Original Article

Evaluation of the Prevalence of Hypomagnesemia and the Related Risk Factors in Patients Admitted to a Referral Heart Hospital in Isfahan

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Abstract

Background: Magnesium is one of the most abundant cations in the body and plays a vital role in the function of the cardiovascular system. Hypomagnesemia can cause severe and dangerous cardiovascular complications. Also, since drugs that can lead to hypomagnesemia are commonly prescribed to cardiac patients, we decided to investigate the prevalence of hypomagnesemia in the population of cardiac patients to be aware of the prevalence of this condition as an important risk factor for cardiovascular events.

Materials and Methods: This study is a retrospective cross-sectional study of an analytical-observational type with a fundamental-applied approach, in which by recording the information of patients in pre-designed forms, the prevalence of hypomagnesemia in them and also the prevalence of hypomagnesemia separation of different heart diseases and the relationship of hypomagnesemia with age, sex, glomerular filtration rate (GFR), and drugs used have been evaluated.

Results: A total of 982 patients were included in the study, of which 636 were men and 346 were women. The average age of the patients in this study was 63 years. Hypomagnesemia was observed in 138 patients (14%), and the prevalence of hypomagnesemia in patients with ventricular arrhythmias was 40%. It was also observed that only 47% of the patients with hypomagnesemia received magnesium, and the rest were not treated.

Conclusion: This study highlights the importance of magnesium status and its relationship with various clinical factors in the studied population. This emphasizes the need to increase attention to hypomagnesemia, especially among vulnerable groups such as women and older adults.

Keywords: Cardiovascular events, cross-sectional study, magnesium, prevalence, risk factor

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Introduction

Magnesium, the second intracellular cation and the fourth abundant cation in our bodies, is an incredibly vital mineral.[1] Within our cardiovascular system, magnesium takes part in numerous regulatory processes, including the modulation of smooth muscle tone within blood vessel walls, the inhibition of angiotensin II activity, the regulation of endothelial cell activity, and the management of myocardial excitability, all factors implicated in the pathophysiology of blood pressure and diverse cardiac ailments.[2] However, serum magnesium levels are not commonly measured, making the deficiency

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of this electrolyte challenging to diagnose for an extended period.[1]

Hypomagnesemia is characterized by an electrolyte imbalance, defined as the serum magnesium falling below 1.46 mg/dL. This state of play often fails to signal a negative effect until serum magnesium levels reach under 1.2 milligrams per deciliter (equivalent to 0.5 millimoles per liter).

When magnesium levels are slightly low and do not cause symptoms, treatment may not be necessary. If the plasma magnesium level is less than 1.9 mg/dl, it may require Mg repletion. The route and dose of magnesium repletion should be selected on the basis of the severity of the clinical manifestations and the degree of hypomagnesemia. Various elements and circumstances may interfere with the body's regulation of serum magnesium levels, commonly broken down into three primary groups: reduced magnesium absorption, cellular uptake displacing the external magnesium, and an increase in the push of magnesium through the kidneys or gastrointestinal framework. Proton pump inhibitors (PPIs) are part of a portfolio of drugs associated with the triggers of hypomagnesemia. However, the basis of how this happens has not yet been thoroughly mapped. However, the leading supposition revolves around the influence of such medications on the body's method of absorbing magnesium within the digestive tract. The consumption of thiazide diuretics and furosemide also causes renal excretion of magnesium, and these drugs are one of the critical risk factors for hypomagnesemia.[3,4]

The various displays of inadequate magnesium levels in the body encompass a wide array. While it might go undetected in mild cases, a significant deficiency of magnesium can result in severe conditions, such as irregular and rapid heart rhythms in both the upper and lower chambers of the heart, specifically atrial and ventricular fibrillation, which can ultimately lead to sudden death.[4,5] Disorders related to hypomagnesemia can lead to a persistent kind of hypokalemia. This type of hypokalemia will remain uncontrollable until the person's magnesium levels are corrected.[6]

