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Assessing Serum Magnesium Levels in Acute Myocardial Infarction: Prognostic Insights and Clinical Implications.

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KEYWORDS

Acute Myocardial Infraction, Serum, Magnesium, High Risk, Coronary

ABSTRACT:

Background: Acute myocardial infarction (AMI) is a critical cardiovascular event with significant morbidity and mortality worldwide. Magnesium, an essential intracellular cation, plays a vital role in myocardial function and vascular tone regulation. This study investigates the serum magnesium levels in patients presenting with AMI and explores the potential prognostic significance of these levels.

Materials and Methods: The study, conducted at a tertiary care hospital's Department of Medicine, focused on ICU-admitted patients with acute myocardial infarction (AMI). Using a Hospital-Based Observational Study design over 24 months, 100 eligible subjects were consecutively sampled. The research aimed to investigate serum magnesium levels' implications in the context of AMI, employing inclusion criteria for individuals over 20 years with acute coronary syndrome (STEMI and NSTEMI) and applying exclusion criteria to enhance reliability and specificity.

Results : This 1.5-year observational study of 100 acute myocardial infarction (AMI) cases, including both ST-segment elevation and non-ST-segment elevation, revealed a male predominance and identified lifestyle factors such as sedentary jobs in 70% of patients. Common symptoms included chest pain, breathlessness, sweating, and palpitations. Complications, including arrhythmia and shock, occurred in 16% of cases during hospitalization. Serum magnesium levels emerged as a significant predictor for complications and mortality, with a cutoff of 1.7 mg% showing high sensitivity and specificity. The study underscores the importance of magnesium levels in predicting outcomes and suggests its potential as a prognostic marker in AMI cases.

Conclusion: Research, along with prior studies, suggests that low magnesium levels in acute myocardial infarction (AMI) independently predict an adverse prognosis, with increased complications and mortality. Serum magnesium levels may serve as a simple indicator for identifying high-risk AMI patients, recommending potential benefits from magnesium treatment. However, further comprehensive multicenter studies are deemed essential to validate these findings.

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INTRODUCTION

Magnesium, an essential element in the human body found naturally in various foods and as a dietary supplement, constitutes approximately 24 g in an adult body, with about 50%-60% located in the bones. The serum magnesium level comprises less than 1% of the total body magnesium [1].

Playing a critical role as a cofactor in over 300 enzymatic reactions, magnesium influences glycemic control, blood pressure, and lipid peroxidation. It acts on platelets, smooth muscles, and myocardial cells, and its deficiency can contribute to hyperlipidemia and atherogenic deposits, particularly in coronary arteries, thereby impacting cardiovascular health [2].

In the realm of myocardial physiology, magnesium is vital; low concentrations destabilize myocardial cell membranes, while high concentrations have stabilizing and antiarrhythmic effects. Even minor fluctuations in ion concentrations can lead to significant consequences [3]. Magnesium's influence extends to acute myocardial infarction (AMI) and its complications, including arrhythmias, as well as its role in the pathogenesis of various cardiovascular diseases [4].

Given that AMI is a substantial health concern globally, with increasing significance in both industrial and developing nations, understanding magnesium's dynamics is crucial. In myocardial infarction, there is a functional deficit of available magnesium due to its sequestration in adipocytes. Studies suggest a decline in serum magnesium levels within the initial 48 hours post-AMI, followed by a gradual increase to normal levels over approximately three weeks [5]. This study investigates the serum magnesium levels in patients presenting with AMI and explores the potential prognostic significance of these levels.

Aims and Objectives

1. Investigating the serum magnesium levels among individuals experiencing acute myocardial infarction (AMI).
2. Examining the correlation between serum magnesium levels and in-hospital mortality in patients with AMI.
3. Exploring the link between serum magnesium levels and complications arising from acute myocardial infarction, such as heart failure, arrhythmia, left ventricular dysfunction, and cardiogenic shock.

The Study was conducted within the Department of Medicine at a tertiary care hospital, focusing on patients who had experienced acute myocardial infarction (AMI) and were admitted to the Intensive Care Unit (ICU) after providing informed consent. Employing a Hospital-Based Observational Study design, consecutive convenient sampling was utilized throughout the 24-month duration, spanning from November 2017 to October 2019. A total of 100 consecutive subjects meeting the eligibility criteria were included in the study, representing a comprehensive effort to understand the implications of serum magnesium levels in the context of AMI within the specified hospital setting.

