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RESEARCH

Clinical factors associated with hypomagnesemia among patients with cardiac conditions: cross-sectional study

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ABSTRACT

Background. Serum magnesium levels are usually measured and corrected, if warranted, among patients with cardiac diseases.

Objective. To determine the rate of and clinical factors associated with hypomagnesemia among patients with cardiac conditions.

Design. Cross-sectional study.

Setting. Davao Regional Medical Center (DRMC) in Tagum City, Philippines, from January 2014 to January 2016.

Participants. 59 males and 53 females with cardiac diagnoses and serum magnesium level determination results.

Main outcome measures. Rate of hypomagnesemia, odds ratios (95% CI) of having hypomagnesemia for selected clinical factors.

Main results. The mean age of the patients was 60.72 ± 16.73 years. The mean serum magnesium level was 0.75 ± 0.23 mmol/L, and 47/112 (41.96%) had hypomagnesemia (serum magnesium <0.7 mmol/L). Unadjusted prevalence odds ratios (POR) for having hypomagnesemia were significantly high for chronic obstructive pulmonary disease (COPD) comorbidity (POR=5.50; 95% CI 1.09 to 27.76; p=0.0392), stroke comorbidity (POR=2.78; 95% CI 1.15 to 6.71; p=0.0227), taking diuretic medications (POR=4.66; 95% CI 1.38 to 15.71; p=0.0132), and having atrial fibrillation during the admission (POR=2.26; 95% CI 1.04 to 4.91; p=0.0394).

Conclusion. In this study, 41.96% of the patients had hypomagnesemia. COPD and stroke comorbidities, diuretic therapy, and atrial fibrillation among patients with cardiac conditions were all significantly associated with hypomagnesemia.

Keywords. serum magnesium, atrial fibrillation, stroke, chronic obstructive pulmonary disease, diuretics

INTRODUCTION

Serum magnesium levels are monitored and, if necessary, corrected as part of the management of patients with cardiac disease.[1-5] Magnesium helps maintain cardiac rhythm,[6 7] and certain cardiac arrhythmias are associated with hypomagnesemia.[8 9] Hypermagnesuria[10 11] and low serum magnesium levels[12 13] have also been observed among patients on digoxin. Outside of these associations, little is known about the relationship of certain clinical characteristics with hypomagnesemia among patients with cardiac disease.

Arrhythmias often complicate structural heart diseases, acute coronary syndromes, and other cardiac conditions, and cause significant morbidity or even death.[14-17] The knowledge of clinical characteristics that frequently accompany hypomagnesemia among patients with different heart diseases can better inform clinicians about the expected course of illness and appropriate diagnostic management of patients in this context. We did this study in order to determine the rate of hypomagnesemia among patients with cardiac conditions and to identify clinical factors associated with low magnesium levels among patients in this subgroup.

METHODOLOGY

Study design and setting

We conducted a cross-sectional study based on the medical records of patients with cardiac diseases admitted at Davao Regional Medical Center (DRMC) in Tagum City, Philippines from January 2014 to January 2016. DRMC is a tertiary care hospital in Southern Philippines. Patients under the Internal Medicine Department with cardiac conditions are usually admitted in the general

IN ESSENCE

For patients with cardiac conditions, keeping serum magnesium levels within normal limits is usually part of the therapeutic management.

In this study among patients with various cardiac diagnoses, 41.96% had hypomagnesemia.

Chronic obstructive pulmonary disease comorbidity, stroke comorbidity, taking diuretic medications, and documented atrial fibrillation during admission were all associated with hypomagnesemia.

medical ward, the medical intensive care unit, or the coronary care unit of the hospital.

Participants

Patients aged 14 years old and over, diagnosed and admitted for any cardiac disease, and with at least one laboratory result of serum magnesium level during admission were eligible for inclusion into the study. We excluded patients with history of recurrent hypokalemia, as well as those who transferred to other institutions or went home against medical advice after serum magnesium level determination. We estimated the sample size for this study using StatCalc from Epi Info 7.1.4.0 based on the assumptions that 30% of patients with cardiac conditions have hypomagnesemia, and that 50% of patients with hypomagnesemia have premature ventricular complexes (PVC), a common type of cardiac arrhythmia, while 21% of patients without hypomagnesemia have PVC.[18] In a computation for odds ratio to determine the association of selected clinical factors with hypomagnesemia carried out with <5% level of significance, a total sample size of 112 patients will have 80% power of rejecting the null hypothesis—no significant increase or decrease in odds ratio—if the alternative holds.

