Original Article

Correlation of Serum Magnesium Level with Severity of Heart Failure with Reduced Ejection

Kamrul Islam[1], Mohammad Ullah[2], Suman Kumar Saha[3], Isha Abdullah Ali[4], Arifur Rahman[4], Kamrun Nahar Juthy[4], Nishat Ali[5], Md. Ahasanul Haque Razib[6]

[1]OSD, DGHS, Mohakhali, Dhaka; [2]Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [3]Department of Cardiology, Dhaka Medical College & Hospital, Dhaka, Bangladesh; [4]Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh; [5]Department of Internal Medicine, Evercare Hospital Limited, Dhaka, Bangladesh; [6]Department of Cardiology, Mymensingh Medical College & Hospital, Mymensingh, Bangladesh

Abstract

Introduction: Heart failure (HF) is a major public health issue. Left ventricular ejection fraction (LVEF) has been used to classify HF into phenotypes. Over the past few years, there has been more evidence that people with lower circulating magnesium concentrations have had more severe HF. This study aimed to evaluate the relationship between serum magnesium levels and the severity of heart failure with reduced ejection fraction (HFrEF).

Methods: This cross-sectional observational study was conducted at the Department of Cardiology, Dhaka Medical College Hospital, for 12 months following ethical approval. A total of 180 patients with HFrEF (<40%) were included after getting written informed consent, wherein 90 patients (Group B) had low magnesium levels (<1.8 mg/dl), and the remaining 90 patients (Group A) had normal magnesium levels (>1.8 mg/dl).

Results: The mean age of the respondents was 63.16±12.57 years in the low magnesium level (Group B) and 63.67±12.96 years in the normal magnesium (Group A). Among respondents with low magnesium levels, dyslipidaemia (75.6%) was predominant, followed by smoking (35.6%), hypertension (30%) & diabetes mellitus (27.8%) with no significant difference between the two groups ($p>0.05$). Severe left ventricular dysfunction was observed in 41.1% of low magnesium level respondents, compared to those with normal magnesium levels (26.7%). Serum magnesium levels showed a significant negative correlation with N-terminal pro-B-type natriuretic peptide (NT-pro BNP) levels ($rs= -0.148$, $p=0.048$), HFrEF levels ($rs= 0.205$, $p=0.006$), and 6 meter walk test (MWT) levels ($rs= 0.329$, $p<0.001$).

Conclusion: Low serum magnesium level is associated with the severity of HFrEF. However, a further larger study is recommended.

Keywords: magnesium levels, heart failure, LVEF.

[JNHFB 2026; 15 (2) : 50-54] doi.10.61819/jnhfb.v15i2.54

Introduction

Heart failure (HF) represents a significant public health challenge. The rate of readmission within one month following hospitalization is approximately 25%, while the mortality rate is reported to be as high as 22% [1]. HF has been categorized into discrete phenotypes predicated on the assessment of left ventricular ejection fraction (LVEF). The reasoning behind this pertains to the initial therapeutic experiments conducted in heart failure, which showed significantly enhanced results in individuals with LVEF of less than 40%. A significant reduction in left ventricular systolic function that is characterized by a reduced LVEF of less than 40% has been classified as heart failure with reduced ejection fraction (HFrEF) [2].

Magnesium is a crucial electrolyte that holds significant importance in metabolic processes and normal myocardial functioning. It plays a crucial role in regulating the function of myocyte and endothelial cells. This ion plays a vital role in transcellular transport and is involved in multiple efflux and influx systems. Due to its vasodilatory, anti-inflammatory, anti-ischemic, and antiarrhythmic properties, this nutrient is considered a significant element that has the potential to serve as an important agent for

Corresponding Author
Dr. Kamrul Islam,
OSD, DGHS
Mohakhali, Dhaka, Bangladesh.
E-mail: kamrul.suzan@gmail.com

cardiovascular diseases such as hypertension, atherosclerosis, acute myocardial infarction (AMI), arrhythmia, and left ventricular hypertrophy [3,4]. Hypomagnesaemia are common electrolyte imbalance observed in patients with HF [5]. These imbalances can be attributed to several factors, including hyperactivity of the renin-angiotensin system(RAS),drug therapy involving loop and thiazide diuretics, under-nutrition, and other factors [6,7]. Additionally, it is prevalent among the elderly population due to a decrease in the absorption of magnesium in the intestines and an increase in the excretion of magnesium through urine [8].