Inclusion Criteria:

The study considered individuals aged over 20 years who were presented with acute coronary syndrome, as per the World Health Organization (WHO) definition. The included patients encompassed those with both ST segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI).

Exclusion Criteria:

The study excluded the subjects with a history of regular alcohol use, chronic diarrhea, excessive urination (as observed in uncontrolled diabetes or during recovery from acute kidney injury), malabsorption syndrome (including conditions like celiac disease and inflammatory bowel disease), and those taking specific medications such as amphotericin, cisplatin, cyclosporine, aminoglycosides, and antibiotics. Additionally, individuals who chose not to participate in the study were also excluded. This stringent set of exclusion criteria aimed to refine the study population and enhance the reliability and specificity of the findings.

METHODOLOGY

Following the randomized patient selection process and subsequent acquisition of informed written consent from all participants enrolled in the study, a thorough examination of pertinent medical history and physical condition was conducted. The patients underwent a comprehensive set of investigations, encompassing a complete blood count, urine examination, blood sugar analysis, blood urea and serum creatinine assessments, fasting lipid profile evaluation, and

cardiac enzyme profiling. Additionally, an electrocardiogram (ECG) was performed for all cases. Serum magnesium levels were meticulously estimated upon admission for both the case and control groups as part of the diagnostic protocol.

Serum magnesium levels were determined using a colorimetric endpoint test with Xylidyl blue as the reagent, calibrated against a standard of 2.5 mg/dL. This method involves an alkaline pH reaction between magnesium and Xylidyl blue, resulting in the formation of a distinctive red chelating compound. The intensity of the red color directly corresponds to the magnesium concentration in the serum. Analysis can be performed on non-hemolyzed serum or lithium heparin plasma, considering the tenfold higher magnesium concentration in red blood cells compared to the extracellular fluid. Timely separation of serum from cells is crucial to prevent hemolysis. Initially, a comparison was made between serum magnesium levels in both cases and controls. Subsequently, an assessment was conducted to compare serum magnesium levels in patients who developed in-hospital complications (such as arrhythmia, cardiogenic shock, heart failure, and left ventricular dysfunction) with those who did not experience such complications.

Statistical Analysis

The mean and standard deviation were utilized to represent quantitative data, while categorical and nominal data were presented as percentages. Quantitative data underwent analysis through the t-test, non-parametric data was assessed using the Mann-Whitney test, and categorical data was examined using the chi-square test. Pearson correlation coefficient was employed to compute the correlation among quantitative variables. The significance threshold for the p-value was established at <0.05. All analyses were conducted using SPSS software version 21.

RESULTS AND OBSERVATION

Our research constituted a prospective observational study conducted within the hospital setting of the current institute from May 2018 to October 2019, spanning approximately 1.5 years. We examined a total of 100 cases of acute myocardial infarction, encompassing both STEMI and NSTEMI. Following the conclusion of the study period, the systematically analyzed data is summarized below.

Table 1: Distribution of study subjects

	N	**%**
Age group		
20-40	16	16%
41-60	41	41.0%
>60	43	43.0%
Total	100	100
Gender		
Male	64	64%
Female	36	36%
Total	100	100%
Type of Occupation		
	30	30%
Active	70	70%
Sedentary	100	100%
Presenting Complaint		
Chest Pain	87	87.0%

Breathlessness	60	60.0%
Sweating	43	43.0%
Palpitations	43	43.0%
Swelling over lower limbs	1	1.0%
Co-morbidities		
Diabetes Mellitus	17	17.0%
Hypertension	38	38.0%
IHD	23	23.0%
Smoking	43	43.0%
Obesity	20	20.0%
Investigation findings		
High CPKMB	35	35.0%
Positive Troponin T	27	27.0%
Complications		
Tachyarrhythmia	7	7%
Bradyarrhythmia	6	6%
VPC	7	7%
Bigeminy	2	2%
Shock	16	16%
Shock and Arrythmia	3	3%
None	65	65%
Total	100	100%
Mortality		
Yes	9	9%
No	91	91%
Total	100	100%

In the current investigation, the minimum age group considered was 20 years. As depicted in Table 1 and Figure 1, there were 16 cases (16%) in the age range of 20-40 years, 41 cases (41%) in the 41-60 years range, and 43 cases (43%) above 60 years. Nevertheless, the average age of the study participants was 55.62 years, with 43% of the cases falling into the category of individuals over 60 years old. Among the randomly selected 100 cases, 36 were female, and 64 were male. The occurrence of myocardial infarction showed a male predominance, with 64% of cases being male and 36% female, resulting in a male-to-female ratio of 1.77.