Data collection

From the medical records of each patient, we collected data on age, sex, cardiac disease diagnosis, comorbidities (hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease (COPD), acute renal failure, chronic renal failure, stroke and malignancy), and use of digoxin, steroids, and diuretics. We also collected data on documented occurrence of any cardiac arrhythmias and/or death during admission. Finally, we also noted the serum magnesium level for each patient. For a patient who had two or more serum magnesium levels in the medical records, we only collected the value of the first serum magnesium level taken closest to the admission date. We considered hypomagnesemia when the patient's serum magnesium level was <0.7 mmol/L.

Statistical analysis

We summarized continuous variables as means and standard deviation and compared means using t-test. We summarized categorical variables as frequencies and percentages and compared proportions using chi-square test or Fisher's exact test. Association of variables were expressed as prevalence odds ratios (POR) and their 95% confidence intervals. We performed univariate logistic regression to determine the unadjusted association of clinical factors with hypomagnesemia. We also performed multivariable logistic regression analysis of individual medical comorbidities, medications, and clinical events for their association with hypomagnesemia adjusted for age, sex, and cardiac diagnosis. For all statistical tests, the level of significance was set at <5%. We uses Epi Info™ 7.2.1 for all our statistical tests.

RESULTS

A total of 112 patients were included in this analysis. There were 59/112 (52.68%) males and 53/112 (47.32%) females, and the mean age of the patients was 60.72 ± 16.73 years (range: 17 to 95 years). The mean serum magnesium level was 0.75 ± 0.23 mmol/L among all the patients, and 47/112 (41.96%) had hypomagnesemia. Table 1 shows the demographic and clinical profile of patients both as total sample and as divided according to the presence or absence of hypomagnesemia. Compared to the group without hypomagnesemia, the group with hypomagnesemia had significantly higher proportions of patients with COPD (7/47, 14.89% versus 2/65, 3.08%; p=0.0336), stroke (17/47, 36.17% versus 11/65, 16.92%; p=0.0203), and documented atrial fibrillation during admission (31/47, 65.96% versus 30/65, 46.15%; p=0.0378). There was also a significantly higher proportion of patients on diuretics in the hypomagnesemia group than in the non-hypomagnesemia group (11/47, 23.40% versus 4/65, 6.15%; p=0.0082).

Table 2 shows the association of selected clinical factors with hypomagnesemia on univariate logistic regression analysis. COPD comorbidity (POR=5.50; 95% CI 1.09 to 27.76; p=0.0392), stroke comorbidity (POR= 2.78; 95% CI 1.15 to 6.71; p=0.0227), diuretic therapy (POR=4.66; 95% CI 1.38 to 15.71; p=0.0132), and documented atrial fibrillation during admission (POR=2.26; 95% CI 1.04 to 4.91; p=0.0394) were all significantly associated with hypomagnesemia. After adjusting for age, sex and cardiac diagnosis (Table 2), COPD comorbidity (adjusted POR=6.54; 95% CI 1.03 to 41.66; p=0.0469), diuretic therapy (adjusted POR= 4.92; 95% CI 1.32 to 18.31; p=0.0175), and documented atrial fibrillation during admission (adjusted POR= 3.12; 95% CI 1.22 to 7.96; p=0.0171) remained

to be associated with hypomagnesemia.

DISCUSSION

Key results

The rate of hypomagnesemia among patients with cardiac conditions in this study was 41.96%. We found out that COPD comorbidity, stroke comorbidity, diuretic therapy, and documented atrial fibrillation during admission among patients with cardiac conditions were associated with hypomagnesemia.

Strengths and limitations

We were able to estimate the rate of hypomagnesemia and determine the factors associated with low serum magnesium levels among patients with cardiac conditions in this study. Since our study had a cross-sectional design, and temporal or causal relationships of the factors associated with hypomagnesemia could not be ascertained, great caution should be exercised in the interpretation of these statistical associations.