The available evidence considering the correlation between serum magnesium levels and the occurrence of heart failure in the general population is limited. Nevertheless, a couple of research studies conducted on middle-aged cohorts have disclosed that low levels of serum magnesium are linked to a heightened probability of heart failure, irrespective of the presence of common risk factors for heart failure and the occurrence of myocardial infarction [9,10]. In the past few years, there have been an increasing number of cases indicating that individuals with lower circulating magnesium concentrations, even within the normal range, are at a heightened risk of developing HF [11]. Studies conducted in both experimental and clinical settings have established a correlation between hypomagnesemia and the pathogenesis of arrhythmias, which is an important risk factor for HF [12]. Some studies also suggest that hypomagnesaemia is a prognostic indicator of heart failure. The objective of our study was to assess the correlation between serum magnesium level and HFrEF.

Methods

This cross-sectional study was conducted in the Department of Cardiology of Dhaka Medical College & Hospital, Dhaka. The study period was 12 months following the approval of the proposal. A total of 180 patients with HFrEF who attended the inpatient and outpatient Department of Cardiology at Dhaka Medical College and Hospital during the study period were included in the study, provided they met the inclusion and exclusion criteria. Patients with known cases of chronic kidney disease (eGFR <30), chronic obstructive pulmonary disease, liver diseases, who are known to be pregnant, who have a history of malignancy and who have heart failure with LVEF ≥ 40% were excluded from the study. After selection, subjects were thoroughly briefed on the aims, objectives, and procedures of the study, following which informed written consent was obtained from all participants. A pre-tested, semi-structured questionnaire was developed and utilized for data collection, with clinical, laboratory, and radiological interpretations documented using a predesigned proforma. Blood samples were collected from all study patients in the post-admission morning for the estimation of serum magnesium levels, which were analyzed using an automated method on conventional Auto-analyzer equipment in the laboratory. Patients were divided into two groups based on their serum magnesium levels: Group A comprised patients with normal magnesium levels (>1.8 mg/dl), while Group B comprised those with low magnesium levels (<1.8 mg/dl). The severity of HF was assessed in these two groups based on parameters such as LVEF, New York Heart Association (NYHA) class, and N-terminal pro-B-type natriuretic peptide (NT-pro BNP) level. Moderate LV dysfunction was defined as an LVEF of 30-39%, while severe LV dysfunction was defined as an LVEF of <30%. 6 meter walk test (MWT) was also performed. The relationship between serum magnesium and the severity of heart failure was then analyzed.

Results

A total of 180 patients were included in this study. Of them, 90 patients (Group B) had low magnesium levels (<1.8 mg/dl), and the remaining 90 patients (Group A) had normal magnesium levels (>1.8 mg/dl). The baseline characteristics of the study patients were outlined in Table 1.

The mean age of the patients was 63.16±12.57 years in the low-magnesium group and 63.67±12.96 years in the normal-magnesium group. Also, the majority of the patients were between 60-69 years in both groups. There was no significant difference in age groups between low and normal magnesium levels. The majority of the respondents in the low magnesium group (Group B) and the normal magnesium group (Group A) were male (70% and 65.6%, respectively).

Table 1: Baseline characteristics of the study patients (n=180)

Variables	Group A Mean±SD/ (%)	Group B Mean±SD/ (%)	p value
Age (Mean±SD) year	63.67±12.96	63.16±12.57	0.97
Age category			0.72
40-49	16.7%	17.8%	
50-59	26.7%	23.3%	
60-69	32.2%	31.1%	
70-79	15.6%	17.8%	
80-89	8.9%	10.0%	
Gender			
Male	65.6%	70.0%	
Female	34.4%	30.0%	

Group A= normal magnesium level; Group B= low magnesium level; SD: standard deviation

There was no significant statistical difference for height, weight, BMI, systolic blood pressure except diastolic blood pressure and heart rate between the two groups (Table 2).

