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***Original research article***

# ASSOCIATION BETWEEN HYPOMAGNESEMIA AND SERUM LACTATE LEVELS IN PATIENTS WITH SEPSIS

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**Abstract:** *Sepsis is a critical condition that often leads to systemic inflammation, organ dysfunction, and high mortality rates. It is well known that metabolic abnormalities play a significant role in the pathophysiology of sepsis.* ***Objective:*** *This study aims to investigate the association between hypomagnesemia and serum lactate levels in patients with sepsis, hypothesizing that low magnesium levels may be linked to increased lactate production and worse clinical outcomes.* ***Methods:*** *A retrospective observational study was conducted at Ghurki Trust Teaching Hospital Lahore from January 2024 to June 2024. Data were collected from 255 adult patients diagnosed with sepsis. Patients were divided into two groups based on their serum magnesium levels: those with normal magnesium levels (≥1.7 mg/dL) and those with hypomagnesemia (<1.7 mg/dL). Serum lactate levels were measured within the first 24 hours of ICU admission.* ***Results:*** *Out of the 255 patients, 108 (42.4%) were found to have hypomagnesemia. Patients with hypomagnesemia had significantly higher serum lactate levels compared to those with normal magnesium levels, with mean lactate levels of 4.1 ± 1.2 mmol/L in the hypomagnesemia group versus 2.7 ± 0.9 mmol/L in the normal magnesium group (p < 0.001).* ***Conclusions:*** *This study shows a significant association between hypomagnesemia and elevated serum lactate levels in patients with sepsis.*

**Keywords:** Sepsis, Hypomagnesemia, Serum Lactate, Retrospective Study, ICU, Mortality, Metabolic Dysfunction.

## Introduction

Sepsis is a severe medical condition characterized by the body's dysregulated response to infection, leading to life-threatening organ dysfunction and high mortality rates (1). The condition still constitutes a serious worldwide threat, contributing to considerable morbidity and mortality amongst seriously ill persons. Sepsis remains one of the most significant sources of preventable mortality worldwide anded only by improved therapeutic and supportive care, and, more crucially, by evidence-based on optimal ICU management (2). The distinct feature of metabolic disturbance including electrolyte modulations in patients with sepsis also plays a pivotal role in worsening organ dysfunction and prognosis. Of these imbalances, hypomagnesemia, or reduced concentration of serum magnesium is found to be common in critically ill, sepsis patients, yet the relevance of this disturbance has not been thoroughly investigated (3). Magnesium also plays a key structural role, being a cofactor in a variety of enzymatic reactions including energy metabolism, protein synthesis, and the stabilization of muscle and nerve cell membranes. It also maintains cardiovascular stability as well as functions in immune responses (4). Because magnesium is involved in so many physiological processes, it is not peculiar that deficiency of this cation may lead to diverse clinical manifestations. Pathophysiologic consequences of hypomagnesemia have included increased risk of cardiac arrhythmias, neuromuscular dysfunction, and immune dysfunction in critically ill patients (5). This implies that in sepsis, low levels of magnesium would jeopardize metabolic and cardiovascular homeostasis and may well play a part in the pathogenesis of the process. The patient with sepsis may have several metabolic derangements, including, importantly, elevated serum lactate levels used as an index of tissue hypoperfusion and impaired oxygen delivery (6). Lactate arises from anaerobic metabolism when tissues are unable to receive sufficient quantities of oxygen, and circulating levels are typically abnormally high in septic patients because the cells they comprise experience hypo-perfusion and have existing disorders of cellular respiration (7). Moderately or highly increased serum lactate concentrations are expected to be associated with disease severity and higher mortality rates, as well as being the indicators of inadequate tissue perfusion and organ dysfunction in sepsis. However, the causes of lactate increase in sepsis are many and this aspect has not been fully explained. Based on energy metabolism interconnection with magnesium, it is possible that hypomagnesemia can deepen lactate production in septic patients, which in turn affects metabolic functions and leads to poorer prognosis (8). While earlier investigations have attempted to establish the link between electrolyte disturbances, generally, and outcomes in critically ill, no prior study has focused particularly on the link between hypomagnesemia concentrations and serum lactate levels in patients with sepsis. Appreciation of this relationship is useful in the enhancement of the management of sepsis because increased levels of lactate are employed in the diagnosis and management of the disease (9). Also, a few measures such as replenishing the total body electrolyte imbalance, in particular magnesium, could be an easily feasible interventional strategy that can be carried out at low cost

