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CORRELATION OF LOW MAGNESIUM LEVELS WITH PROGNOSIS IN PATIENTS WITH SEPSIS

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ABSTRACT

Aims: To correlate serum magnesium levels with prognosis and clinical outcome of sepsis patients

Materials and methods: In this prospective, observational case-control study, we analyzed a total of 100 cases, 50 cases (sepsis with low magnesium) and 50 controls (sepsis with normal magnesium), respectively.

Results: There is statistically significant difference between the patient groups was seen with respect to the serum magnesium (p=0.001). The mean serum magnesium was found to be decreasing with increase in the Q-SOFA score among the patients in the case group.The mean serum magnesium was found to be decreasing with increase in the Q-SOFA score in control group, and statistically significant difference between the scores was seen. A statistically significant association between the patients groups and the need for mechanical ventilation, duration of ventilatory support, need for ionotropic support and mortality. Mean serum magnesium in the group of patients died was 1.13, while the mean serum magnesium in the group of patient's lives was 1.46. A statistically significant difference between the patient groups (alive and dead) was seen with respect to the serum magnesium (p=0.001). The mean Q-SOFA score in the group of patients died was 2.79, while the mean Q-SOFA score in the group of patient's lives was 1.92, respectively. A statistically significant difference between the patient groups (alive and dead) was seen with respect to the Q- SOFA

scores (p=0.001). The sensitivity of the Q-SOFA cut-off value >2 was 90.62%, sensitivity of 51.47%, and the accuracy was 64%, respectively.

Conclusion: Hypomagnesemia, when detected require correction for the management of those with critical illness for better outcomes.
Keywords: Hypomagnesemia, Quick Sequential Organ Failure Assessment(Q-SOFA), Sepsis, mechanical ventilation, ventilatory support

INTRODUCTION

Magnesium is of great importance in biology. It is a co-factor for ATP in all its actions and is a co-factor for a very large number of enzymes of plants and animals.It is the fourth most abundant total cation and the second most abundant intracellular cation in the human body. Vast majority of magnesium is found in the bone and soft tissues, primarily muscle. Less than 5% is in the extracellular fluid, with small portion of it in the intravascular portion, 20% to 30% is protein-bound. Often, the signs of Magnesium deficiency can occur with normal or minimally low serum levels which could be related to the slowing down of its mobilisation from other tissues. This could result in acute hypomagnesemia. Owing to its protein bound nature, it is not feasible to clinically determine precise amount of intracellular Magnesium, and, therefore, the serum level is most often used as an indicator of total body Magnesium. Despite, magnesium has been considered the “fifth forgotten ion”, of late, it has become a growing interest among clinicians in the determination of the total Mg concentration in serum. It was found that the requests for the measurement of total Mg concentration in serum in the Academic Medical Center increased during the period 1990 to 1998 by almost 30%, to a total of 4,450 per year.7 This increased interest among clinicians, especially in ICUs could be due to high incidence of hypomagnesemia in patients admitted to an ICU. Literature have shown high prevalence of low magnesium levels and linked its link with poor outcome.[1,2,3]

Hypomagnesemia may present with neuromuscular, neurologic, psychiatric and cardiac manifestations, which may considerably increase the morbidity of such patients. It is one of the most common electrolyte abnormalities of hospitalized patients. The etiology of magnesium deficiency in ICU is multifactorial. Drugs (diuretics, aminoglycosides), renal and gastrointestinal losses, comorbidities like diabetes mellitus and chronic alcoholism, metabolic disorders like Barter's and Gittleman's syndromes and magnesium redistribution are the postulated causes. It has been estimated that 20 to 65% of critically ill patients develop hypomagnesemia during the course of their ICU stays. It has been found that both extracellular and cytosolic magnesium have significant effects on cardiac ion channels and it found to have significant effect on action potential duration, cell excitability, and contractility. In patients with acute myocardial infarction who have mild hypomagnesemia, it is found to have a two or threefold increase in the frequency of atrial and ventricular arrythmias, cardiac insufficiency, coronary vasospasm, sudden death, skeletal and respiratory muscle weakness, tetany, seizures and other neuromuscular manifestations, as well as a number of metabolic abnormalities such as hypokalaemia, hyponatremia, hypocalcemia or hypophosphatemia.[4,5]

The prevalence of hypomagnesemia (measuring total serum magnesium) has a wide range (11- 61%), and a considerable controversy exists regarding its effects on morbidity and mortality. The incidence of hypomagnesemia is reported to be 2% in the general population, 10- 20% in hospitalized patients, 50- 60% in intensive care unit (ICU) patients, 30- 80% in persons with alcoholism, and 25% in outpatients with diabetes.[6,7]There is a paucity of data in Indian literature, addressing this common, but underdiagnosed electrolyte deficiency. Present study was undertaken against this backdrop at a teaching hospital to estimate the

serum magnesium levels in patients admitted with Sepsis in Critical care unit in Princess Esra Hospital /Owaisi Hospital and Research Center,Deccan College of Medical Sciences.