Table 2: Clinical evaluation of patients (n=180)

Variable	Group A mean±SD	Group B mean±SD	p-value
Height (m)	1.57±0.07	1.57±0.07	0.959
Weight (kg)	56.7±5.73	57.35±6.46	0.473
BMI (kg/m²)	23.01±3.06	23.3±3.34	0.533
SBP (mmHg)	114.57±11.35	114.72±11.23	0.926
DBP (mmHg)	78.18±9.18	68.72±10.42	<0.001
HR (perminute)	55.78±10.53	79.2±6.62	<0.001

Group A= normal magnesium level; Group B= low magnesium level; SD: standard deviation; m: meter; kg: kilogram; BMI: body mass index; SBP: systolic blood pressure; mmHg: millimeters of mercury; DBP: diastolic blood pressure; HR: heart rate.

Among Group A respondents (Table 3), the majority had dyslipidemia (82.2%), followed by hypertension (51.1%), smoking (46.7%) & diabetes mellitus (40%). On the other hand, the majority of Group B patients had dyslipidaemia (75.6%) followed by smoking (35.6%) hypertension (30%) & diabetes mellitus (27.8%).

Table 3: Distribution of co-morbidities among patients (n=180)

Variables	Total n(%)	Group A n(%)	Group B n(%)	p-value
Diabetes mellitus	61(33.9)	36(40)	25(27.8)	0.083
Hypertension	73(40.6)	46(51.1)	27(30.0)	0.004
Dyslipidemia	142(78.9)	74(82.2)	68(75.6)	0.273
smoking	74(41.1)	42(46.7)	32(35.6)	0.130

Group A= normal magnesium level; Group B= low magnesium level.

No significant difference was found between the two groups regarding the usage of heart failure medications, between the two groups except for SGLT2 inhibitors (Table 4).

Table 4: Distribution of past medication history among patients (n=180)

Variables	Total n (%)	Group A n (%)	Group B n (%)	p-value
Loop diuretics	95(52.8)	50(55.6)	45(50)	0.455
Thiazide	60(33.3)	38(42.2)	22(24.4)	0.011
MRA	39(21.7)	23(25.6)	16(17.8)	0.205
ARB/ACEI	116(64.4)	60(66.7)	56(62.2)	0.533
SGLT2 inhibitor	46(25.6)	31(34.4)	15(16.7)	0.006
Beta-blocker	60(33.3)	32(35.6)	28(31.1)	0.527

Group A= normal magnesium level; Group B= low magnesium level; MRA = Mineralo-corticoid receptor antagonists; ARB: angiotensin receptor blocker; ACEI: angiotensin-converting enzyme inhibitor; SGLT2: sodium-glucose cotransporter 2.

The majority of the respondents with both low and normal magnesium groups had class III (28.9% and 51.17%, respectively) NYHA classification of heart failure (Figure1). Also, low magnesium level respondents (Group B) had more Class IV HF (14.4%) than normal magnesium level respondents (Group A) (12.2%), though no significant association was found (p value=0.285).

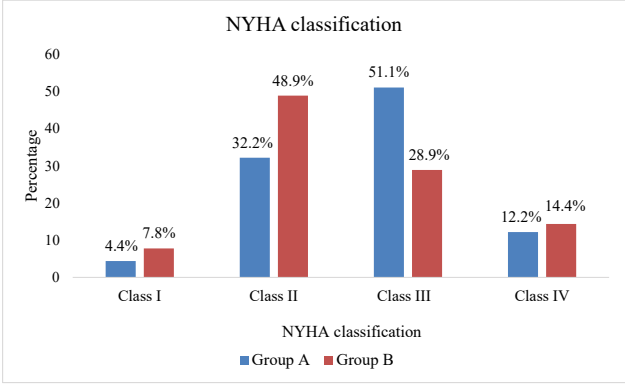


Figure 1: Distribution of NYHA classification among Group A and Group B (n=180) Group A= normal magnesium level; Group B= low magnesium level; NYHA: New York heart association.

According to the investigation parameters, Group B patients had significantly lower Hb levels, low LVEF and higher NT pro-BNP levels compared to Group A (Table 5).