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and possibly have a pull for enhancing the septic patient's outcome (10). However, the role of treating hypomagnesemia in sepsis to improve the patient's clinical status is still inconclusive, specifically because the effects of correcting hypomagnesemia in sepsis on important indicators of septic severity, such as the patient's lactate levels, have not been investigated in other clinical trials (11).

This study aims to investigate the association between hypomagnesemia and serum lactate levels in patients with sepsis, hypothesizing that low magnesium levels may be linked to increased lactate production and worse clinical outcomes.

## Methodology

A retrospective observational study was conducted at Ghurki Trust Teaching Hospital Lahore from January 2024 to June 2024. Data were collected from 255 adult patients diagnosed with sepsis. Patients with chronic kidney disease, those on magnesium supplementation before ICU admission, or patients with incomplete medical records that lacked essential data, such as serum magnesium or lactate levels.

Data was extracted from electronic medical records, including demographic information, age, gender, clinical characteristics, source of infection, laboratory results, and clinical outcomes. Serum magnesium and lactate levels were measured within the first 24 hours of ICU admission. Serum magnesium levels were categorized into two groups: normal magnesium (≥1.7 mg/dL) and hypomagnesemia (<1.7 mg/dL). Serum lactate levels were recorded as continuous variables, with elevated levels defined as >2.0 mmol/L. Data also included clinical outcomes such as ICU length of stay, 30-day mortality, and the need for mechanical ventilation. White blood cell count, serum creatinine, C-reactive protein (CRP), and arterial blood gas measurements were also measured. The SOFA score was calculated for each patient on admission to assess the severity of sepsis.

Statistical analyses were performed using SPSS version 26.0. Descriptive statistics were used to summarize patient characteristics and clinical outcomes. Categorical variables, such as gender and the presence of hypomagnesemia, were reported as frequencies and percentages.

## Results

Data were collected from 255 patients with 108 having hypomagnesemia and 147 with normal magnesium levels. The mean age was similar between the groups (58.5 ± 14.9 years in the hypomagnesemia group vs. 61.2 ± 16.4 years in the normal magnesium group, p = 0.18). Gender distribution was equal, with 56.5% males and 43.5% females in both groups. Common comorbidities such as hypertension, diabetes mellitus, chronic kidney disease, COPD, and heart failure showed no significant differences between the groups. (Table 1)

**Table 1: Demographic Data of Patients**

| Characteristic | All Patients (n=255) | Hypomagnesemia (n=108) | Normal Magnesium (n=147) | p-value |
|---|---|---|---|---|
| Age (years), mean ± SD | 59.3 ± 15.7 | 58.5 ± 14.9 | 61.2 ± 16.4 | 0.18 |
| Male, n (%) | 144 (56.5%) | 61 (56.5%) | 83 (56.5%) | 0.99 |
| Female, n (%) | 111 (43.5%) | 47 (43.5%) | 64 (43.5%) | 0.99 |
| Hypertension, n (%) | 87 (34%) | 41 (38%) | 46 (31%) | 0.23 |
| Diabetes mellitus, n (%) | 71 (28%) | 34 (31%) | 37 (25%) | 0.32 |
| Chronic kidney disease, n (%) | 22 (9%) | 12 (11%) | 10 (7%) | 0.36 |
| Chronic obstructive pulmonary disease (COPD), n (%) | 36 (14%) | 16 (15%) | 20 (14%) | 0.74 |
| Heart failure, n (%) | 41 (16%) | 18 (17%) | 23 (16%) | 0.81 |
| Source of infection, n (%) | | | | |
| - Respiratory | 113 (44%) | 49 (45%) | 64 (44%) | 0.88 |
| - Abdominal | 66 (26%) | 28 (26%) | 38 (26%) | 0.99 |
| - Urinary tract | 51 (20%) | 22 (20%) | 29 (20%) | 0.93 |
| - Other | 25 (10%) | 9 (9%) | 16 (11%) | 0.59 |