MATERIALS AND METHODS

Prospective observational case- control study from January 2021 to July 2022 . Patients with sepsis admitted to the CCU in Deccan College of Medical Sciences teaching hospitals viz Princess Esra Hospital and Owaisi Hospital and Research Center, Hyderabad, Telangana.

A total of 10036 cases were selected in the view of this study. Patients with sepsis with low magnesium were taken as cases (n= 50) and patients with sepsis with normal magnesium were taken as controls (n= 50). The research protocol was reviewed and approved by the Institutional Review Board. Ethical clearance was obtained to collect and review the data of the patients retrospectively.

Inclusioncriteria: Patients with sepsis
Exclusioncriteria : Patients on diuretics, Chronic alcoholics , Patients who had already received magnesium prior to admission to the ICU.

All those patients meeting the inclusion criteria , serum magnesium was sent within 24 hours of admission to the ICU. Serum magnesium measured was the total magnesium, estimated by Calmagite.

Detailed history and thorough physical examination as indicated for a particular case was done. qSOFA score was calculated for each patient. Relevant blood and urine investigations were sent. Other investigations as needed for a patient were performed. Each patient in the study group was followed till discharge or death.

qSOFA score i.e., the quick sequential related organ failure assessment was proposed as a risk stratification tool that is more specific than the Systemic Inflammatory Response Syndrome (SIRS) criteria in order to urge the assessment of organ failure, initiate or escalate appropriate sepsis therapy, refer patients to the Intensive Care Unit (ICU). This simple model has been developed for quick use at the bedside while providing a valid diagnostic performance outside the ICU. The clinical criteria for sepsis in intensive care unit (ICU) patients were de- fined as suspected infections with two or more increments in the Sequential Organ Failure Assessment (SOFA) score. For non-ICU patients, a suspected infection with a quick Sepsis-related Organ Failure Assessment (qSOFA) score of two or higher was defined as an early warning tool for sepsis. The qSOFA consists of the following

systolic blood pressure (BP) measurement ≤100 mmHg, a respiration rate of 22 bpm or higher, andan altered mentation.

Sequential Organ Failure Assessment (Quick) qSOFA

Assessment	qSOFA score
Low blood pressure (SBP< 100mmHg)	1
High respiratory rate (>22 breaths/min)	1
Altered mentation (GCS <15)	1

A score is assigned by the following variables.
Variable & Associated Points

0 points = Not high risk
1 point = Not high risk
2 points = High risk
3 points = High risk

A qSOFA score of 2 or 3 predicted a 3-14 times greater in-hospital mortality than those with a score of 1 or 0. The authors from the derivation and validation study support qSOFA as a tool for assessing mortality in patients with suspected infection, noting that clinical suspicion for infection is derived separately.
The parameters were looked into are LengthofstayinICU, Needforventilatorysupport,durationofventilatorysupport, needforionotropicsupport and Mortality. The study did not interfere with the patient management. Each patient received treatment as per the case requirement.

Statistical Analysis:
Statistical analysis was performed using the statistical software IBM SPSS Version 22.0. The data was collected and compiled in Microsoft Excel. To analyse the data, descriptive statistics was used to draw the graphs and frequencies and percentages, and quantitative data was analysed using student's t test. Then qualitative data was analysed using qualitative chi square test. If p- value is ≤ 0.05, it is considered statistically significant at 5% level of Significance.

RESULTS
Table 4 and Graph 2 shows the age distribution of the study sample in both case and control groups. The mean age of the overall sample was 53.16 years. The mean age of the patients in the case group was 54.62 years, while the mean age of the patients in control group was 52.52 years, respectively. The output of the independent t- test showed that there was no statistically significant difference between the two groups with respect to the age i.e., t(df)= 0.625 (98) and p- value= 0.533, respectively.

Table-1: Sex distribution in the study groups

			Group		Total	Chi- square	p-value
			Cases	Controls			
Sex	Male	Count	34	32	66	0.178	0.673
		Percent	68	64	66		
	Female	Count	16	18	34		
		Percent	32	36	34		
Total		Count	50	50	100		
		Percent	100	100	100		

It was found that among cases, 68% were males and, 32% were females. On the other hand, in controls, 64% were males and 36% females, respectively. The output of the Chi-square test of association showed that there was no statistically significant association between study groups and sex, respectively.

