

Dysmagnesemia in Critically Ill Patients: Prevalence and Nature of Magnesium Disorder.

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Abstract:

Background: Magnesium, ranks on number four for its abundancy in the body. It is known as “the forgotten electrolyte” in the literature. It is second most abundant intracellular cation. Altered magnesium level is frequently encountered electrolyte imbalance in critically ill patients. It increases ICU related morbidity and mortality. Identification and prompt management of magnesium disorder helps in reducing ICU related mortality.

Methods: We performed a prospective interventional study in which we collected data from intensive care unit of liaquat national hospital. We included only those patients who were having critical illness. We then measured serum magnesium level in all patients and reported the findings.

Results: A total of 107 patients from the Medical ICU were included in this study .56 were females (52%) and 51(47.7%) were males. The mean age was 59.6 years. We found that 63.3 % of patients had deranged levels of magnesium. 47.7 % of patients had hypermagnesemia whereas 15.9% of patients had hypomagnesemia.

Conclusion: Dysmagnesemia is significantly common in critically ill patient.

Key words: Dysmagnesemia, hypomagnesemia, hypermagnesemia, intensive care unit, critical illness.

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Introduction:

Magnesium is intracellular ion of the body and has many physiologic roles including regulation of defense system of the body. ^[1] Magnesium disorders have been studied in hospitalized patients with different clinical scenarios including critical illness and literature have reported negative impact of altered magnesium level on morbidity and mortality of ICU patients. Dysmagnesemia i.e altered magnesium level could be either hypomagnesemia or hypermagnesemia. However, clinically, both extremes of magnesium level presents similarly. Clinical manifestation includes muscular weakness, respiratory depression, cardiac arrhythmia, heart failure, and eventually, may lead to cardiac arrest. In one study, conducted on cancer patients, hypomagnesemia was found as pre-dominant magnesium disorder. ^[2] Hypomagnesemia leads to neuromuscular hyper excitability e.g. seizures and asthenia (lack of energy). ^[3] Patients with cardiovascular disease were found to have hypermagnesaemia more

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commonly.^[4] In a study conducted on hospitalized patients, hypermagnesaemia was more common (31.5%) than hypomagnesaemia (20.2%), however, any alteration in serum magnesium levels were found to have poor outcomes.^[5] Altered magnesium level causes progression of systemic inflammatory response syndrome (SIRS) to sepsis. Examination of magnesium disorder in critically ill patients showed that patients with hypomagnesaemia had increased need for mechanical ventilation, prolonged ICU stay and higher mortality. [6]

Hypomagnesemia is a risk factor for certain bacterial infections including bacterial urinary tract infection and bronchopneumonia.^[7] Patients with critical illness are prone to develop magnesium disorder and specially to develop hypomagnesemia. It is pivotal to identify the type of magnesium disorder in patients admitted to intensive care units and high dependency units so that mortality associated with altered magnesium levels and poor outcomes can be prevented. Review of data from Pakistan reports association between hypomagnesemia and poor glycemic control.^[8] and low magnesium has been reported in 65.3% in diabetes patients. [9] Some work on serum magnesium level in stroke patients have been performed and hypomagnesaemia has signified as etiologic factor for acute stroke while 24% prevalence of low magnesium in acute stroke has been reported^[10] The aim of this research is to comprehensively examine the prevalence of dysmagnesemia in critically ill patients and to systematically appraise the nature of magnesium disorder in critically ill patients.

Objective: To establish the prevalence of Magnesium disorder (dysmagnesemia) in critically ill patients. Furthermore, to understand the nature of prevalent magnesium disorder in critically ill patients.

Methods:

Study population and data source:

This study is a single-center, prospective, cross sectional analysis of critically ill patients. Study was performed at a teaching hospital of Pakistan. Study was conducted over a period of 6 months and data regarding Age, sex, nature of critical illness, admission diagnosis, co-morbidities, drug history and serum magnesium level were obtained from the electronic medical record system (EMR) of the ICU by a principle investigator.