Lifestyle stands out as a significant risk factor in the occurrence of acute coronary events. Therefore, we categorized patients based on their occupation or type of work, distinguishing between active and sedentary roles. Among the total of 100 cases, 70% were engaged in sedentary jobs, while only 30% were involved in active occupations. Among these patients, 87 reported chest pain, 60 experienced breathlessness, and 43 each presented with sweating and palpitations. Notably, lower limb swelling was uncommon during acute events. The most frequently reported symptom was chest pain (87%), followed by breathlessness (60%) and

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equal incidences of sweating and palpitations (43% each). Sixteen cases presented solely with isolated chest pain (without any of the other mentioned complaints), and four cases presented exclusively with palpitations.

The most prevalent underlying health condition was hypertension (38%), followed by ischemic heart disease (IHD) at 23%, and diabetes at 17%. Approximately 43% of cases had a history of smoking, and 20% had a body mass index (BMI) exceeding 23 kg/m². The diagnosis of acute coronary events relied on ECG changes and cardiac enzyme markers. Patients exhibiting significant ST-T changes underwent investigations for CPKMB and TROPONIN. Quantitative measurement was employed for CPKMB, while Troponin T was assessed qualitatively. According to Table 1, elevated CPK-MB levels were observed in 35% of cases, and positive Troponin T was reported in 27% of cases.

In our current investigation, complications following myocardial infarction (MI), such as cardiogenic shock and arrhythmia, were observed during the hospitalization period. The recorded arrhythmias included premature ventricular contractions, ventricular bigeminy, ventricular tachycardia, and bradyarrhythmia. The most frequently associated complications were arrhythmia (16%) and shock (16%). Cases with both arrhythmia and shock accounted for 3%. Notably, 65% of cases did not report any complications.

Table: 2 Association of serum electrolytes with associated complications

Electrolyte	Mean Value (Std. Deviation)		Test
	Complicated N= 37	Uncomplicated N=63	
Mg	1.69 (0.11)	2.16 (0.35)	<0.01
Na	140.14 (6.46)	140.24 (8.16)	0.946
K	4.03 (0.39)	4.02 (0.75)	0.69
Ca	8.55 (0.7)	8.77 (0.66)	0.112

In our research, we investigated electrolyte levels, including sodium, potassium, calcium, and magnesium, in both complicated and uncomplicated cases of myocardial infarction (MI) during the hospitalization period. The results presented in Table 2 indicate a significant decrease in mean magnesium levels among MI cases with associated complications (1.69 vs. 2.16 mg%; $p<0.01$). However, there were no notable differences in the mean values of other electrolytes, such as sodium, potassium, and calcium ($p>0.05$).

Table: 3 Association of serum electrolytes with type of Myocardial infarction

Electrolyte	Mean Value (Std. Deviation)		Test
	STEMI N=74	NSTEMI N=26	
Mg	1.97 (0.38)	2,01(0.32)	0.649
Na	139.41 (7.9)	142.42 (5.96)	0.08
K	4.02 (0.67)	4.17 (0.56)	0.32
Ca	8.61 (0.71)	8.91 (0.54)	0.52

The electrolyte levels were examined and compared between the STEMI (ST-elevated myocardial infarction) group and the NSTEMI (non-ST-elevated myocardial infarction) group. According to Table 3, there were no discernible variations in the average values of electrolytes, including magnesium, sodium, potassium, and calcium, between cases of ST and non-ST elevated myocardial infarction ($p>0.05$).