Table 1 Clinical characteristics of patients

Characteristics	Total n=112	With Hypomagnesemia n=47	Without Hypomagnesemia n=65	p-value
Mean age ± SD, *years*	60.72 ± 16.73	62.38 ± 17.69	59.52 ± 16.03	0.3715
Sex, *frequency(%)*				0.9263
Male	59 (52.68)	25 (53.19)	34 (52.31)	
Female	53 (47.32)	22 (46.81)	31 (47.69)	
Cardiac diagnoses, *frequency(%)**				
Stable angina	38 (33.93)	19 (40.43)	19 (29.23)	0.2168
Unstable angina	8 (7.14)	2 (4.26)	6 (9.23)	0.4644†
NSTEMI	30 (26.79)	14 (29.79)	16 (24.62)	0.5419
STEMI	16 (14.29)	6 (12.77)	10 (15.38)	0.6959
Congenital heart disease	1 (0.89)	0 (0)	1 (100.00)	1.0000†
Dilated cardiomyopathy	10 (8.93)	3 (6.38)	7 (10.77)	0.5158†
Rheumatic heart disease	5 (4.46)	1 (2.13)	4 (6.15)	0.3966†
Valvular heart disease	3 (2.68)	1 (2.13)	2 (3.08)	1.0000†
Thyrotoxic heart disease	7 (6.25)	2 (4.26)	5 (7.69)	0.6970†
Medical comorbidities, *frequency(%)**				
Heart failure	71 (63.39)	28 (59.57)	43 (66.15)	0.4757
Hypertension	69 (61.61)	32 (68.09)	37 (56.92)	0.2452
Diabetes mellitus	25 (22.32)	11 (23.40)	14 (21.54)	0.8150
Dyslipidemia	9 (8.04)	3 (6.38)	6 (9.23)	0.7319†
COPD	9 (8.04)	7 (14.89)	2 (3.08)	0.0336†‡
Acute renal failure	28 (25.00)	13 (27.66)	15 (23.08)	0.5804
Chronic renal failure	7 (6.25)	5 (10.64)	2 (3.08)	0.1283†
Stroke	28 (25.00)	17 (36.17)	11 (16.92)	0.0203‡
Medications, *frequency(%)**				
Digoxin	7 (6.25)	4 (8.51)	3 (4.62)	0.4505†
Steroids	5 (4.46)	4 (8.51)	1 (1.54)	0.1594†
Diuretics	15 (13.39)	11 (23.40)	4 (6.15)	0.0082†‡
Clinical events, *frequency(%)**				
Atrial fibrillation	61 (54.46)	31 (65.96)	30 (46.15)	0.0378‡
Ventricular tachycardia	5 (4.46)	1 (2.13)	4 (6.15)	0.3966†
Died	18 (16.07)	5 (10.64)	13 (20.00)	0.1830

*One patient may have more than one cardiac diagnosis, medical comorbidity, medication, or clinical event.
†Compared using Fisher's exact test.
‡Significant at p<0.05.
COPD—chronic obstructive pulmonary disease; NSTEMI—Non-ST-elevation myocardial infarction; STEMI—ST-elevation myocardial infarction.

Table 2 Logistic regression analysis showing the association of selected clinical factors with hypomagnesemia

Clinical factors	Unadjusted Prevalence odds ratio (95% CI) n=112	Unadjusted p-value	Adjusted* Prevalence odds ratio (95% CI) n=112	Adjusted* p-value
Medical comorbidities				
Hypertension	1.61 (0.74 to 3.54)	0.2321	1.26 (0.51 to 3.11)	0.6120
Heart failure	0.75 (0.35 to 1.64)	0.4761	0.79 (0.32 to 1.91)	0.5949
Diabetes mellitus	1.11 (0.45 to 2.73)	0.8142	0.94 (0.36 to 2.41)	0.8903
Dyslipidemia	0.67 (0.16 to 2.83)	0.5863	0.64 (0.14 to 2.94)	0.5646
COPD	5.50 (1.09 to 27.76)	0.0392†	6.54 (1.03 to 41.66)	0.0469†
Acute renal failure	1.27 (0.54 to 3.02)	0.5809	1.34 (0.52 to 3.43)	0.5450
Chronic renal failure	3.75 (0.69 to 20.23)	0.1244	3.18 (0.56 to 18.19)	0.1933
Stroke	2.78 (1.15 to 6.71)	0.0227†	2.48 (0.95 to 6.43)	0.0624
Medications				
Digoxin	1.92 (0.41 to 9.03)	0.4075	13.69 (0.91 to 207.11)	0.0589
Steroids	5.95 (0.64 to 55.10)	0.1161	6.44 (0.54 to 76.91)	0.1412
Diuretics	4.66 (1.38 to 15.71)	0.0132†	4.92 (1.32 to 18.31)	0.0175†
Clinical events				
Atrial fibrillation	2.26 (1.04 to 4.91)	0.0394†	3.12 (1.22 to 7.96)	0.0171†
Ventricular tachycardia	0.33 (0.04 to 3.07)	0.3307	0.31 (0.03 to 3.31)	0.3296
Death	0.48 (0.16 to 1.44)	0.1905	0.48 (0.15 to 1.57)	0.2265

*For age, sex, and cardiac diagnosis.
†Significant at p<0.05.
COPD—chronic obstructive pulmonary disease; NSTEMI—Non-ST-elevation myocardial infarction; STEMI—ST-elevation myocardial infarction.

