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Pathology

Low Serum Magnesium Level is Associated with Severity of Acute Stroke

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Abstract **Original Research Article**

***Background*:** Incidence of stroke is increasingly prevalent around the world. It is necessary to assess the severity of acute stroke early for better patient management and also to predict treatment option and disease outcome. Serum magnesium (Mg) remarkably associated with vascular risk factor and has a neuro-protective role in stroke. ***Objective*:** To assess the correlation between serum magnesium level with severity of acute stroke. ***Methods*:** This cross-sectional study was conducted at Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from March 2021 to February 2022. A total of 60 diagnosed patients of acute stroke were enrolled. A through neurological examination of the study patients were done, the severity of acute stroke was leveled by the National Institutes of Health Stroke Scale (NIHSS) score. Then, their serum magnesium levels were measured following standard procedure. Data were analyzed and compared by statistical tests. ***Results*:** The mean (±SD) age of the study patients was 61.7 (±12.2) years, with a range of 28-95 years. A male to female ratio was 1.6:1. Of them; 75% study patients had low level of serum magnesium, mean serum magnesium level was 1.52±0.30 (mg/dl) in acute stroke patients and it was significantly decreased with increasing severity of acute stroke (p= 0.048). A significant negative correlation was observed between serum magnesium level and stroke severity (r= -0.374, p= 0.003). ***Conclusion*:** Majority of the patients with acute stroke has low serum magnesium level and serum magnesium is negatively related with severity of the acute stroke.

Keywords: Acute Stroke, Correlation, NIHSS Score, Serum Magnesium Level.

1. INTRODUCTION

Stroke is a common neurological emergency and is the third most common cause of death in developing nations after ischemic heart disease and cancer [1]. According to the World Health Organization (WHO) stroke is defined as a rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin [2-4]. An acute stroke is characterized by the rapid appearance (usually over minute) of a focal deficit of brain function, most commonly a hemiplegia with or without signs of focal higher cerebral dysfunction (such as aphasia), hemisensory loss, visual field defect or brain stem deficit [3]. Globally, incidence of stroke is 0.03% and prevalence is 1.12% [4]. Stroke is mainly two types: ischemic and hemorrhagic; ischemic stroke accounts for 80-85% and hemorrhagic stroke accounts for 15-20% [5]. Stroke has multifactorial etiopathogenesis with multiple modifiable and non-modifiable risk factors [6]. The common modifiable risk factors are hypertension, diabetes mellitus, smoking/tobacco use, ischemic heart disease, obesity, dyslipidemia and drugs (oral contraceptive pills use in female); non-modifiable ones are advancing age, sex and family history of stroke etc [6, 7]. There are various stroke scales used to quantify

neurological deficits, functional outcome, global outcome, or health-related quality of life in patients after a stroke. The National Institutes of Health Stroke Scale (NIHSS) is a systematic assessment tool used to provide an accurate assessment of the neurological deficits of a patient with stroke during initial presentation [8]. During recent years it has been documented that stroke is associated with alterations in the balance of some trace elements [9-15]. Trace elements are essential for maintaining the metabolism of neurons and glia [9]. Magnesium (Mg) is an important trace element within the vascular system and it has a key role in the pathogenesis of stroke and restoration of brain cells [10]. In the body, Mg is a naturally occurring antagonist of calcium ions and helps to maintain blood pressure and blood flow in the vessels by modulating vasomotor tone [11]. Decreased Mg enhances vascular endothelial damage and vasoconstriction; thus it promotes to the development and progression of atherosclerosis [12]. In the nervous system, magnesium is essential for optimal nerve transmission and neuromuscular coordination, thus gives protection against excitotoxicity (excessive excitation leading to cell death) [13, 14]. It was reported that, patients with acute stroke having low serum magnesium levels, which are associated with worse clinical outcome [15-17]. On the other hand, increased serum magnesium level was correlated with a decreased stroke severity in acute stroke [18-20]. The correlation between serum magnesium level and severity of acute stroke had shown inconsistent results in different previous studies. As magnesium act as a neuroprotector against excitotoxocity and it is essential for optimal neuronal transmission, therefore it has a key role in the pathogenesis of stroke. In this background this study aimed to assess the serum magnesium level in acute stroke patients and its relationship with the severity of acute stroke.