According to prior research findings, the occurrence of hypomagnesemia shows significant variations. For instance, it ranges from 5.14% in the general non-select German population to 8.11% in Indian individuals aged 50–84 and 5.2% in healthy hospital staff and blood donors.[7–9] Furthermore, the prevalence of low magnesium levels in patients receiving medical care in hospitals is approximately 0.7–0.11%, rising to 65% among patients admitted to critical care units.[10] A study conducted in 2022 revealed a higher probability of hypomagnesemia in individuals who use PPI medications. The occurrence of hypomagnesemia was approximately 22% in people using PPIs, while it was around 16% in those who did not take these medications.[11] In Iran, several studies have been conducted on the prevalence of hypomagnesemia in different conditions. For instance, a study at Mashhad's Imam Reza Hospital, involving 60 patients, showed that the occurrence of hypomagnesemia in hospitalized patients ranged between 10% and 15%. However, this rate escalates to 40–60% among intensive care unit (ICU) patients.[12] Considering that hypomagnesemia can lead to significant and dangerous cardiovascular consequences, and considering that drugs capable of inducing hypomagnesemia are commonly prescribed to these cardiac patients, we initiated to examine the prevalence of hypomagnesemia across different underlying diseases and explore the association with related factors (medications, age, and gender) in patients who visit Chamran Heart Hospital. As there is currently no research available on the occurrence of hypomagnesemia in Isfahan, this study has the potential to provide valuable insights into its epidemiology.

Materials and Methods

The researchers utilized a cross-sectional observational methodology with an analytical-observational perspective. The main goal was to explore the prevalence of hypomagnesemia and its related risk factors, such as drugs, in patients referred to Chamran Heart Hospital in Isfahan.

The participants in this study were individuals who came to the emergency department of Shahid Chamran Heart Hospital in Isfahan in September 2021.

During the specified timeframe, all eligible patients entering the study were included. The inclusion criteria encompassed all patients seeking emergency care at Chamran Heart Hospital in Isfahan during the second half of 2022.

Patients who received oral or intravenous magnesium medication within one week before measuring blood magnesium levels were excluded.

The main goal of this research was to evaluate the occurrence of hypomagnesemia in the study patients. As part of our research goals, we aimed to examine reduced magnesium levels in cardiac ailments and delve into the links between age, gender, and the medications employed by individuals experiencing magnesium deficiency. We gathered blood samples from all eligible patients and subsequently analyzed the concentrations of magnesium and potassium in the blood serum.

The potassium levels, similar to magnesium, were measured at the entrance for the patients under study.

In this study, hypomagnesemia and hypokalemia were defined by serum magnesium concentrations <1.8 mg/dL (<0.74 mmol/L) and serum potassium concentrations <3.5 mg/dL. Additionally, serum magnesium concentrations >2 mg/dL were considered safe in patients with cardiovascular disease. These findings and the rest of the test outcomes were documented upon admission to update the physician on the patient's potassium and magnesium levels.

To investigate the prevalence of hypomagnesemia and its association with the use of drugs causing this condition, all medications taken by patients at home, along with the dosage used in the past three days, were recorded. Patients were

categorized into different groups based on drug dosage for further analysis of the relationship between hypomagnesemia and drug dosage.

To assess patients' arrhythmia, a 12-lead electrocardiogram (EKG) was obtained upon admission. Additionally, to examine ejection fraction (EF) status and heart failure diagnosis, all patients underwent an echocardiogram performed by a cardiac specialist at admission. Patient details, including age, gender, medical record number, prescribed medications, diagnosis, and various tests, such as potassium and magnesium levels and creatinine, were recorded on dedicated forms. After data collection, the relationship between hypomagnesemia, age, gender, and medication use was analyzed. The prevalence of hypomagnesemia was also investigated based on diagnosis, underlying heart conditions, and the simultaneous occurrence of hypomagnesemia and hypokalemia.

Categorical variables were represented as frequencies and proportions, whereas quantitative variables were reported as means ± standard deviations. Independent t-tests and Chi-square tests were employed to investigate disparities between means for quantitative and qualitative variables, respectively. Regression models and analysis of covariance were employed for adjusting confounding effects. Pearson correlation coefficient assessed the relationship between risk factors and dependent variables. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 20, and significance was considered for *P* values less than 0.05.

Results

During this research, 1073 individuals sought attention at the Chamran Heart Hospital emergency department. However, 91 people were not included in the study, as they had taken magnesium-containing medications before their serum magnesium levels could be measured. Therefore, the study sample consisted of 982 patients, comprising 636 males (64.7%) and 346 females (35.3%). The average age of the participants in this study was 63 (±18) years old.

