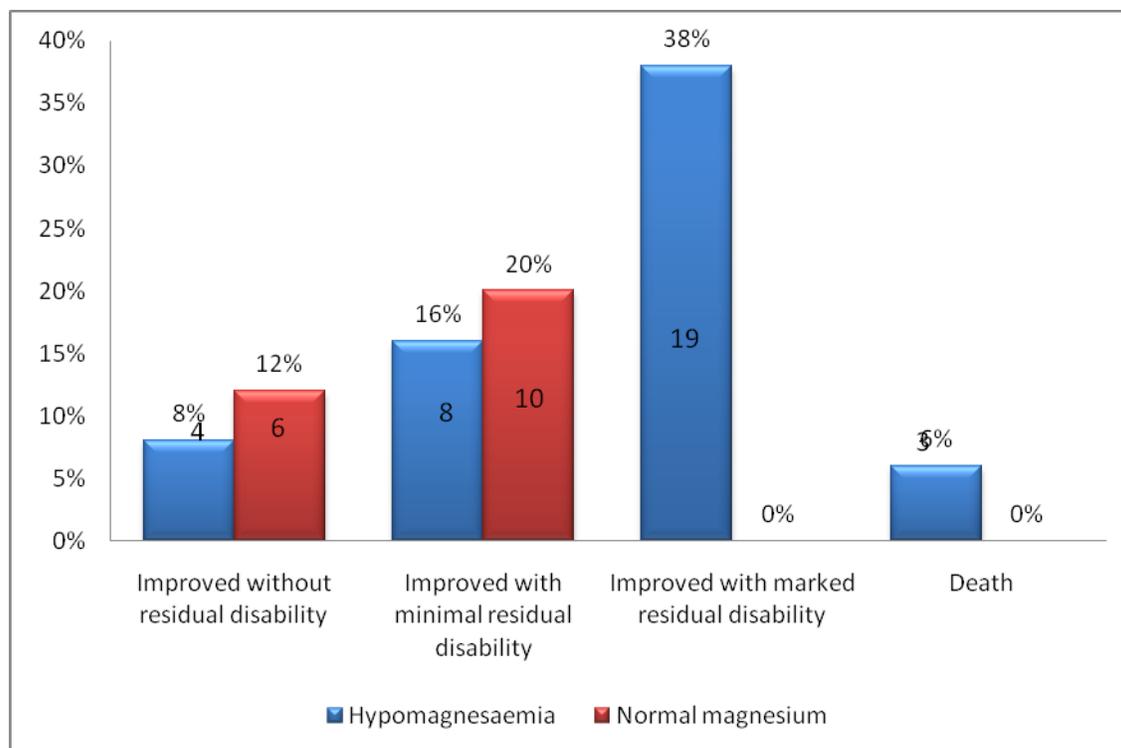
Table III Comparison of serum magnesium level between Ischemic and hemorrhagic stroke

Serum magnesium (mg/dl)	Ischemic stroke		Hemorrhagic stroke		P-value
	Number	Percentage	Number	Percentage	
1.0-1.4	17	34	03	06	0.0017
1.5-1.8	11	22	05	10	0.1336
1.9-2.0	04	08	03	06	0.705
$>$ 2.0	01	02	06	12	0.0588

Effect of serum magnesium levels on acute stroke patient's outcome was shown in this figure 1. Most of the patients with acute stroke were improved with marked residual disability [19 (38.0%)], improved with minimal residual disability were 08 (16%), improved without residual disability were 04 (08%) and

death were 03 (6%) , having hypomagnesaemia compared to the patients who have normal serum magnesium level maximum [10 (20.0%)] improved with minimal residual disability, 06 (12%) were improved without residual disability, improved with marked residual disability and death were [0 (0%)]. Gross clinical outcome disability of acute stroke patients was worse who had hypomagnesaemia. P-value (0.001) was significant.

Figure 1 Effect of serum magnesium levels on acute stroke patient’s outcome



Discussion

In this present study, out of 50 patient , the age of the patients ranged from 21 to 90 years with the mean age of 66.44 (SD ± 14.8) years. The age of the male patients ranged from 40 to 90 years with the mean age of 66.26 (SD ± 12.80) years, while the age of the female patients ranged from 21 to 90 years with the mean age of 66.20 (SD ± 17.90) years and amongst the 50 patients, 30 (60%) are males and 20 (40%) are females with a ratio of male to female was 1.5:1. The mean age of the patients was significantly higher in stroke patients and male predominance.