2. METHODOLOGY

This cross-sectional study was conducted at Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from March 2021 to February 2022. This study was approved by the Ethical Review Committee of BSMMU, Dhaka, Bangladesh. A total of 60 diagnosed patients of acute stroke were enrolled following selection criteria. Adult (age >18 years) patients of both gender, diagnosed as acute stroke (both ischemic and hemorrhagic) within 7 days of the onset of symptoms were included. Patients of recurrent stroke, patients having renal failure, patients with any types of malignancy and pregnant patients were excluded from the study. The diagnosis of stroke was done by neurologist and was confirmed by neuroimaging techniques [computed tomography scan (CT-scan)/magnetic resonance imaging (MRI) of brain].

Study Procedure

A total of 60 diagnosed patients with acute stroke were selected following selection criteria. The aims and objectives of the study and the necessity of the investigation were explained to study participants. Informed written consent was obtained from each patient or next of kin (when the patient with a stroke was unable to provide informed consent). Then a detailed case history was taken and clinical examinations including NIHSS scoring were done accordingly. All relevant data were recorded in data collection sheet. Demographic information such as age and gender was noted. Risk factor profiles including- family history of stroke, diabetes mellitus, hypertension, heart disease, dyslipidemia, smoking/tobacco using and oral contraceptive pills use (in female patients) were recorded. A separate data collection sheet was used for each study patient to maintain the confidentiality.

National Institute of Health Stroke Scale (NIHSS)

The National Institutes of Health Stroke Scale (NIHSS) is an 11- item impairment scale used to measure stroke severity [8]. It was originally developed in 1989. In the current National Stroke Foundation guidelines, the NIHSS is recommended as a valid tool to assess stroke severity in emergency departments [21]. It is measured by a scoring system based on different domains. It‘s scoring range is 0-42 points. The higher score points indicate the greater severity of stroke. A score 0 means no stroke symptoms, 1-4 means minor stroke, 5-15 means moderate stroke, 16-20 means moderate to severe stroke and 21-42 means severe stroke. It is widely used to assess stroke severity, treatment efficacy and to predict outcomes [21].

Collection, Processing and Analysis of Blood Samples

With all aseptic precaution 3 ml venous blood were collected in a red screw capped plain tube (without anticoagulant) from the median cubital vein of each study patient. After collection, tubes were labeled with the patient‘s identification number. The tube was kept standing for 30 minutes. Then the blood was centrifuged at 3000 rpm for 5 minutes in room temperature (22˚C - 24˚C) and separated into Eppendorf tubes for analysis. Serum magnesium was assessed by the automated biochemistry analyzer SIEMENS Dimension EXL with LM by the principle of photometric technique using a commercially available cartridge in the Department of Laboratory Medicine, BSMMU, Dhaka, Bangladesh.

Normal Range of Serum Magnesium

The reference normal range of serum magnesium in the Department of Laboratory Medicine, BSMMU, Dhaka, Bangladesh was 1.82-2.43 mg/dl (0.75-1.0 mmol/l).

Statistical Analysis of Data

Collected data were cross-checked, compiled and verified. All data were analyzed by computer based software program Statistical Package for Social Sciences

(SPSS) version- 26. The mean and standard deviation (mean±SD) of serum magnesium level were calculated. Then, levels of serum magnesium (mean±SD) were calculated in different categories of acute stroke severity. Association between serum magnesium level and severity of acute stroke (minor, moderate, moderate to severe and severe stroke) was determined by ANOVA test. The Spearman correlation (r) test was performed to determine the relationship between serum magnesium levels with severity of stroke. A p value < 0.05 was considered as statistically significant.

3. RESULTS AND OBSERVATIONS

This study was intended to assess the correlation of serum magnesium level with severity of acute stroke. A total of 60 clinically diagnosed acute stroke patients, age more than 18 years irrespective of gender were selected for the study. The mean age of the study patients was 61.7±12.2 years with age ranged from 28-95 years and maximum [22 (36.7%)] patients belonged to age 61-70 years (Table- 1). Of them, maximum 37 (61.7%) patients were male and rest 23 (38.3%) patients were female; a male to female ratio was 1.6:1 (Table- 1).

Table 1: Basic data of the study patients (N= 60)

Variables	Number of patient (n)	Percentage (%)
Age (years)		
≤40	3	5.0
40-50	8	13.3
51-60	19	31.7
61-70	22	36.7
>70	8	13.
Mean±SD	61.7±12.2	
Range (minimum-maximum)	28-95	
Gender		
Male	37	61.7
Female	23	38.3
Male to female ratio	1.6:1	

Data were expressed as frequency, percentage, mean ± SD and range (minimum-maximum)

It was observed that among the study population, 39 (65.0%) patients had ischemic stroke and 21 (35.0%) patients had hemorrhagic stroke (Figure- 1).