Out of the patients who came to Shahid Chamran Heart Hospital in Isfahan, the prevalence of hypomagnesemia reached 138 individuals, representing 14% of the overall number. In this group of people, only around 47% were given magnesium as treatment while they were in the hospital, while the remaining individuals did not undergo any form of therapy. Furthermore, considering gender, 16% of the women and 12% of the men had low levels of serum magnesium in this study, and 58.7% were of the male gender, while around 41.3% were female. This examination unveiled the high prevalence of insufficient magnesium levels in the bloodstream.

In this study, we also measured the prevalence of hypomagnesemia in various underlying diseases. It was found that the prevalence of hypomagnesemia in heart failure patients with reduced EF (≤40) was 13.82%, in patients with myocardial infarction 12.67%, in atrial fibrillation 17.54%, and in patients with ventricular arrhythmias (Ventricular fibrillation (VF) Ventricular tachycardia (VT)) were 40%. The prevalence of hypomagnesemia by demographic characteristics is shown in Table 1.

The present investigation aimed to analyze and scrutinize the correlation among age, gender, glomerular filtration rate (GFR), and medication utilization among patients. This research involved comparing two groups: individuals who have hypomagnesemia and those who do not. According to the data in the table, the statistical analysis found no difference between the two groups regarding the examined factors [Table 2].

Scientists investigated the connection between the dosage of thiazide diuretics, PPI, and furosemide and the occurrence of hypomagnesemia. They divided patients into categories based on their medication dosages and individually assessed the prevalence of hypomagnesemia in each category. However, no significant correlation was found between varying doses of hydrochlorothiazide, furosemide, and PPI and the occurrence of hypomagnesemia.

The study's secondary objective was to explore the frequency of hypokalemia among individuals admitted to the Shahid

Table 1: Prevalence of hypomagnesemia by demographic characteristics

	Group population *n*	Hypomagnesemia, *n* (%)
All the patients, *n* (%)	982	138 (14), Mg <1.8 mg/dL 400 (40), Mg <2 mg/dL
Males, *n* (%)	636	81 (58.69)
Age, years, 65 ≤, *n* (%)	436	75 (54.34)
Age, years, 65 >, *n* (%)	519	63 (45.65)
Cardiac diseases		
Heart failure with reduced EF	492	68 (13.82)
Myocardial infarction	505	64 (12.67)
Atrial fibrillation	57	10 (17.54)
Ventricular fibrillation or ventricular tachycardia	30	12 (40)

Data are presented as number (%) of patients. EF: ejection fraction

Table 2: Correlation between serum magnesium and age, gender, GFR, and drugs

	Hypomagnesemia *n*: 138	Non-hypomagnesemia *n*: 844	*P*
Age (year)	64±13.5	62.8±13.6	0.32
Male, *n* (%)	81 (58.7)	555 (65.8)	0.10
GFR (ml/min)	68.21±27.81	72.02±75.76	0.58
Furosemide, *n* (%)	29 (21)	195 (23.1)	0.29
PPI, *n* (%)	37 (26.8)	168 (22)	0.21
Thiazide diuretics, *n* (%)	12 (8.7)	78 (9.2)	0.83
Digoxin, *n* (%)	8 (5.8)	63 (7.5)	0.48

GFR: glomerular filtration rate; PPI: proton pump inhibitor

Chamran Heart Hospital emergency ward in Isfahan. The results indicated that among the 982 participants, 74 individuals (around 7.5%) encountered low potassium levels.

Additionally, among the 138 patients diagnosed with hypomagnesemia, it was observed that 16 of them (approximately 11.59%) simultaneously experienced low potassium levels as well.

Moreover, this research examined the connection among age, sex, GFR, hypomagnesemia, and the utilization of medications by patients with the incidence of hypokalemia levels in males. To accomplish this objective, patients were categorized into two cohorts: individuals with hypokalemia and individuals without. The variables investigated in both cohorts are displayed in There were significant differences between the two groups regarding age and the occurrence of hypomagnesemia [Table 3].

Discussion

The primary objective of this study was to examine the prevalence of hypomagnesemia and the related risk factors among individuals seeking help at Shahid Chamran Heart Hospital in Isfahan. This investigation took place between late 2021 and early 2022. This research defined hypomagnesemia as magnesium levels to or below 1.8 milligrams per deciliter (mg/dL). The results revealed that out of the entire cohort of 982 patients enrolled in the study, 138 individuals (which is equivalent to 14%) had hypomagnesemia. The occurrence rate of hypomagnesemia observed in the present research participants corresponds with the findings of earlier studies that have emphasized a significant prevalence of hypomagnesemia in individuals with heart problems.[13] A study was carried out on a cohort of 11,000 American inhabitants, ranging from 45 to 64 years old, which revealed fascinating discoveries. It was observed that a modest percentage, precisely 2.5% of the participants, displayed magnesium concentrations less than 0.7 millimoles per liter.

