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Prevalence of hypomagnesemia and its association with clinical outcomes in patients with acute coronary syndromes

Munir Ahmad [a], Muhammad Yasir [a], Omer Qadeer [b], Farah Naz [c], Ahmad Salman [c], Jasia Shahid [c]

[a] Associate Professor, Department of Cardiology, Faisalabad Institute of Cardiology, Faisalabad.
[b] Senior Registrar, Department of Cardiology, Faisalabad Institute of Cardiology, Faisalabad.
[c] Assistant Professor, Department of Cardiology, Faisalabad Institute of Cardiology, Faisalabad.
Correspondence: drmunir2000@hotmail.com*

ABSTRACT

BACKGROUND & OBJECTIVE: Acute coronary syndromes (ACS), including unstable angina, NSTEMI, and STEMI, remain the leading causes of morbidity and mortality. Hypomagnesemia (<1.7 mg/dL) occurs in 29–76% of ACS patients and predicts worse outcomes, including arrhythmia's, larger infarction size, and higher in-hospital mortality. Limited studies have explored its prevalence and prognostic value in low- and middle-income countries like Pakistan. This study aimed to assess the prevalence of hypomagnesemia in ACS patients and its impact on early clinical outcomes.

METHODOLOGY: This descriptive cross-sectional study was conducted over one year at the Faisalabad Institute of Cardiology. A total of 185 ACS patients were recruited through consecutive sampling. Serum magnesium was measured within 24 hours of admission. Clinical outcomes, including arrhythmia's, infarction size, and in-hospital mortality, were analyzed using SPSS 25.

RESULTS: Hypomagnesemia was observed in 85(45.9%) of patients. Those with hypomagnesemia had significantly higher rates of arrhythmia's (41.2% vs. 20%, p≤0.001), larger infarction size (52.9% vs. 30%, p≤0.001), and higher in-hospital mortality (23.5% vs. 10%, p=0.012). Logistic regression identified hypomagnesemia (OR: 2.5, p=0.01), advanced age (OR: 1.8, p=0.03), and diabetes (OR: 1.6, p=0.04) as key predictors of mortality.

CONCLUSION: Hypomagnesemia is common in ACS and linked to poor outcomes. Routine screening and management, especially in resource-limited settings, are crucial. Further studies are needed to confirm findings and optimize treatment strategies.

KEYWORDS: Acute Coronary Syndromes, Magnesium Deficiency, Myocardial Infarction, In-Hospital Mortality, Magnesium , Cardiovascular Disease.

INTRODUCTION

Acute coronary syndromes (ACS), encompassing unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), are leading causes of morbidity and mortality worldwide, including in Pakistan [1].Abbreviated forms of acute coronary syndromes (ACS) and their short-term outcomes such as arrhythmias, infarct size, and in hospital mortality remain significant challenges, often linked to the biochemical disturbance of hypomagnesemia [2]. Cardiovascular health requires many enzymatic reactions and modulators of myocardial excitability, vascular spasm, and platelet aggregation. Serum magnesium concentrations below the normal range interfere with these physiological processes and expose patients to arrhythmia's, increased infarction size, and compromised cardio myocyte salvage [3]. Hypomagnesemia has been associated with an increased incidence of ventricular arrhythmia, increased length of hospital stay, and increased mortality. Independent predictors of poor outcomes include hypomagnesemia, in which patients do not respond well to standard ACS therapies, including anti-platelet agents and beta blockers [4].

Epidemiological data shows that hypomagnesemia is common in critically ill patients with CVD, accounting for more than 50% of this population [5]. Potential causes of hypomagnesemia include increased magnesium excretion in the stool or urine due to gastrointestinal or renal disease and the use of drugs like diuretics and proton pump inhibitors. Notably, regional disparities in Diabetes Mellitus (DM) intake aggravate the risk, especially in low- and middle-income countries, including Pakistan, with inadequate nutrition and low socioeconomic status [6]. Surprisingly,

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literature examining large-scale data analyzing frequency and outcomes of hypomagnesemia in ACS is scarce, and critical research gaps are present hence [7].

The purpose of this study is to provide a quantitative review of the literature regarding the relationship between serum magnesium levels and multiple short-term prognostic markers in ACS, such as ventricular arrhythmia, myocardial infarction size, and in-hospital mortality. The study aims to address the deficiency of magnesium or hypomagnesemia on clinical and practical levels that require research-based solutions for early risk assessment and management.