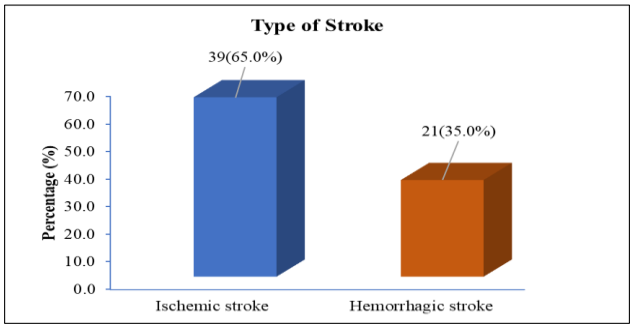

Figure 1: Bar-diagram displaying the distribution of stroke types among the study patients (N= 60)

Risk factors analysis revealed that, 73.3% study patients had hypertension (HTN) followed by dyslipidaemia (35%), diabetes mellitus (31.7%), smoking (31. &%), heart disease (18.3%), family history of stroke (11.7%) and oral contraceptive pill (3.3%) (Table-2).

Table 2: Distribution of risk factors among the study patients (N= 60)

Risk factors*	Frequency (n)	Percentage (%)
Family history of stroke	7	11.7
Diabetes mellitus (DM)	19	31.7
Hypertension (HTN)	44	73.3
Heart disease	11	18.3
Dyslipidaemia	21	35.0
Smoking	19	31.7
Oral contraceptive pill (OCP)	2	3.3

*Multiple response, Data were expressed as frequency and percentage

Among the study patients according to NIHSS scores; 26.7% had minor stroke, 33.3% had moderate stroke, 25.0% had moderate to severe stroke and 15.0% had severe stroke (Table- 3).

Table 3: Distribution of the study patients according to the stroke severity based on NIHSS scores (N= 60)

Severity of acute stroke (According to NIHSS score)	Frequency (n)	Percentage (%)
Minor stroke	16	26.7
Moderate stroke	20	33.3
Moderate to severe stroke	15	25.0
Severe stroke	9	15.0

Data were expressed as frequency and percentage

In this study, 45 (75%) patients had low level of serum magnesium and 15 (25%) patients had serum magnesium level within normal reference range; the mean serum magnesium level of the study population was 1.52±0.30 mg/dl, which ranged from 0.8 mg/dl to 2.0 mg/dl (Table- 4).

Table 4: Serum magnesium (Mg) level in acute stroke patients (N= 60)

Serum magnesium (mg/dl)	Number of patient (n)	Percentage (%)
Low level (<1.82 mg/dl)	45	75.0
Normal level (1.82-2.43 mg/dl)	15	25.0
Mean±SD	1.52±0.30 mg/dl	
Range (minimum-maximum)	0.8 mg/dl - 2.0 mg/dl	

Data were expressed as frequency and percentage, mean ± SD and range (minimum-maximum)

Among the study population; mean serum magnesium level was found significantly low in ischemic stroke patients than hemorrhagic stroke patients (1.44±0.31 mg/dl versus1.67±0.22 mg/dl, p=0.004) (Table- 5).

Table 5: Comparison of serum magnesium levels in ischemic stroke and hemorrhagic stroke among study patients (N= 60)

Serum magnesium level	Ischemic stroke (n=39)	Hemorrhagic stroke (n=21)	p value
Mean±SD	1.44±0.31 mg/dl	1.67±0.22 mg/dl	0.004[s]
Range (minimum-maximum)	0.8 mg/dl - 2 mg/dl	1.3 mg/dl - 2.0 mg/dl	

Data were expressed as mean±SD and range, Unpaired t-test was performed to compare the data, s= significant

The association of serum magnesium level with severity in acute stroke is depicted in table-6. The mean magnesium level was 1.64±0.24 (mg/dl) in minor stroke, 1.58±0.31 (mg/dl) in moderate stroke, 1.41±0.30 (mg/dl) in moderate to severe stroke and 1.37±0.28 (mg/dl) in severe stroke. The difference was statistically significant (p= 0.048). It was observed that serum magnesium level was gradually decreased according to the severity in acute stroke (Table- 6).