Patients with hypomagnesemia had significantly higher serum lactate levels (4.1 ± 1.2 mmol/L) compared to those with normal magnesium (2.7 ± 0.9 mmol/L, p < 0.001), with 92% of the hypomagnesemia group having elevated lactate levels (>2.0 mmol/L) versus 68% in the normal magnesium group (p = 0.002). The 30-day mortality rate was also significantly higher in the hypomagnesemia group (35%) compared to the normal magnesium group (22%, p = 0.03). ICU length of stay was longer for hypomagnesemic patients (median of 12 days) compared to those with normal magnesium levels (9 days, p = 0.01). (Table 2)

**Table 2: Clinical Characteristics, and Outcomes of Patients**

| Characteristic/Outcome | Hypomagnesemia (n=108) | Normal Magnesium (n=147) | p-value |
|---|---|---|---|
| Serum lactate (mmol/L), mean ± SD | 4.1 ± 1.2 | 2.7 ± 0.9 | < 0.001 |
| Elevated lactate (>2.0 mmol/L), n (%) | 99 (92%) | 100 (68%) | 0.002 |
| 30-day mortality, n (%) | 38 (35%) | 32 (22%) | 0.03 |
| ICU length of stay (days), median (IQR) | 12 (8–15) | 9 (6–12) | 0.01 |

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| | | | |
|---|---|---|---|
| Mechanical ventilation, n (%) | 56 (52%) | 56 (38%) | 0.07 |
| pH (arterial blood gas), mean ± SD | 7.31 ± 0.09 | 7.35 ± 0.07 | 0.02 |
| White blood cell count (×10^3/µL), mean ± SD | 13.5 ± 4.8 | 12.9 ± 5.2 | 0.45 |
| C-reactive protein (mg/L), mean ± SD | 176 ± 62 | 169 ± 58 | 0.32 |
| Serum creatinine (mg/dL), mean ± SD | 2.1 ± 1.0 | 2.0 ± 0.9 | 0.29 |