METHODOLOGY

This cross-sectional study was carried out in the emergency department of the Cardiology unit at the Faisalabad Institute of Cardiology, a large tertiary care teaching hospital with a high patient turnover, especially for those presenting with acute coronary syndrome (ACS).

The purpose of the study was to estimate the proportion of patients with hypomagnesemia among those diagnosed with ACS and to compare the clinical characteristics of patients with and without hypomagnesemia. The study was conducted from January 2022 to December 2022, analyzing a total of 185 patients with ACS, with the sample size determined by prevalence studies and the desired level of accuracy.

Non-probability consecutive sampling was used to select eligible patients, ensuring that all consecutive patients meeting the inclusion criteria were included. Inclusion criteria included adults over 18 years of age with ACS, defined as STEMI, NSTEMI, or unstable angina, and those who provided informed consent. Exclusion criteria included patients with chronic kidney disease (CKD) or end-stage renal disease (ESRD), individuals on magnesium supplements or medications that interfere with magnesium levels, patients with known electrolyte imbalances other than magnesium, and pregnant or lactating women. Upon presentation to the Emergency Department, patients were screened based on the inclusion and exclusion criteria, and detailed demographic and clinical data were recorded. Baseline data included age, gender, BMI, comorbidities such as diabetes, hypertension, and prior cardiac events, the type of ACS, the onset of symptoms, and initial management.

Blood samples were collected within 24 hours of admission to measure serum magnesium levels using the ion-selective electrode method, with hypomagnesemia defined as magnesium levels below 1.7 mg/dL. Patients were followed throughout their hospital stay to assess clinical outcomes such as arrhythmia, heart failure, recurrent ischemia, and mortality, with detailed records of interventions and complications. All data were cross-verified by a second investigator for accuracy, and missing data were minimized through regular monitoring. Prior to their inclusion in the trial, all participants or their legal guardians provided written informed permission, which was evaluated and approved by the Faisalabad Institute of Cardiology's Institutional Review Board (No.12-2018/MEC/FIC/FSD / Dated: 10-09-2018).

SPSS version 25.0 was used to analyze the data. Categorical data were presented as percentages and frequencies, and continuous variables as mean ± standard deviation. Independent t-tests for continuous variables and chi-square tests for categorical variables were used to determine the prevalence of hypomagnesemia and examine its relationship to clinical outcomes. A multi-variable logistic regression analysis was conducted to account for any potential influences. Statistical significance was established at a p-value of less than 0.05.

RESULTS

In this study, a total of 185 patients were enrolled based on inclusion criteria. The mean age of patients with hypomagnesemia (n=85) was significantly higher at 62 ± 12 years compared to 58 ± 11 years in those without hypomagnesemia (n=100) (P-value=0.04). The proportion of males was slightly higher among patients with hypomagnesemia at 60 (70.6%) compared to 65 (65%) in the no hypomagnesemia group, while females comprised 25(29.4%) and 35(35%) in the respective groups, with both gender differences showing no statistical significance (P-value=0.418). Hypertension was more prevalent among patients with hypomagnesemia, affecting 50(58.8%) compared to 40(40%) in those without hypomagnesemia (P-value=0.01). Similarly, diabetes Mellitus was reported in 40 (47.1%) of the hypomagnesemia group versus 30(30%) in the no hypomagnesemia group (P-value=0.02). Smoking was also significantly more frequent in the hypomagnesemia group, observed in 30(35.3%) compared to 20(20%) of patients without hypomagnesemia (P=0.01) Table-I.

Table-I: Baseline Characteristics (n = 185).

Variable	Hypomagnesemia (n=85) n(%)	No Hypomagnesemia (n=100) n(%)	P-value
Age (Mean ±SD)	62 ± 12	58 ± 11	0.04
Male	60 (70.6)	65 (65)	0.418
Female	25 (29.4)	35 (35)	
Hypertension	50 (58.8)	40 (40)	0.01
Diabetes Mellitus	40 (47.1)	30 (30)	0.02
Smoking	30 (35.3)	20 (20)	0.01

Table-II: Relationship of hypomagnesemia with clinical outcomes (n = 185).