Table 6: Association of serum magnesium level with severity in acute stroke (N= 60)

Stroke severity by NIHSS score	Serum magnesium (mg/dl)		p value
	Mean±SD	Range (minimum-maximum)	
Minor stroke	1.64±0.24	1.2-2.0	0.048[s]
Moderate stroke	1.58±0.31	1.0-2.0	
Moderate to severe stroke	1.41±0.30	1.0-1.9	
Severe stroke	1.37±0.28	0.8-1.7	

Data were expressed as mean ±SD and range, ANOVA test was performed to analyze the data, s= significant

Spearman correlation showed that there was a significant negative correlation between serum magnesium level and stroke severity in acute stroke patients (r= -0.374; p= 0.003) (Figure-2).

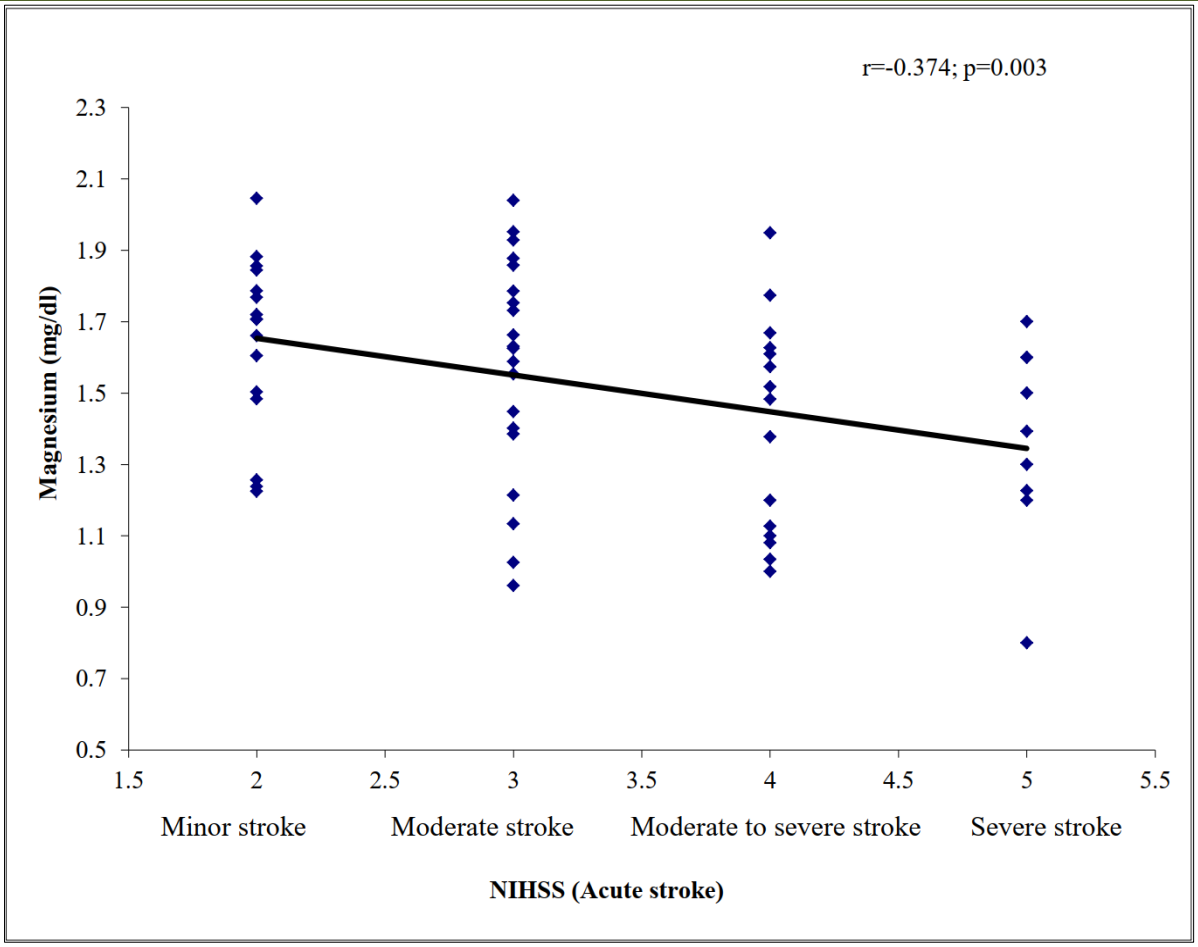

Figure 2: Scatter diagram showing correlation between serum magnesium level and stroke severity

4. DISCUSSION

Stroke is one of the leading causes of disability and mortality worldwide [1]. Incidence of stroke is increasingly prevalent that has a miserable impact on patients, their families and health care system ultimately created a significant economic burden [3]. Early assessing the severity of acute stroke is necessary for patient management and to predict treatment option with disease outcomes. The NIHSS is a well-established and useful scale for assessing the severity and functional outcome of acute stroke [8]. It was reported that serum magnesium (Mg) is significantly related with vascular risk factor [10]. There are no reliable biomarkers in NIHSS to assess stroke severity. Serum magnesium level could be the valuable test for clinician to assess severity of stroke. In this regard, the relationship of serum magnesium level with severity of acute stroke was evaluated in this study.