Table 5: Distribution of investigation parameters among Group A and Group B (n=180)

Variable	Group A mean±SD	Group B mean±SD	p-value
HB%(gm/dl)	11.68±1.31	8.95±2.6	<0.001
RBS (mg/dl)	123.34±47.33	122.46±45.65	0.899
S. Creatinine(mg/dl)	0.99±0.15	1.22±0.36	<0.001
S. sodium(mg/dl)	130.13±6.79	140.23±3.02	<0.001
S. Chloride(mg/dl)	103.23±4.9	103.12±5.05	0.882
S. Potassium(mg/dl)	3.78±1.08	4.09±0.98	0.052
LDL (mg/dl)	133.88±23.08	132.98±23.09	0.794
HDL (mg/dl)	40.94±8.77	41.03±7.81	0.943
Total cholesterol(mg/dl)	158.48±25.12	155.14±25.12	0.996
Triglyceride(mg/dl)	121.74±16.88	121.73±15.34	0.375
LVEF (%)	34.82±7.53	25.36±10	<0.001
NT pro BNP(pg/ml)	837.13±331.66	3049.87±393.75	<0.001

Group A= normal magnesium level; Group B= low magnesium level; SD: standard deviation; HB: hemoglobin; gm/dl: grams per deciliter; RBS: random blood sugar; mg/dl: milligram per deciliter; LDL: low density lipoprotein; HDL: high density lipoprotein; LVEF: left ventricular ejection fraction; NT-pro BNP: N-terminal pro-B-type natriuretic peptide; pg/ml: pictograms per milliliter.

Among low magnesium level patients, 41.1% had severe LV dysfunction (Table 6), which was significantly higher compared to normal magnesium level patients (26.7%).

Table 6: Association of severity of LV dysfunction among Group A and Group B (n=180)

Variables	Total n(%)	Group A n(%)	Group B n(%)	p-value
Moderate LV dysfunction (30-39%)	119(66.1)	66(73.3)	53(58.9)	0.041
Severe LV dysfunction (<30%)	61(33.9)	24(26.7)	37(41.1)	

Group A= normal magnesium level; Group B= low magnesium level; LV: left ventricular.

According to the Spearman correlation test (Figure 2), a significant negative correlation was found between serum magnesium and NT proBNP level (rs= -0.148, p=0.048).

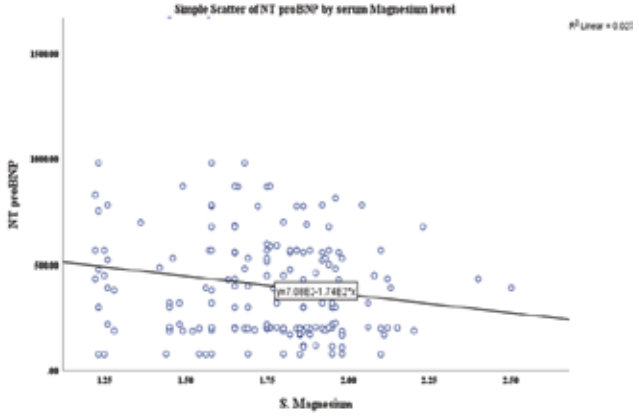


Figure 2: Scattered plot diagram of the relation between serum magnesium level and NT proBNP level NT-pro BNP: N-terminal pro-B-type natriuretic peptide.

According to the Spearman correlation test (Figure 3), there was a significant negative correlation between serum magnesium and HFrEF level (rs= 0.205, p=0.006).

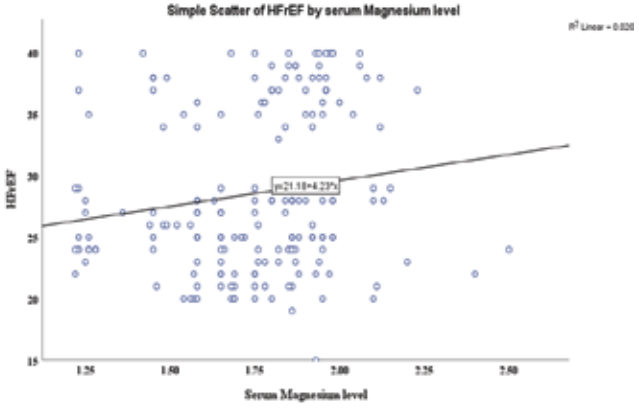


Figure 3: Scattered plot diagram of the relation between serum magnesium level and HFrEF level

HFrEF: heart failure with reduced ejection fraction.