Operational definitions:

- Dysmagnesemia (Altered magnesium level): Any disorder in serum Magnesium level from normal level which is 1.6-2.5mg/dl
- Critically ill patient: Patients having multiple organ dysfunction mandating monitoring setup for proper management.
- Hypomagnesemia: serum magnesium level less than 1.6mg/dl
- Hypermagnesemia: serum magnesium level more than 2.5mg/dl

Magnesium measurement in serum:

We measured serum magnesium level with in 1st 24 hours of hospital admission. To measure serum magnesium concentration, venous samples were taken using a vacuum technique with lithium heparin solution container by a trained nursing staff. Sample analysis was done immediately. These samples were analyzed by trained laboratory technician at the central biochemistry lab of the hospital using COBAS 501 analyzer based on spectrophotometric method. Results were obtained through electronic database system of central laboratory. Values enrolled on excel sheet by a principle investigator. Serum magnesium level less than 1.6mg/dl was considered as hypomagnesemia and greater than 2.5mg/dl was considered as hypermagnesemia.

Statistical Analysis:

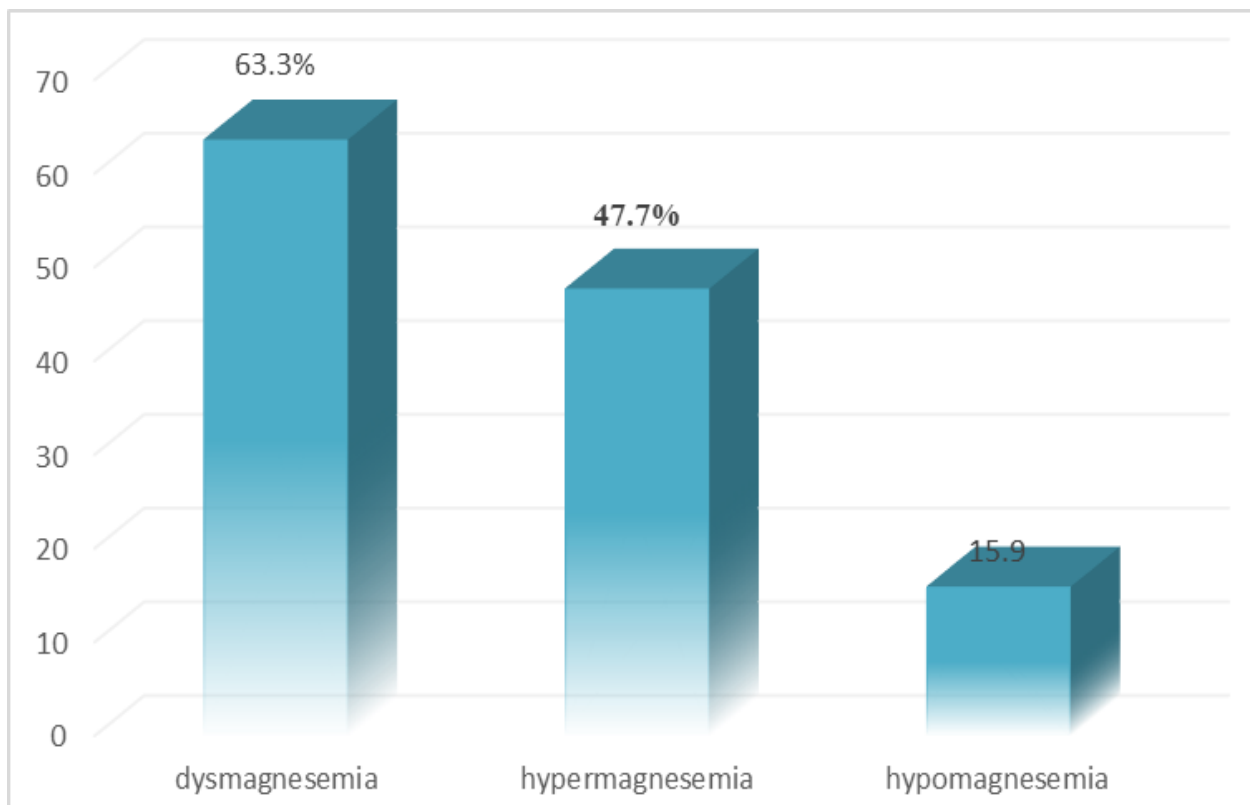
Data was entered on SPSS version 25. Qualitative variables were presented as frequency and percentages such as gender, co-morbidities, admission diagnosis, medication history and alteration in serum magnesium levels. Quantitative variables were presented as Mean \pm SD such as age and serum magnesium. Post stratification chi-square test were applied for finding association between categorical variables.