Table 3: Correlation between serum potassium and age, gender, GFR, hypomagnesemia, and drugs

	Hypokalemia *n*: 74	Non-hypokalemia *n*: 908	*P*
Age±average (year)	60.01±13.41	63.2±13.57	0.05
Male, *n* (%)	34 (45.9)	312 (34.4)	0.4
GFR±average (ml/min)	73.73±27.76	71.30±73.43	0.77
Hypomagnesemia	16 (21.6)	122 (13.4)	0.05
Furosemide, *n* (%)	23 (31.1)	201 (22.1)	0.07
Thiazide diuretics, *n* (%)	9 (12.2)	81 (8.9)	0.51
Digoxin, *n* (%)	8 (10.8)	63 (6.9)	0.21
ACEI, *n* (%)	3 (4.1)	58 (6.4)	0.42
ARB, *n* (%)	25 (33.8)	309 (34)	0.96
Spironolactone, *n* (%)	11 (14.9)	128 (14.1)	0.85

GFR: glomerular filtration rate; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker

Furthermore, 5% of the participants had magnesium levels lower than 0.75 millimoles per liter. Notably, this state was discovered to be twice as elevated among the 4,000 individuals with African lineage.[14] Delving further into the study, it was revealed that hypomagnesemia was more frequent in females compared to males. Roughly 12.7% of males were identified as possessing this state, whereas a slightly greater percentage of 16.4% was observed among females. These discoveries offer additional substantiation to the current proof of a heightened prevalence of low blood magnesium levels among females relative to males within the particular population being scrutinized. These findings support studies conducted by Worwag and colleagues, who also observed low magnesium levels in females compared to males.[9,15] Hormonal factors, such as estrogen levels, regulate magnesium levels. Research has shown that estrogen affects magnesium absorption, excretion through the kidneys, and transport within cells. These factors can influence magnesium levels in females.

Additionally, dietary preferences and eating habits may differ between genders, leading to variations in magnesium intake and subsequent body levels. Magnesium plays a role in bodily functions, including the health of our bones and heart. As a result, low levels of magnesium in women could increase their vulnerability to diseases associated with magnesium deficiency, such as osteoporosis, cardiovascular conditions, and metabolic disorders.[16]

In this study, the participants were divided into two categories: those above 65 and those below 65. Among individuals aged 65 years and above, around 16.19% had hypomagnesemia (low magnesium levels), while among those below 65 years, it was 12.13%. These findings suggest that hypomagnesemia is 4% more prevalent among the population. In a case-control study, a high incidence of hypomagnesemia (50%), age, inadequate glycemic control, and a low estimated glomerular filtration rate (eGFR) were significant risk factors for lower serum magnesium levels.[17] The increased frequency of hypomagnesemia among older individuals holds considerable importance in a clinical setting. As individuals grow older, the lack of magnesium can exacerbate health issues associated with aging. Increase the chances of experiencing cardiovascular problems, high blood pressure, and other ailments that accompany aging.[18] In older people, magnesium consumption is generally lower than in younger individuals, possibly due to changes in eating habits, decreased appetite, or limited access to foods rich in magnesium. Furthermore, age-related changes may affect how the body absorbs and eliminates magnesium through the kidneys, resulting in decreased magnesium levels within the body.[8]

This study analyzed the relationship between age, gender, GFR, and medication consumption in patients with and without hypomagnesemia. The outcomes revealed no notable distinctions between the two groups concerning these variables. This suggests that none of them can be considered significant risk factors for hypomagnesemia in this study. Another

research study explored the occurrence of hypomagnesemia in individuals who experienced side effects while using proton PPI. Out of a total of 66,102 individuals, 1.0% (n = 693) reported experiencing hypomagnesemia. Through the analysis of the information using logistic regression, it was discovered that all PPI, except esomeprazole, were linked to a higher likelihood of developing hypomagnesemia. Among the PPIs, pantoprazole presented the most significant risk.