Outcomes	Hypomagnesemia (n=85) n(%)	No Hypomagnesemia (n=100) n(%)	P-value
Arrhythmia's	35 (41.2)	20 (20)	≤0.001
Increased Myocardial Infarction Size	45 (52.9)	30 (30)	≤0.001
In-hospital Mortality	20 (23.5)	10 (10)	0.012

The association between hypomagnesemia and clinical outcomes in patients with acute coronary syndromes was significant in this study. Among patients with hypomagnesemia (n=85), arrhythmia's were observed in 35(41.2%) individuals, which was notably higher compared to 20(20%) individuals without hypomagnesemia (n=100), with a P-value of ≤0.001. Similarly, an increased myocardial infarction size was documented in 45(52.9%) patients with hypomagnesemia, compared to 30(30%) patients without hypomagnesemia, showing statistical significance with a P-value of ≤0.001. Furthermore, in-hospital mortality occurred in 20(23.5%) patients with hypomagnesemia, which was more than double the 10 patients (10%) observed in the no-hypomagnesemia group, with a P-value of 0.012. These findings highlight a strong correlation between hypomagnesemia and adverse clinical outcomes in this cohort Table-II.

Table-III: Total mean serum magnesium concentration (n = 185).

Clinical Outcomes	Mean Magnesium Level in Patients with Outcome (mg/dL)	Mean Magnesium Level in Patients without Outcome (mg/dL)	P-value
Arrhythmia's	1.6 ± 0.2	1.9 ± 0.1	≤0.001
Increased Myocardial Infarction Size	1.5 ± 0.3	2.0 ± 0.2	≤0.001
In-hospital Mortality	1.4 ± 0.2	2.1 ± 0.1	≤0.001

In this study, hypomagnesemia was significantly associated with adverse clinical outcomes in patients with acute coronary syndromes. Patients who experienced arrhythmia's had a mean serum magnesium level of 1.6 ± 0.2 mg/dL compared to 1.9 ± 0.1 mg/dL in those without arrhythmia's, demonstrating a statistically significant difference (p-value≤0.001). Similarly, those with increased myocardial infarction size had a mean magnesium level of 1.5 ± 0.3 mg/dL versus 2.0 ± 0.2 mg/dL in patients without this outcome (p-value≤0.001). In-hospital mortality was notably associated with the lowest mean serum magnesium levels, measuring 1.4 ± 0.2 mg/dL in deceased patients compared to 2.1 ± 0.1 mg/dL in survivors (p-value≤0.001) Table-III.

Table-IV: Multiple linear regression of predictors of In-hospital mortality among patients (n = 185).

Variable	Odds Ratio (95% CI)	P-value
Hypomagnesemia	2.5 (1.3–4.8)	0.01
Age > 60 years	1.8 (1.1–3.0)	0.03
Diabetes Mellitus	1.6 (1.0–2.7)	0.04
Smoking	1.4 (0.8–2.5)	0.1
Increased Myocardial Infarction Size	3.0 (1.5–6.0)	<0.001

In the multivariate analysis of predictors of in-hospital mortality among patients with acute coronary syndromes (n = 185), hypomagnesemia was identified as a significant predictor, with an odds ratio (OR) of 2.5 (95% CI: 1.3–4.8), accounting for 2.5 times higher odds of mortality (p = 0.01). Advanced age (>60 years) also significantly increased the odds of mortality, with an OR of 1.8 (95% CI: 1.1–3.0) or 80% higher odds (p = 0.03). Similarly, diabetes mellitus was associated with a 1.6-fold (95% CI: 1.0–2.7) increase in odds of mortality (p = 0.04). While smoking demonstrated a non-significant association with mortality, with an OR of 1.4 (95% CI: 0.8–2.5), increased myocardial infarction size was the strongest predictor, exhibiting three times higher odds of mortality (OR: 3.0, 95% CI: 1.5–6.0; p < 0.001). These findings highlight the importance of addressing hypomagnesemia, age, diabetes, and infarct size in managing in-hospital outcomes in this patient population Table-IV.

DISCUSSION

Acute Coronary Syndrome or act as also known as acute myocardial infarction or both is among the leading causes of morbidity and mortality. These syndromes consist of several positions - unstable angina, non-st elevation myocardial infarction(NSTEMI), and ST-elevation myocardial infarction (STEMI) – all having a common pathological basis of plaque rupture and subsequent thrombus formation. A second mineral of considerable importance is magnesium, which is present in the intracellular compartment and is implicated in enzyme activities, stabilization of myocyte membranes and control of vascular tension. Although hypomagnesemia has been identified as a widespread problem with strong clinical relevance, it is considered to be relatively unnoticed in clinical practice.