This observation matches with a study done in north India.²¹ In the Kaur Jaspreet et al study, 50

diagnosed cases of acute ischemic stroke, 10 cases of TIA and 60 age and sex matched healthy controls. Among 50 patients of acute ischemic stroke in the age group of 40 to 89 years whereas the presenting age group of patients with transient ischemic attack was 50-89 years. This study carried out in north Indian population supported the result that the average age of the stroke patients were found to be above 50 years but below 80 years. 40% of Cases were recorded in the sixth decade. This is in accordance with the Indian²² as well as western studies .²³

Among 50 acute stroke patients 36 (72%) patients had low serum magnesium and 14 (28%) had normal serum magnesium level. Male patients had more hypomagnesaemia 22 (61.2%) than female

14 (38.8%). Serum magnesium level more low in ischemic stroke 28 (56%) patients out of 33 patients than hemorrhagic stroke 08 (16%) out of 17 patients. This study shows that ischemic stroke as well as hemorrhagic stroke patients, the serum magnesium levels were significantly lower. Kaur J et al., Conducted a study on 120 patients, which includes 50 patients with stroke, 10 transient ischemic attacks and 60 age and sex matched controls, stated that serum magnesium levels are reduced in ischemic strokes, hemorrhagic strokes and transient ischemic attacks when compared to controls and significant decrease in serum magnesium levels was seen in patients with ischemic stroke, the levels of serum magnesium are observed to be further decreased in cases of ischemic stroke patients when compared with hemorrhagic stroke Cases.²¹ which is almost similar to our present study.

In the present study of 50 patients, the mean serum magnesium level in all 50 patients was 1.59 (SD ± 0.37) mg/dl and among 33 ischemic stroke patients was 1.47 (SD ± 0.32) mg/dl, 17 hemorrhagic stroke patients was 1.83 (SD ± 0.34) mg/dl. It is quite similar to a recent North Indian study which reported ischemic Stroke (42 cases) mean serum magnesium $2.05 \pm .48$, Hemorrhagic stroke (8 cases) $2.19 \pm .48$ ($P > 0.05$).²¹ Kaur J et al study reviewed of 60 consecutive patients with an admission criteria of acute stroke. Serum magnesium level were low in patients who had acute stroke (mean 2.07 ± 0.47 mg/dl, $P < 0.001$) but not in the control group (mean 3.58 ± 0.16 mg/dl).²¹

Cojocarui IM et al. conducted a study on forty patients with acute ischemic stroke, which included 26 women and 14 men, and 21 sex- and age-matched controls, stated that serum magnesium levels were reduced in ischemic strokes, mean value of serum magnesium was 1.39 ± 0.213 mmol/L (on admission), 1.47 ± 0.181 mmol/L at 48 hours after the onset of stroke versus 1.66 ± 0.138 mmol/L in controls and severity of paresis degree was higher in the patients with low Mg levels ($p < 0.05$).²⁴ The finding is quite similar to our study.

In our study most of the patients with acute stroke were improved with marked residual disability [19 (38.0%)], improved with minimal residual disability [08 (16%)], improved without residual disability [04 (08%)] and death [03 (6%)] having hypomagnesaemia while patients who have normal serum magnesium level maximum [10 (20.0%)] improved with minimal residual disability, [06 (12%)] improved without residual disability, improved with marked residual disability and death were [0 (0%)]. Gross clinical outcome disability of acute stroke patients was worse who had hypomagnesaemia (P -value 0.001 significant). In the present study shows that patients with hypomagnesaemia during acute stroke has worsen clinical outcome. Cojocarui IM et al. study, serum magnesium level was measured in forty patients involved by ischemic stroke in the event and their neurologic deficits were assessed in first day and after 48 hours by NIHSS Scale and there was a significant statistical correlation between serum magnesium level in the first 48 hours after the stroke and patient ($P < 0.05$).²⁴ Saberi A et. al conducted a study on total of 67 ischemic stroke patients and stated that the serum magnesium level in the first hours after ischemic stroke or in better word before the event had reciprocal correlation with patient's disability in the first hours and 1 week after the stroke, but it didn't have any correlation with the mean of changes of disability score in this period of times.²⁵ It is worthy of attention that the results of this study is similar to our results, although their measure of disability assessment differed from our measure, (NIHSS vs. gross clinical outcome). But in another study assigned by Ovbiagele et al.; in 2009 in USA the admission magnesium level was not an independent clinical outcome prognosticator.²⁶

Conclusion

Cerebrovascular disease predominates in the middle and later years of life. Men are more prone to stroke compared to women. Incidences of stroke were observed more in 60-69 age groups. Magnesium levels are significantly decreased in acute stroke; both ischemic stroke patients as well as patients of hemorrhagic stroke also had

magnesium deficiency. The decrease of the magnesium serum level during the acute phase of stroke seems to correspond with worse neurological status. Further study is needed to confirm the association of dietary or serum magnesium with acute stroke in additional large prospective studies. Limitation of the study was, small sample size therefore the sample lacks representation of the population. The results were limited by the absence of a formal control group chosen from the population.