Interpretation

In this study, the odds of having hypomagnesemia were 4.6 times as high among patients on diuretic medications than among those who were not taking diuretics. The use of diuretic agents have been linked to hypomagnesemia.[19] Thiazides and loop-diuretics are mainly responsible for renal magnesium loss.[20 21] It has been proposed that loop diuretics and osmotic diuretics increase magnesium excretion by increasing flow rate into the Henle's loop and decreasing sodium chloride transport.[22]

Magnesium has been thought to play a role in the relaxation of bronchial smooth muscles.[23] Low levels of serum magnesium have been associated with impaired pulmonary function, hyper-reactivity of the airways, and exacerbation of COPD.[24] On the other hand, magnesium sulfate administration for acute bronchospasm has been reported to improve airway function.[25-27] One interpretation of the association of hypomagnesemia with COPD comorbidity in our study is that it follows this exposure-outcome framework. However, based on the retrospective data that we collected in this study, we could not establish the exacerbation status of patients with recorded COPD comorbidity.

Cardiac arrhythmias and hypomagnesemia have been reported to occur concomitantly.[20 28] Atrial fibrillation is the most common dysrhythmia, which occurs in 0.4% to 1.0% of the population.[29] Magnesium is a cofactor in the sodium-potassium pump, and during hypomagnesemia, disruption in the function of the sodium-potassium pump can lead to abnormalities in the cardiac conduction system.[4] Clinically, magnesium administration has a role in restoring sinus rhythm during atrial fibrillation.[30] In our study, the odds of having atrial fibrillation were 2.26 times as high among patients with hypomagnesemia than among those without hypomagnesemia. Patients with atrial fibrillation would benefit from strict monitoring to detect hypomagnesemia that needs correction.[31]

It is not completely understood whether low magnesium levels promote the occurrence of stroke or vice versa. Relatively low serum magnesium levels have been observed among patients with stroke, and it has been suggested

that the severity of cerebrovascular injury is inversely proportional to the serum magnesium levels.[32] The neurological symptoms of hypomagnesemia, including mental status changes and acute focal deficits notably, can also mimic stroke in the clinical setting.[33] Another possible explanation for the association of stroke with hypomagnesemia in this study is the strong association of hypomagnesemia and atrial fibrillation, which is a risk factor for stroke.[34 35] After adjustment for age, sex, and cardiac diagnosis in this study, however, the association of stroke and hypomagnesemia did not show statistical significance, suggesting that the association is possibly mediated by other factors that modify stroke, hypomagnesemia, or both.

Hypomagnesemia is present in 20.2% of hospitalized patients.[36] Several other studies reported varying rates of hypomagnesemia among different patient subgroups—6.59% among patients in the emergency room,[37] 8.75% to 18% among patients on dialysis,[38-40] 17.4% among patients with congestive heart failure,[21] 23.96% among patients in intensive care units,[41] 33.6% among patients with intracerebral hemorrhage,[42] and 36% among elderly patients on long-term care.[43] The rate of hypomagnesemia among patients with cardiac conditions in our study (41.96%) is higher than those reported in previous studies. The presence of several conditions associated with hypomagnesemia, such as concomitant COPD, stroke, or atrial fibrillation, can possibly account for this high rate of hypomagnesemia. Diuretic agents are commonly prescribed to patients with cardiac conditions complicated by heart failure, and this may also—at least partly—explain the high rate of hypomagnesemia among the patients with cardiac conditions in our study.

Generalizability

The results of this study are applicable to most patients with cardiac diagnoses since the clinical and demographic characteristics of our patients are similar to those of patients in other tertiary care hospitals. Males and females were equally represented in our study, and the age range of patients we included was quite broad. The most common cardiac diagnoses and their comorbidities were also well-represented among the patients in our study sample.

CONCLUSION

Among patients with cardiac conditions in this cross-sectional study, 41.96% had hypomagnesemia. COPD comorbidity, stroke comorbidity, diuretic therapy, and documented atrial fibrillation during admission were significantly associated with low serum magnesium levels.

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Ethics approval

This study was reviewed and approved by the Department of Health XI Cluster Ethics Review Committee (DOH XI CERC reference P16060701).

Reporting guideline used

STROBE Checklist (http://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_combined.pdf)

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None declared

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