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Table: 4 Association of serum electrolytes with survival

Electrolyte	Mean Value (Std. Deviation)		p- value
	Survivors N=91	Non-Survivors N=9	
Mg	2.02 (0.36)	1.62 (0.68)	<0.01
Na	140.21 (7.83)	140.11 (3.62)	0.97
K	4.06 (0.67)	4.06 (0.37)	0.97
Ca	8.76 (0.64)	8.04 (0.76)	<0.01

The study also investigated and compared serum electrolyte levels between groups of survivors and non-survivors. According to Table 4, the average serum magnesium (1.62 vs. 2.02 mg%; p<0.01) and calcium levels (8.04 vs. 8.76 mg%; p<0.01) were notably reduced in non-survivors.

Table: 5 Association of serum electrolytes with complications and survival

Electrolyte	Mean Value (Std. Deviation)		p- value
	Survivors (Within Complicated) N=28	Non-Survivors (Within Complicated) N = 9	
Mg	1.72 (0.11)	1.62 (0.063)	0.017
Na	140.14 (7.19)	140.11 (3.62)	0.99
K	4.02 (0.41)	4.056 (0.37)	0.826
Ca	8.71 (0.61)	8.04 (0.76)	0.01

The investigation also explored and compared the connection between serum electrolytes and survival outcomes in complicated cases. Table 5 demonstrates that the average serum magnesium (1.62 vs. 1.72 mg%; p<0.01) and calcium levels (8.04 vs. 8.71 mg%; p<0.01) were markedly diminished in non-survivors with complications in comparison to survivors with complications.

In the multivariate analysis, only serum magnesium emerged as a significant predictor for the occurrence of complications in myocardial infarction cases (p<0.01). Similarly, in the multivariate analysis, serum magnesium was identified as the sole significant predictor of mortality among myocardial infarction cases (p<0.01)

A noteworthy correlation was noted between magnesium levels and mortality in cases of acute myocardial infarction (AMI), with an area under the curve of 0.94 (confidence interval: 0.893-0.986). The ideal magnesium level cutoff was determined to be 1.7 mg%, exhibiting a sensitivity of 100% and specificity of 86.8%.

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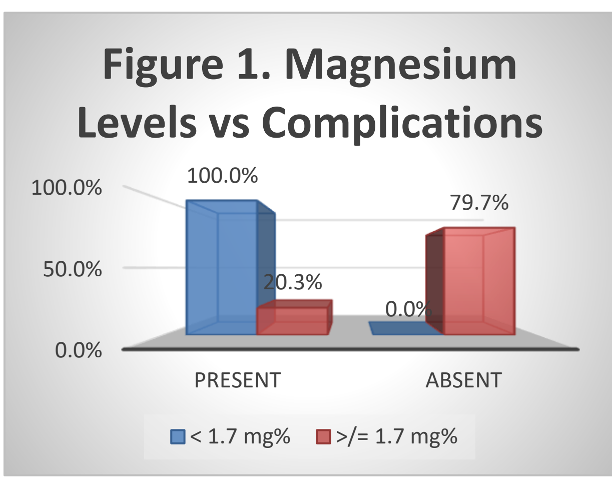
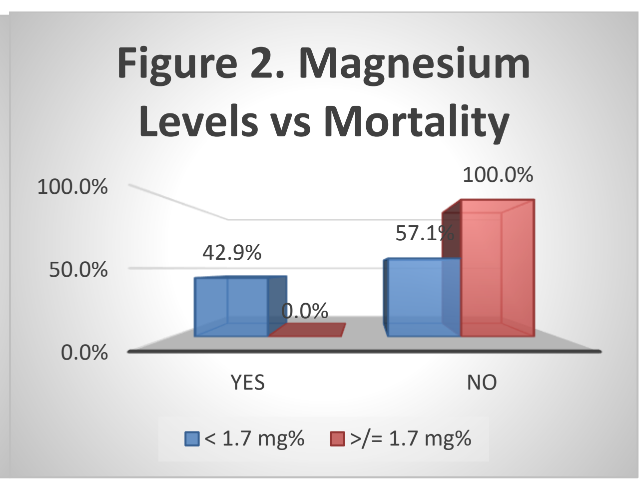
Table: 6 Multivariate analysis for identification of predictor of complications and Mortality