According to the Spearman correlation test (Figure 4), there was a significant negative correlation between serum magnesium and 6MWT level (rs= -0.329, p<0.001).

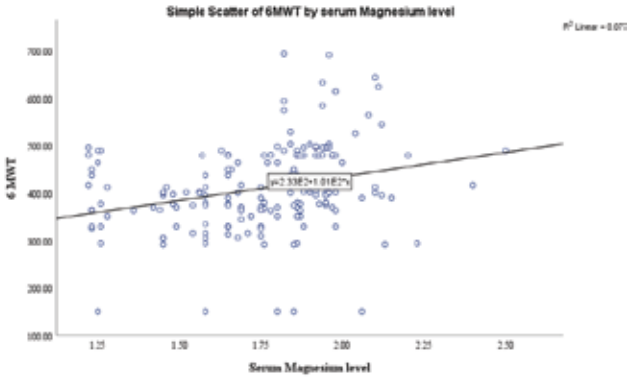


Figure 4: Scattered plot diagram of the relation between serum magnesium level and 6MWT.
MWT: meter walk test.

Discussions

The study reveals that there were no significant differences in age distribution between the low-magnesium level group and the normal-magnesium level group. However, the majority of the respondents were in their sixties in both low and normal magnesium level HF respondents. Also, male respondents with heart failure commonly had low magnesium levels in this study. These findings were quite similar to those of Savarese et al. [13] where increasing age, male respondents, hypertension, and smoking habits were contributing factors for heart failure with reduced ejection fraction level. Also Rahman et al. [14] showed that most of the patients with heart failure (65%) were of the 51-70 years age group and 75% (1584) of the patients were male. However, there was a higher prevalence of males in the low magnesium level group, along with a higher prevalence of smoking and anemia. These factors could potentially influence the outcomes and need to be considered in the interpretation of the results.

While there were no significant differences between comorbidities and magnesium levels, it's noteworthy that there was a higher prevalence of dyslipidemia, hypertension, and diabetes mellitus in the low magnesium level group. Oost et al. [15] showed that low magnesium levels in heart failure patients might also be associated with hypertension, dyslipidemia, and diabetes mellitus, with related complications such as diabetic foot. Additionally, the use of loop diuretics, thiazides, and mineralocorticoid receptor antagonists (MRAs) was more common in the low magnesium level group. Previous literature stated that diuretics used for heart failure might induce hypokalemia and hypomagnesemia [16]. These findings support this study's results.

The majority of respondents in both groups were classified as NYHA class III, indicating that the severity of heart failure was similar between the groups. However, there

were a greater number of NYHA class IV patients in the low magnesium group, indicating a pattern toward more severe heart failure in this population in this study. This result was similar to Cidade-Rodrigues et al. [17] where class III and class IV NYHA classifications were more common in lower magnesium levels of HF patients.

According to the investigation parameters of this study, NT pro-BNP levels were significantly increased in low magnesium, and the ejection fraction showed a significant decrease in low magnesium level respondents compared to normal magnesium levels. Also, HFrEF (rs= 0.205, p=0.006) and 6MWT (rs= 0.329, p<0.001) had a significant positive correlation with higher magnesium levels in this study. These findings have coincided with Nishihara et al. [18] study where HFrEF had a high relative risk of low magnesium levels in heart failure patients. Another study showed HFpEF and BNP levels were lower in low magnesium HF respondents, which suggests reduced EF level, was more common in low magnesium HF respondents. Furthermore, the low magnesium level group exhibited a higher prevalence of severe left ventricular dysfunction (78.9%), which aligns with the observed trends in investigation parameters.

Limitations of this study were: it was a single-center study with a short duration; population was relatively small.