References

1. Bergen DC. The world wide burden of neurological disease. *Neurology* 1996; 47(1):21-5.
2. Weir CJ, Muir SW, Walters MR, Lees KR. Serum urate as an independent predictor of poor outcome and future vascular events after acute stroke. *Stroke* 2003; 34:1951-7.
3. Ropper AH, Brown RH. Cerebrovascular disease. Adam's and Victor's Principles of neurology. 8th ed. New York: McGraw-Hill; 2005:661-740.
4. Allen CMC, Lueck CJ, Dennis M. Neurological disease. In: Boon NA, Colledge NR Walker BR, Hunter JAA, eds. Cerebrovascular disease: Stroke. New York Churchill Livingstone: Davidson Principles & Practice of Medicine; 2006:1245-1256
5. Shi F, Hart RG, Sherman DG, Tegeler CH. Stroke in the People's Republic of China. *Stroke* 1989; 20:1581-5.
6. Murray CJL, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global burden of disease study. *Lancet* 1997; 349:1498-1504.
7. Mathers CD, Loncar D. Updated projections of global mortality and burden of disease, 2002-2030: data sources, methods and results. Evidence and information for policy working paper. Geneva: World Health Organization. *Plos Med* 2006; 3: 442.
8. Prasad K. Epidemiology of cerebrovascular disorders in India. In: Recent concepts in stroke by Bansal BC (ed) Indian college of Physicians, New Delhi; 1999:4-19.
9. Ebe H, Gunther T. magnesium metabolism: a review. *J Clin Chem. Clin Biochem* 1980;18:257-70.
10. Shivakumar K. Model of cardiovascular injury in magnesium deficiency. *Med Hypotheses* 2001; 56:110–13.
11. Ouchi Y, Tabata R, Stergiopoulos K, Sato F, Hattori A, Orimo H. Effect on dietary magnesium on development on magnesium on development of atherosclerosis in cholesterol-fed rabbits. *Arteriosclerosis* 1990; 10:732-7.
12. Sjogren A, Floren C, Nilsson A. Magnesium deficiency in IDDM related to the level of glycosylated hemoglobin *Diabetes* 1986; 35:459-63.
13. Howard B Lipoprotein metabolism in Diabetes mellitus. *J lipid Res.*1987; 28:613-28.
14. Garcia M, Mc Namara P, Crordon T, Kannell WB. Morbidity and mortality in diabetes in the Framingham study. *Diabetes* 1976; 23:105-11.
15. Jee SH, Miller E R, Guallar E, et al. Type 2 diabetes mellitus: the Atherosclerotic risk in communities Study. *Arch Intern Med* 1999; 159(18):2151-9.
16. Peacock JM, Folsom AR, Arnett DK, et al. Relationship of serum and dietary magnesium to incident hypertension: the Atherosclerosis Risk in Communities (ARIC) Study. *Ann Epidemiol.*1999; 9(3):159-65.
17. Lampl Y, Gilad R, Geva D, Eshel Y, Sadeh M. Intravenous administration of magnesium sulfate in acute stroke: a randomised double-blind study. *Clin Neuropharmacol* 2001; 24:11-5.
18. Smith D. A, Connick J. H, Stone T. W. Effect of changing extracellular levels of magnesium on spontaneous activity and glutamate release in the mouse neocortical slice. *Br. J. Pharmacol*1989; 97(1):475.
19. Yang Y, Li Q, Ahmad F, Shuaib A. Survival and histological evaluation of therapeutic window of post- ischemia treatment with magnesium sulfate in embolic stroke model of rat. *Neurosci Lett* 2000; 285:119-22.
20. Saberi A, Hatamian HR, Esmaeilzadeh K, Heydarzadeh A. The relationship between magnesium level and first 72hours Rankin score and Rankin score in 1 week after an ischaemic stroke. *Ir J neurol* 2011; 10(1-2):26-28.
21. Kaur J, Prabhu K M, Thakur L C. Serum magnesium levels in ischaemic cerebrovascular disorders. *Journal of Pharmaceutical and biomedical sciences* 2012; 17(2):12.
22. Dhamija SB. Prevalence of stroke in rural community: An overview of Indian expression. *JAPI* 14. Kao WH, Falson AR, Nieto FJ, et al. Serum and dietary magnesium and the risk for 1998; 46:351- 4.
23. WoifPa D, Agostino R B, Belanger A J. Are blood lipid risk factor for stroke. *Stroke* 1991; 22:26.
24. Amighi J, Sabeti S, Schlager O, Mlekusch W, Exner M, Lalouschek W, et al. Low Serum Magnesium Predicts Neurological Events in

Patients With Advanced Atherosclerosis Stroke
2004; 35:22- 7.

25. Mehrdokht M, Saadat T. Comparison of Serum Levels of Magnesium and Potassium in Stroke Patient and Healthy Controls. Journal of fasa university medical science 2011; 1(2):7-13.

26. Ovbiagele B, Liebeskind DS, Starkman S, et al. Are elevated admission calcium levels associated with better outcomes after ischemic stroke? Neurology 2006; 67:170- 3.

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