Logistic Regression: Complications (Y/N)								
Variables	B	S.E.	Wald	Df	p- value	Odds Ratio	95% C.I.for EXP(B)	
							Lower	Upper
Mg	17.176	3.609	22.653	1	<0.01	28812604.5	24420.1	33995259278
Ca	-0.21	0.595	0.124	1	0.725	0.811	0.253	2.601
Logistic Regression: Mortality (Y/N)								
Mg	13.499	5.24	6.637	1	0.01	728565.693	25.248	21023899852
Ca	0.973	0.67	2.109	1	0.146	2.645	0.712	9.828

A significant link was established between lower magnesium levels and the incidence of complications, with over half of the cases (56.7%) experiencing complications having magnesium levels below 1.7 mg%. Likewise, there was a noteworthy association between diminished magnesium levels and mortality, as all deaths occurred in individuals with magnesium levels below 1.7 mg%. (Figure 1 & 2)





DISCUSSION

In this current investigation, our objective was to establish a connection between acute ischemia and serum magnesium levels, while also prospectively monitoring these patients for in-hospital mortality. The study encompassed 100 patients, all aged 20 years or above, diagnosed with acute myocardial infarction, admitted to our hospital, and providing informed consent. The assessment of serum magnesium levels was conducted upon admission for each case, alongside the analysis of other electrolytes.

The average age of the participants in the study was 55.62 +/- 13.73 years, with 43% of the individuals being over the age of 60. Among the cases, 16% fell within the age range of 20-40, and 41% were between 41 and 60 years old. The incidence of myocardial infarction exhibited a male predominance, with 64% of cases being male and 36% female.

The demographic distribution observed in our study aligns with findings from various other studies. In a study conducted by Siddiuqi et al. [6] , the mean age at presentation was 56.6 years (SD ± 11.48), and the male-to-female ratio was 8:1 (88.5% males to 11.5% females). Another study by Senthil KP et al. [7] reported the peak incidence in the age group of 50–64, with a mean age of 57 years and 90% male participants compared to 10% female participants. Nour MK et al. [8] observed a mean age of 51.8 years in the study group, with 56% males and 44% females. Similarly, Parale GP et al. [9], in their study of 300 myocardial infarction cases, noted a mean age of 60 years, with 220 males and 80 females. Mhaskar M et al. [10] reported a mean age of myocardial infarction cases as 59.3 years in their study, with a male-to-female ratio of 2.7:1.

The average age of individuals in our study was 55.62 +/- 13.73 years, with 43% of cases being over 60 years old. Chest pain was the predominant presenting complaint, reported by 87% of patients, followed by breathlessness (67%), sweating (43%), and palpitations (43%). A combination of all four symptoms was observed in 24% of patients, while 16% presented with isolated chest pain not associated with other symptoms.

This demographic distribution aligns with findings from various studies. Siddiuqi et al. reported chest pain as the most common presentation (100%), followed by sweating (61%), breathlessness (50%), and nausea and vomiting (21%). Similar observations were noted by Senthil KP et al. and Nour MK et al.

Regarding risk factors and comorbidities, 43% of cases had a history of smoking, and 20% had a body mass index (BMI) over 23 kg/m². The most commonly associated morbidity was hypertension (38%), followed by ischemic heart disease (IHD) (23%) and diabetes (17%). Smoking was identified as a risk factor in 70% of acute myocardial infarction cases in a study by Akila A et al. [5], consistent with results from Senthil KP et al. and Siddiuqi et al.

In our study, 26% of cases were classified as non-ST-elevated myocardial infarction (NSTEMI), while 74% had ST-elevated myocardial infarction (STEMI). Among STEMI cases, anterior wall MI was predominant (44 cases), followed by inferior wall MI (30 cases). This distribution is consistent with findings from other studies, such as Akila A et al. and Vaidya V et al. which also reported anterior wall MI as the most common.

Post-MI complications, including cardiogenic shock and arrhythmias, were observed in our study. Arrhythmia (16%) and shock (16%) were the most common complications, and both were reported in 3% of cases. Arrhythmias were diverse, including premature ventricular contractions, ventricular bigeminy, ventricular tachycardia, and bradyarrhythmia. Similar observations were made in other studies, with approximately 90% of AMI patients developing some form of cardiac arrhythmia during or after the event. The incidence of arrhythmia and shock varied across studies, with risk highest in the first hour after AMI. Studies by Akila et al. and Mhaskar M et al. reported comparable findings regarding the incidence of arrhythmia and shock.