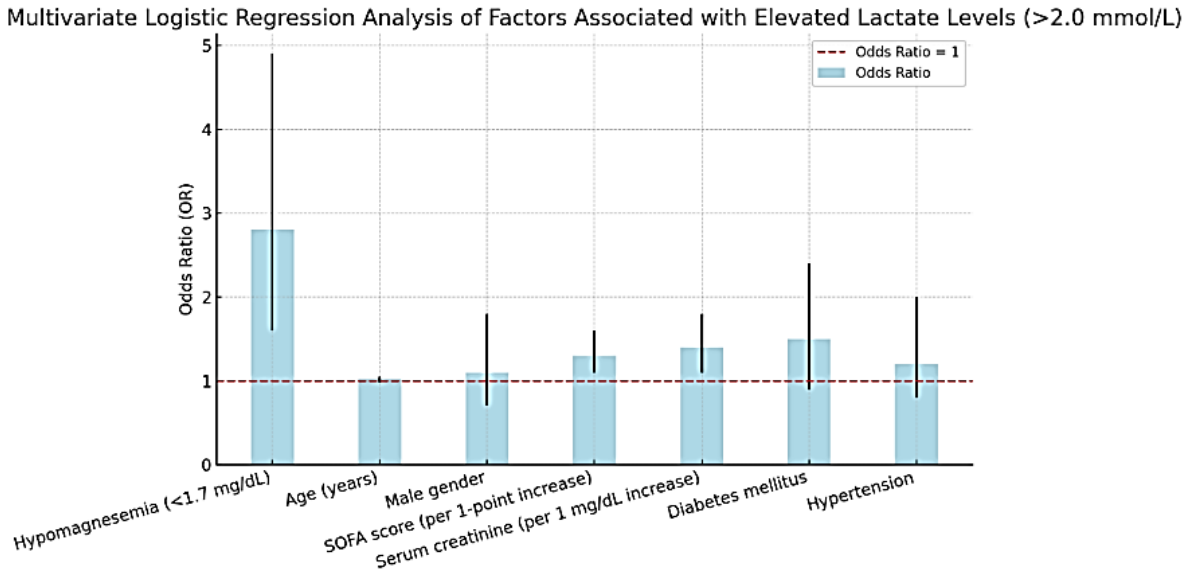


**Figure 01: Graph of Multivariate Logistic Regression Analysis of Factors Associated with Elevated Lactate Levels (>2.0 mmol/L)**

## Discussion

This study aimed to investigate the association between hypomagnesemia and elevated serum lactate levels in patients with sepsis (12). This finding accords with published works showing that magnesium plays multiple physiological functions such as muscle and neuronal actions, and further supports speculations that magnesium depletion in septic patients could worsen metabolic abnormalities (13, 14). Additionally, the SOFA score was positively correlated with elevated lactate levels (OR: 1.3, 95% CI: 1.1 to 1.6, p = 0.001) to strengthen the previous finding that the high level of organ dysfunction correlates with the worsening of the metabolic condition in septic patients (15). This is due to the impressionistic idea that sepsis brings multi-organ dysfunction and an increase in levels of lactate due to metabolism dysregulation and tissue hypoperfusion and hypoxia. Serum creatinine levels also emerged as a significant predictor of elevated lactate (OR: 1.4, 95% CI: 1.1–1.8, p = 0.01), indicating that minimal renal dysfunction is responsible for the metabolic disorders in septic patients (16). High levels of creatinine affect the kidney's ability to filter electrolytes and maintain metabolic body balance because of their filtration abilities. There is evidence that as kidney function declines the ability of the body to regulate lactate becomes impaired, leading to increased disturbance of the acid-base balance (17). Peculiarly, other predisposing factors like age, male gender, diabetes mellitus, and hypertension were not associated with raised lactate levels. This may indicate that although these factors can be used as a parameter in the management of sepsis and in general the condition of a patient these factors may have less impact on lactate levels than hypomagnesemia and markers of organ failure (18). Our results also have significant clinical relevance. The relationship between hypomagnesemia and increased lactate indicates that maintaining proper magnesium levels in septic patients could be useful in differentiating patients who will experience metabolic abnormalities and poor prognosis (19). Further, the treatments intended to rectify magnesium deficiency could have therapeutic implications and promote a better clearance of lactate and favorable outcomes for patients. Furthermore, research about the outcome effect of magnesium supplementation and lactate levels for both septic and metabolic status should also performed in subsequent studies, more particularly randomized controlled trials with large sample sizes, and multi-center studies to reduplicate the results.

## Conclusion

It is concluded that hypomagnesemia is significantly associated with elevated serum lactate levels in patients with sepsis, indicating that low magnesium levels may contribute to metabolic derangements and worse outcomes in this population. Our findings suggest that patients with hypomagnesemia are more than twice as likely to have

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elevated lactate, emphasizing the importance of monitoring magnesium status in septic patients.

## Declarations

**Data Availability statement**
All data generated or analyzed during the study are included in the manuscript.
**Ethics approval and consent to participate.**
Approved by the department concerned. (IRBEC-TL-0024/23)
**Consent for publication**
Approved
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Not applicable

## Conflict of interest

The authors declared an absence of conflict of interest.

## Authors Contribution

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