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Results:

A total of 107 patients from the Medical ICU were included in this study. 56 were females (52%) and 51(47.7%) were males. 58.8% of patients with dysmagnesemia were greater than 60 years of age. The mean age was 59.6 years. According to the cause of admission of patients with dysmagnesemia; 35.5 % patients had Community-acquired pneumonia, 31.7 % patient had septicemia, 14.9% patient had Acute Kidney Injury, 4.6% had NSTEMI, 5.6% had CNS related pathology including stroke, CNS trauma and seizure disorder and other noted admission diagnosis included Chronic Liver Disease, Acute Gastroenteritis, pulmonary hemorrhage, Urinary Tract Infection, diabetic foot, and drug toxicity. According to the patients, past medical histories 19% of patients had NKCM, 57% had Hypertension, 47.6% had diabetes, 4.7% had Chronic Kidney Disease, 12% had Ischemic Heart Disease, and 3.7% had End-Stage Renal Disease. Only 13% of patients were using diuretics, 8% of patients were using Proton Pump Inhibitors, 12% were using Antacids and 58.9 % of patients were on other medications. We found that 63.3 % of patients had deranged levels of magnesium. 47.7 % of patients had hypermagnesemia whereas 15.9% of patients had hypomagnesemia.

Figure 1: Frequency of dysmagnesemia and hypo/hypermagnesemia



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Figure:2 Age distribution of dysmagnesemia