In summary, our study provides valuable insights into the demographics, risk factors, and clinical characteristics of patients with acute myocardial infarction, and these findings are consistent with observations from other relevant studies in the literature.

The mortality rate in our current study stood at 9%, with all nine cases experiencing associated complications. Among these, four cases had cardiogenic shock, two had ventricular tachycardia as an arrhythmia, and three had both complications simultaneously. Comparable mortality rates were reported by Shechter et al. [11] (12.3%) and Hashmi SF et al. [12] (11%), with complications related to acute myocardial infarction (AMI) being the common factor in cases that did not survive. Similar mortality rates ranging from 3% to 21% were documented in various other studies.

The role of magnesium ion in cardiovascular health has gained prominence, implicating its involvement in AMI pathogenesis and complications such as arrhythmias. Magnesium plays a crucial role in maintaining ATP activation, sodium-potassium pump function, and exerting a calcium-

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blocking effect, thereby influencing arrhythmias and rhythm disturbances post-AMI. Hypomagnesemia in AMI patients is linked to heightened catecholamine-induced myocardial necrosis, increased inflammatory cytokine levels, and larger infarct size during coronary occlusion. The stress of AMI can elevate magnesium requirements due to myocardial and urinary losses.

Studies have reported a decrease in serum magnesium following acute MI, though it remains unclear whether the low cardiac content precedes or results from myocardial infarction. Intravenous magnesium treatment in post-infarction individuals has shown a lower risk of dying from ischemic heart disease-related complications. Therefore, establishing an association between low serum magnesium and its prognostic significance in AMI has become imperative.

In our study, mean magnesium levels were significantly lower in cases with complications and mortality. On multivariate analysis, serum magnesium emerged as the only significant predictor of complications like arrhythmia and mortality in AMI cases. The ROC analysis revealed an area under the curve of 0.94, signifying the prognostic value of magnesium in predicting mortality. The optimal cut-off for magnesium levels was identified as 1.7 mg%, with high sensitivity (100%) and specificity (86.8%). Notably, all mortality cases and more than half of the complications occurred in individuals with magnesium levels below 1.7 mg%.

Studies by Dyckner T et al. [13] Akila A et al., and Shafiq et al. [147] also supported the significance of magnesium in predicting complications and mortality in AMI cases, emphasizing the heightened risk associated with hypomagnesemia.

In conclusion, our study underscores the vulnerability of AMI patients with low magnesium levels to increased morbidity and mortality. The routine use of intravenous magnesium early during AMI is recommended to mitigate mortality, arrhythmias, and shock. However, further large multicentric studies are warranted to validate and strengthen the findings of our study.

CONCLUSION

The findings from our current study, in conjunction with those of previous researchers, consistently highlight that diminished magnesium levels in individuals experiencing acute myocardial infarction independently predict a less favorable prognosis. Instances of complications, particularly arrhythmias, and mortality were notably higher in individuals with lower magnesium levels, and the severity of hypomagnesemia correlated with a worsened prognosis. As such, serum magnesium levels emerge as a straightforward indicator for identifying patients at elevated risk. Considering magnesium treatment for individuals with acute myocardial infarction and low magnesium levels should be contemplated. Nevertheless, further extensive multicentric studies are imperative to corroborate and reinforce the conclusions drawn from our study.

LIMITATIONS

The study possesses certain limitations that warrant cautious interpretation of its findings. Firstly, being a single-centric study, there exists a potential for regional bias, limiting the generalizability of the results to the broader population. The outcomes and observations made in this study may not necessarily reflect the diversity inherent in a more comprehensive and varied demographic. Additionally, the absence of a control group in the study design poses a limitation, as the lack of a comparative reference group makes it challenging to discern whether the observed trends are specifically linked to the studied variables or if they might be influenced by other factors. Lastly, the study did not investigate the effects of magnesium therapy in patients with myocardial infarction, which could have provided valuable insights and further substantiated the relevance of serum magnesium levels in predicting outcomes. Future research endeavors with larger, multicentric designs and the inclusion of control groups and intervention analyses could help address these limitations and enhance the robustness and applicability of the study's findings.

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