A total of 60 clinically diagnosed acute stroke patients, age more than 18 years irrespective of gender were selected for this study. In this study, the mean age of stroke patients was 61.7±12.2 years which ranged from 28-95 years. These findings were consistent with related previous studies [15, 22]. In this present study, highest (36.7%) patients belonged to age group of 61-70 years in acute stroke. This finding was closely resembled with a couple of related study [11, 15]. A male predominance was observed in our study that was supported by related previous studies [11, 22-24]. In this current study, it was observed that 65.0% patients had ischemic stroke and 35.0% patients had hemorrhagic stroke. This result was comparable with similar studies [15-16]. Regarding the risk factors associated with acute stroke; hypertension (73.3%) was the most commonly appearing risk factor followed by dyslipidaemia (35%), diabetes mellitus (31.7%), smoking (31.&%), heart disease (18.3%), family history of stroke (11.7%) and taking oral contraceptive pill (3.3%). These findings were in a line of previous reports [25, 26, 27]. In this study severity of stroke was determined according to the National Institute of Health Stroke Scale (NIHSS) criteria; it was observed that 26.7% had minor stroke, 33.3% had moderate stroke, 25.0% had moderate to severe stroke and 15.0% had severe stroke. These findings were an agreement of a related previous study [20].

In this current study, the mean serum magnesium level of the study patients was 1.52±0.30 mg/dl, which was ranged from 0.8 mg/dl to 2.0 mg/dl. Among the study population, 75% had low level of serum magnesium and 25% had serum magnesium level within normal reference range. The mean serum

magnesium level was found significantly low in ischemic stroke than hemorrhagic stroke (p= 0.004). In accordance, Hossain *et al.,* reported that mean serum magnesium level was low in acute stroke patients [15]. Another previous study reported a significant difference in serum magnesium level between two types of stroke (p= 0.001) [16]. These findings were closely resembled with this present study. In this study it was found that the mean serum magnesium level was 1.64±0.24 (mg/dl) in minor stroke, 1.58±0.31 (mg/dl) in moderate stroke, 1.41±0.30 (mg/dl) in moderate to severe stroke and 1.37±0.28 (mg/dl) in severe stroke among the study patients. The mean serum magnesium level was significantly (p= 0.048) decline with increased severity in acute stroke. In this context, Hossain *et al.,* found that serum magnesium level was significantly decreased in acute stroke (p= 0.001) and it correspond with worse neurological status [15]. Similarly, one previous study also found serum magnesium level was significantly reduced with increased stroke severity (p<0.001) [11]. Feng *et al.,* also found that lower serum magnesium concentration was associated with risk of higher NIHSS score (p<0.05) [19]. A couple of related study have obtained that serum magnesium level was significantly lower in acute stroke patients with increased risk of hemorrhagic transformation after intravenous thrombolysis [16, 28]. These findings were consistent with this current study. In this study it was observed that, a significant negative correlation was found between serum magnesium level and NIHSS score (r=-0.450; p=0.004) in acute stroke. One previous study observed a statistically significant correlation between stroke severity and serum magnesium level (p<0.001), which was consistent with this current study [16].

CONCLUSION

This current study documented that majority of the patients with acute stroke has low serum magnesium level. Serum magnesium level is significantly low in ischemic stroke patients than hemorrhagic stroke patients. Low serum magnesium level has a significant correlation with severity of acute stroke. A low serum magnesium level could be used as a simple biochemical tool to assess the severity of acute stroke.

Limitations of the Study

It was a single centre study with a relatively small sample size. The patients excluded from the study on the basis of history and clinical features.

Recommendations

A multicentre broad-based prospective cohort study is required to confirm the findings of the present study. Follow up studies are recommended for better evaluation of serum magnesium level with prognosis and outcome of acute stroke.

Conflicts of Interest: All author declared that they have no conflict of interest regarding this publication.

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