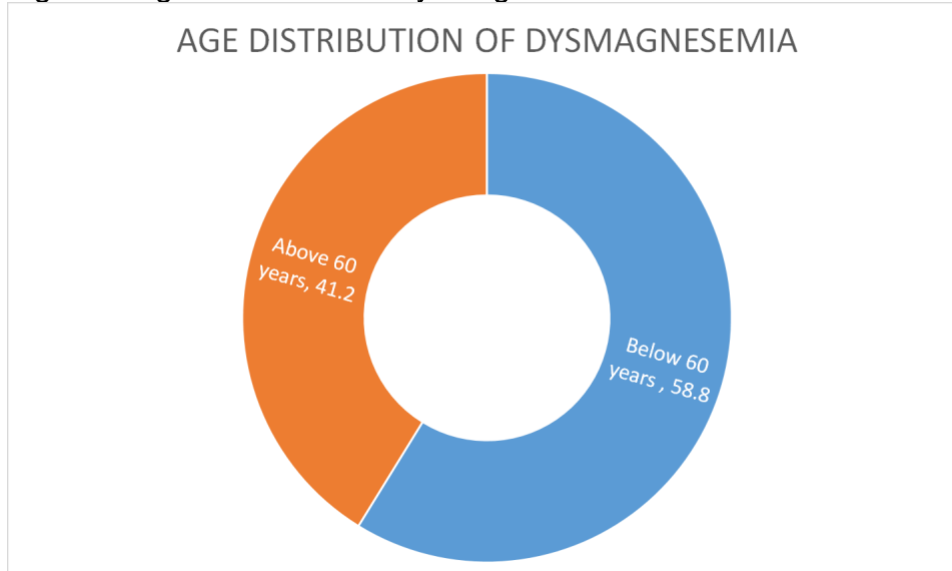
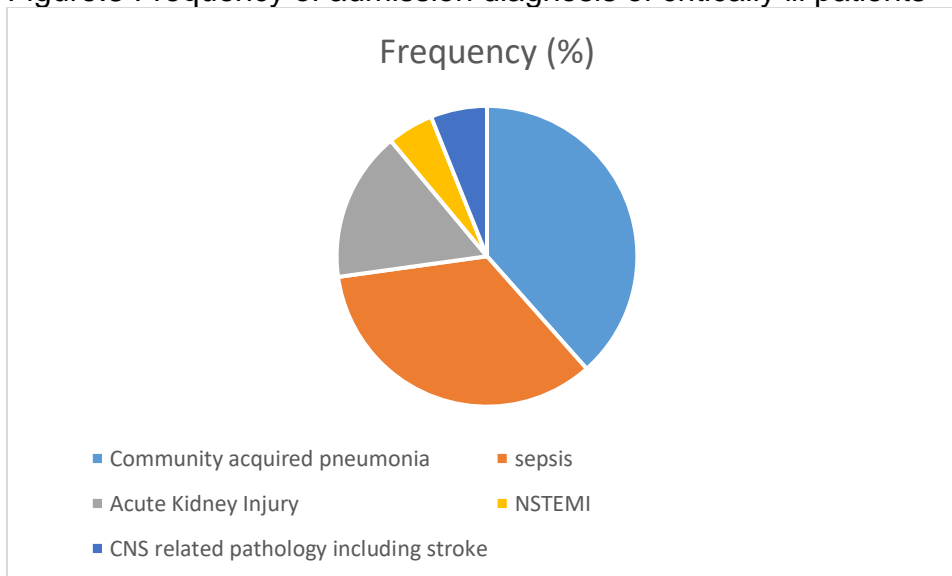


Figure:3 Frequency of admission diagnosis of critically ill patients



Discussion:

Physiologic importance of magnesium:

Magnesium (Mg) is a cation (positive ion) that plays in enhancing immune system of the body to work against infections by producing cytokines and nitric oxide.^[1,11] It is one of the prime intracellular ions. It plays a crucial role as a catalyst in several physiological functions and cellular reactions e.g., calcium regulation, protein synthesis, energy-requiring metabolic processes, neurotransmitter release, muscle contraction and many more.^[12] The nervous alterations are one of the important clinical manifestation of chronic magnesium deficiency.^[3] Furthermore, Magnesium deficiency increases endothelial cell susceptibility to oxidative stress, promotes endothelial dysfunction, reduces fibrinolysis, and increases coagulation. The level of magnesium in natural killer

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cells and CD8 killer T cells modulates their cytotoxic capacity. A dis-balance of magnesium levels affects the immune response and cellular resilience; it may increase the risk of infection or decrease the speed of recovery.^[7]

Study Findings: This study is from the Pakistan to document the prevalence of dysmagnesemia in an intensive care unit. We aimed to study magnesium disorder in critically ill patients of the medical ICU. Higher incidences of both hypomagnesemia and hypermagnesemia were observed in the intensive care setting. The results of our study revealed the incidence of hospital acquired dysmagnesemia was 63.3% out of which 47.7% had hypermagnesemia and only 15.9% patients had hypomagnesemia. All these patients had critical illness with 2 or more than 2 organ failures. On cross tab examination we found that magnesium disorder was greater in patients with ages greater than 60 in comparison to less than 60 (58.8% vs 41.2%). Presence of an underlying co-morbid condition has been observed as risk factor for magnesium disorder in our study. In hypertensive patients we reported dysmagnesemia in 55.9% of patients while in diabetes 57.4% of patients were reported. However, only 16.6% patients without any co-morbid condition had altered magnesium level.