In this study, the mean age of patients with hypomagnesemia was significantly higher (62 ± 12 years) compared to those without hypomagnesemia (58 ± 11 years), aligning with studies suggesting that older individuals are more prone to electrolyte imbalances due to physiological and pathological changes associated with ageing [8]. Moreover, the male-to-female ratio was not statistically significant, further supporting earlier literature that suggested that there seems to be no strong male or female susceptibility to hypomagnesemia in cardiovascular circumstances [9].

Hypertension and diabetes mellitus were found to be higher in patients with hypomagnesemia at 58.8% and 47.1%, respectively. This is in consonance with epidemiological evidence that magnesium deficiency causes endothelial dysfunction, oxidative stress, and inflammation, which is potent in hypertension and diabetes mellitus [10,11]. Importantly, Guerrero-Romero and Kostov (2019) meta-analysis paid attention to the relationship between magnesium deficiency and insulin resistance, which supports our study [12].

Smoking was more common in the hypomagnesemia group (35.3% vs. 20%), and smoking has been related to oxidative stress, which may result in cardiovascular complications. This correlation confirms the desirability of smoking-cessation programs in cardiovascular risk, especially where magnesium is deficient [13].

Hypomagnesemia was significantly linked with arrhythmias, with 41.2% prevalence compared with 20% among non-hypomagnesemia patients (P < 0.001). The results are parallel in nature to the previous work done by Kostov et al., 2019, in which the author elucidated that magnesium has a co-factor impact on myocardial electrical stability [12]. It has been established that the lack of magnesium worsens intracellular calcium overload, thus increasing the risk of arrhythmias [13].

That larger infarction size was found in hypomagnesemia patients (52.9% vs.30%) underscores the role of magnesium in the prevention of ischemic damage. Experimental works of Alateeq et al (2024) presented the concept that Mg-deficient population was at a greater risk of myocardial damage due to a lack of vasodilation and perfusion during ischemia and that magnesium supplementation could reverse this effect [14]. This claim is further evidenced by clinical trials showing improved cardiovascular outcomes with magnesium repletion [15].

The overall in-hospital mortality was significantly higher in patients with hypomagnesemia: (23.5% vs 10%, p=0.01). This observation is consistent with current literature from observational studies and meta-analysis of studies where hypomagnesemia is established as an independent risk factor for mortality in patients with ACS [14]. Thus, there is a strong need to recognize and treat the deficiency of magnesium on time, especially among patients with ACS: the level of magnesium in dead patients was 1.4 ± 0.2 mg/dL, while in survivors, it was 2.1 ± 0.1 mg/dL.

Hypomagnesemia was a significant predictor of in-hospital mortality (OR: 2.5, P = 0.01), supported by Taha et al. (2024) [16]. Being an independent predictor, age superior to 60 years can also be referred to as a traditional risk factor for unfavourable outcomes of ACS, including diabetes mellitus [17]. The strongest predictor is increased MI size (OR: 3.), which confirms that hypomagnesemia patients require the strictest control to prevent infarct-related complications.

Magnesium's role in cardiovascular health is multifaceted. It controls vascular tone, cardiac contractility, electrical activity, and mechanical properties [18]. Low magnesium concentration intensifies both oxidative stress and inflammation, shifts haemostasis to pro-thrombotic potential, and modulates the risk of fatal arrhythmia [19]. Therefore, this study demonstrates the need to adopt and sustain appropriate magnesium supplementation in patients who have suffered an ACS to minimise adverse outcomes.

The observed strong and consistent link between hypomagnesemia and worse clinical outcomes implies that serum magnesium testing should become a standard part of ACS care. Therefore, it is likely that in-patient interventions, both dietary and pharmacological, could help improve the prognosis, as added by Owusu et al. (2024) [20].

The limitations of this study include its observational nature, which does not allow inferring causality, and the small sample size, which necessitates further evaluation of this hypothesis in future large-scale, multi-centre, randomized controlled trials.

CONCLUSION

Hypomagnesemia is a common and independent predictor of adverse outcomes in ACS patients, including arrhythmia's, larger infarct size, and increased in-hospital mortality. Monitoring and correcting serum magnesium levels, especially in high-risk groups such as the elderly and diabetics, may improve clinical outcomes. Further large-scale studies are warranted to validate these findings and optimize treatment strategies.

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Authors' Contribution:

Munir Ahmad : Substantial contributions to the conception and design of the work.
Muhammad Yasir : The acquisition and analysis of data for the work.
Omer Qadeer: Analysis of data for the work.
Farah Naz: Interpretation of data for the work.
Ahmad Salman: Drafting the work and reviewing it critically for important intellectual content.
Jasia Shahid: Final approval of the version to be published.

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