Moreover, the inquiry unveiled a notable connection linking low magnesium in the blood, decreased levels of calcium, and hypokalemia (40). Additionally, an extensive analysis of various studies showcased that people who made use of PPIs had an approximately 40% increased likelihood of encountering a deficiency in magnesium compared to individuals who refrained from using such medications.[19] Hypomagnesemia caused by a specific category of drugs usually occurs only if the patient has been on the medication continuously for at least several years. There is a suspicion that our study did not find a connection between using PPIs and the development of hypomagnesemia. This may be because we needed to consider how long the participants had used PPIs.

Both thiazide and loop diuretics can cause magnesium to be excreted in urine at certain levels. Research has shown that using these diuretics for over a week can reduce plasma magnesium concentration by 5–10% on average. A study involving 404 patients with congestive heart failure undergoing at least three months of furosemide therapy observed a 12.3% prevalence of hypomagnesemia. They concluded that doses exceeding 80 milligrams of furosemide per day, along with female gender, congestive heart failure, and hypocalcemia, are significantly associated with hypomagnesemia.[20]

In our analysis, there was no significant link between thiazide and furosemide diuretics, though the study also explored the relationship between their use and hypokalemia. It was observed that the consumption of thiazide diuretics, like hydrochlorothiazide, is associated with hypokalemia, suggesting these medications could be considered a risk factor for this condition; however, such an association was not found for furosemide. It is crucial to highlight that individuals who employ furosemide typically encounter heart failure and regularly consume a combination of angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blocker (ARB), and mineralocorticoid receptor antagonist (MRA) alongside it. These additional medications contribute to a rise in the potassium levels in the bloodstream, which could elucidate the absence of a significant association with decreased potassium.

One of the main goals of this study was to examine how common low levels of magnesium are in patients with different cardiovascular diseases. The findings showed that a significant number of patients with atrial fibrillation (17.54%) and ventricular arrhythmia (40%) had low magnesium levels. Based on these findings, it appears that the occurrence of low magnesium levels (known as hypomagnesemia) is approximately three times more common in patients with arrhythmia compared to the normal population. Furthermore, the results suggest that individuals with hypomagnesemia have four times the chance of experiencing ventricular arrhythmias compared to those with normal magnesium levels. These findings highlight the significance of magnesium in both atrial and ventricular arrhythmias. In a study conducted in 2007, it was also observed that there is a link between magnesium deficiency and cardiac arrhythmias.[21–23]

In addition to hypomagnesemia, we also evaluated the prevalence of hypokalemia in this study. Out of 982 patients, 74 patients exhibited hypokalemia. A meaningful association was identified between hypokalemia, age, hypomagnesemia, and hydrochlorothiazide usage. Notably, older individuals and those with hypomagnesemia were more likely to develop hypokalemia. Furthermore, among the 138 patients diagnosed with hypomagnesemia, an additional 16 were also found to have hypokalemia. These findings provide valuable insights into the contributing factors of hypokalemia risk and the interplay between age, hypomagnesemia, and medication usage in patients with cardiovascular conditions.

Conclusion

Our investigation unveils a greater occurrence of hypomagnesemia in women as opposed to men. Moreover, we observed a correlation between age and the prevalence of hypomagnesemia, with individuals aged 65 years and above displaying the highest occurrence. There is a pressing need to pay more attention to the intake of magnesium and effectively manage hypomagnesemia, especially among vulnerable groups such as women and older adults. The results emphasize magnesium's crucial role in developing irregular heart rhythms, as individuals with hypomagnesemia have a four-fold increased risk of experiencing ventricular tachycardia compared to those with normal magnesium levels. It is strongly advised to incorporate assessments of magnesium levels into regular cardiac tests for patients, and there should be a greater focus on treatment due to the potentially severe consequences of hypomagnesemia, which do not require excessive financial resources.

Limitations of the study

Patients can arrive at the emergency facility at any moment, with a chance that some individuals may be discharged before the researcher can identify them and gather blood samples. As a result, these patients would have to be excluded from the study. Additionally, the study fails to address the duration of PPI usage, which serves as another limitation.

Ethics approval and consent to participate

The authors have entirely observed ethical issues (including plagiarism, data fabrication, and double publication). The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of the Isfahan University of Medical Sciences approved this study. The institutional ethical committee at Isfahan University of Medical Sciences approved

all study protocols (IR.MUI.RESERCH.REC.1400.386). Accordingly, written informed consent was obtained from all participants before any intervention.

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Conflicts of interest

There are no conflicts of interest.

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