Reason for critical illness is one the factor associated with magnesium disorder. In one study on patients with critical illness secondary to community acquired pneumonia (CAP) both hypermagnesemia and hypomagnesemia on admission were found to be associated with increased 30-day mortality.^[13] In our study 35.3% patients had CAP. Literature is extensively contaminant with findings on magnesium disorder in sepsis. Review of data reveals increased mortality as well as morbidity in septicemia due to altered magnesium level.^[14,15] In our study, we reported that 31.7% patients had septicemia. Hypomagnesemia holds etiologic importance in stroke patients.^[10] In our study, 5.6% patients had stroke. It is difficult to identify the more prevalent type of dysmagnesemia as previous literature reported hypomagnesemia rates ranging from 9 – 65% and hypermagnesemia rates ranging from 5.7 – 23.6%^[16,17]. Several studies have documented different patterns of dysmagnesemia, from previous studies identifying hypomagnesemia as more prevalent in compare to recent studies which identify hypermagnesemia as more prevalent.^[17] The variations in these results can be explained by several reasons. Firstly, due to the detrimental effects of hypomagnesemia researched and proven over the years, hospital-acquired hypermagnesemia is induced commonly by prophylactic use of Mg in practice e.g., administration of magnesium-contained medications. Such clinical decisions are influenced due to the several published benefits reporting reductions in serum lipids, hyperglycemia, metabolic syndrome, obesity, insulin resistance, and diabetes mellitus and when given in conjunction with taurine or potassium, lowers blood pressure, retards atherogenesis, prevents arrhythmias, and stabilizes platelets even though these findings have not been confirmed. Secondly, because of the high number of kidney related issues which may cause hypermagnesemia. Thirdly, administration of antacids or intravenous magnesium infusions in the elderly or in those with impaired renal function^[18]. Just in our study, 12% patients were using antacids and 8% of the patients were using proton pump inhibitors (PPI).

In contrast hospital-acquired hypomagnesemia is attributed to decreased intake or absorption by the gastrointestinal tract e.g. due to vomiting, nasogastric suction, diarrhea, enteritis, inflammatory bowel disease, intestinal and biliary fistulas, intestinal surgery resections, and pancreatitis. Another important reason for hypomagnesemia in hospitalized patients is increased renal loss, due to effects of medications, such as amphotericin, chemotherapeutic agents, diuretics, or other tubular toxins. Metabolic acidosis due to diabetic ketoacidosis, starvation, or alcoholism also causes renal Mg wasting. Thirds and important cause of hypomagnesemia in admitted patients is redistribution triggered by severe illnesses, such as acute pancreatitis, refeeding syndrome or cardiopulmonary surgeries^[19]. Hypomagnesemia may in turn influence other electrolytes and may cause hypokalemia and hypocalcemia causing worsening of critical illness related complications.^[20]

One of the most well established facts about Mg are its cardio-protective effects. It not only provides cellular protection during myocardial ischemia but is one of the most widely accepted and practiced use in the prevention and treatment of cardiac arrhythmias. Mg acts as a calcium antagonist in post ischemia calcium overload. It

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conserves ATP and it reduces oxygen consumption by lowering the heart rate, contractility, and systemic afterload. Likewise, it modulates the myocardial excitability to prevent arrhythmias.^[21]

Magnesium is proven to contribute in the immune response and correlate with the levels of several immune mediators such as interleukin-1, tumor necrosis factor-alpha, interferon-gamma, and substance P.

There were several limitations to this study. Firstly; it was an experience from single centered hospital. Secondly, due to small sample size of data, there is potential for systemic error. Although an extensive data was collected and adjustments were made to reduce confounding factors, it was difficult to stratify due to Magnesium's multi-systemic influence in the human body.

Conclusion:

Magnesium should not be a forgotten electrolyte in patients with critical illness. It should be frequently measured and optimized due to the drastic effects of dysmagnesemia

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