Conclusion

This study observed a higher prevalence of severe left ventricular dysfunction in patients with low magnesium levels compared to those with normal magnesium levels. Furthermore, serum magnesium demonstrated a significant negative correlation with NTpro-BNP levels, HFrEF, and 6MWT. These findings align with previous research, albeit with slight variations. Therefore, it can be concluded that low serum magnesium levels are associated with the severity of HFrEF.

Acknowledgments: The authors were grateful to the staff of the Department of Cardiology of Dhaka Medical College and Hospital.

References

1. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart Failure Incidence and Survival (from the Atherosclerosis Risk in Communities Study). The American Journal of Cardiology. 2008;101(7):1016-1022.
2. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal. 2021;42(36):3599-3726.
3. Reffelmann T, Ittermann T, Dörr M, Völzke H, Reinthaler M, Petersmann A, et al. Low serum magnesium concentrations predict cardiovascular and all-cause mortality. Atherosclerosis. 2011;219(1):280-284.
4. Kolte D, Vijayaraghavan K, Khera S, Sica DA, Frishman WH. Role of Magnesium in Cardiovascular Diseases. Cardiology in Review. 2014;22(4):182-192.
5. Enselberg CD, Simmons HG, Mintz AA. The effects of magnesium upon cardiac arrhythmias. American Heart Journal. 1950;39(5):703-712.
6. Singer P, Berger MM, Van den Berghe G, Biolo G, Calder P, Forbes A, et al. ESPEN Guidelines on Parenteral Nutrition: Intensive care. Clinical Nutrition. 2009;28(4):387-400.
7. Taylor BE, McClave SA, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient. Critical Care Medicine. 2016;44(2):390-438.
8. Barbagallo M, Belvedere M, Dominguez LJ. Magnesium homeostasis and aging. Magnesium Research. 2009;22(4):235-246.
9. Lutsey PL, Alonso A, Michos ED, Loehr LR, Astor BC, Coresh J, et al. Serum magnesium, phosphorus, and calcium are associated with risk of incident heart failure: the Atherosclerosis Risk in Communities (ARIC) Study. The American Journal of Clinical Nutrition. 2014;100(3):756-764.
10. Kunutsor SK, Khan H, Laukkanen JA. Serum magnesium and risk of new-onset heart failure in men: the Kuopio Ischemic Heart Disease Study. European Journal of Epidemiology. 2016;31(10):1035-1043.
11. de Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in Man: Implications for Health and Disease. Physiological Reviews. 2015;95(1):1-46.
12. Markovits N, Kurnik D, Halkin H, Margalit R, Bialik M, Lomnicky Y, et al. Database evaluation of the association between serum magnesium levels and the risk of atrial fibrillation in the community. International Journal of Cardiology. 2016;205:142-146.
13. Savarese G, Stolfo D, Sinagra G, Lund LH. Heart failure with mid-range or mildly reduced ejection fraction. Nature Reviews Cardiology, Springer US. 2022;19(2):100-116.
14. Rahman MT, Majumder A, Rahman A, Chowdhury AW. Clinical Presentation of Heart Failure Patients Admitted in the National Institute of Cardiovascular Diseases, Dhaka. Journal of Medicine. 2014;15:18-22.
15. Oost LJ, van der Heijden AAWA, Vermeulen EA, Bos C, Elders PJM, Slieker RC, et al. Serum Magnesium Is Inversely Associated With Heart Failure, Atrial Fibrillation, and Microvascular Complications in Type 2 Diabetes. Diabetes Care. 2021;44(8):1757-1765.
16. Lindenfeld J, Albert NM, Boehmer JP, Collins SP, Ezekowitz JA, Givertz MM, et al. HFSA 2010 Comprehensive Heart Failure Practice Guideline. J Card Fail. 2010;16:e1-e194.
17. Cidade-Rodrigues C, Cunha FM, Elias C, Oliveira D, Bettencourt P, Lourenço P. The prognostic impact of uric acid in acute heart failure according to the coexistence of diabetes Mellitus. Nutrition, Metabolism and Cardiovascular Diseases. 2021;31(12):3377-3383.
18. Nishihara T, Yamamoto E, Sueta D, Fujisue K, Usuku H, Oike F, et al. Clinical significance of serum magnesium levels in patients with heart failure with preserved ejection fraction. Medicine (United States). 2019;98(38):1-8.