Table-2: Mean Q-SOFA score and ICU stay between cases and controls

	Group	Mean	Std. Deviation	t (df)	p-value
Q-SOFA	Cases	2.34	0.745	7.519 (98)	0.001*

	Controls	1.12	0.872		
ICU Stay	Cases	50	6.64	3.042	4.700 (98)
	Controls	50	3.88	2.826	

The mean Q-SOFA score in the case group was 2.34, while the mean Q-SOFA score in control group was 1.12, respectively. there was a statistically significant difference between the two groups with respect to the Q-SOFA score i.e., t(df)= 7.519 (98) and p- value= 0.001, respectively.

The mean number of ICU stay in the case group was 6.64 days, while the mean number of ICU stay in the control group was 3.88 days, respectively. There was a statistically significant difference between the two groups with respect to the mean number of ICU stay in the i.e., t(df)= 4.700 (98) and p- value= 0.001, respectively.

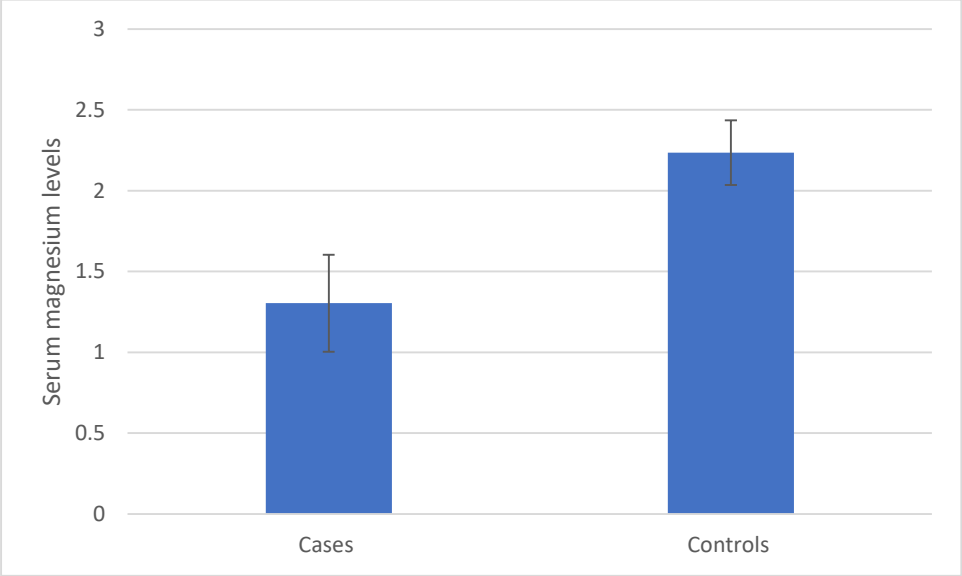

Figure-1: Mean serum Magnesium between cases and controls

The mean serum magnesium in the case group was 1.304, while the mean serum magnesium in the control group was 2.236, respectively. The output of the independent t- test showed that there was a statistically significant difference between the two groups (cases and controls) with respect to the mean serum magnesium in the i.e., t(df)= 15.399 (98) and p-value= 0.001, respectively.

Table-3: Mean serum magnesium levels according to Q-SOFA scores.

	N	Mean	Std. Deviation	F value	p-value
Q-SOFA in controls	0	2.31	0.187	10.080	0.001*
	1	2.26	0.232		
	2	2.22	0.165		
	3	1.50	0.141		
	Total	2.23	0.247		
Q-SOFA in cases	0	1.80	--	1.734	0.173
	1	1.42	0.2775		

	2	1.365	0.3897		
	3	1.208	0.3078		
	Total	1.304	0.3493		

*Statistically significant (p<0.05)

The mean serum magnesium was found to be decreasing with increase in the Q-SOFA score in control group, respectively. The output of the ANOVA test showed that there was a statistically significant difference between the Q-SOFA scores and serum magnesium i.e., F value= 10.080 and p- value= 0.001, respectively.

The mean serum magnesium was found to be decreasing with increase in the Q-SOFA score in case group, respectively. However, the output of the ANOVA test showed that there was no statistically significant difference between the Q-SOFA scores and serum magnesium i.e., F value= 1.734 and p- value= 0.173, respectively.

Table-4: Need for Mechanical ventilation

			Group		Total	Chi- square	p-value
			Cases	Controls			
Need for Mechanical ventilation	Yes	Count	38	16	54	19.485	0.001*
		Percent	76	32	54		
	No	Count	12	34	46		
		Percent	24	68	46		
Total		Count	50	50	100		
		Percent	100	100	100		

In the case group, 76% were in need for mechanical ventilation while in the control group only 32% were in need for mechanical ventilation, respectively. The output of the Chi-square test of association showed that there was a statistically significant association between the cases and controls, and the need for mechanical ventilation, respectively (p= 0.001).

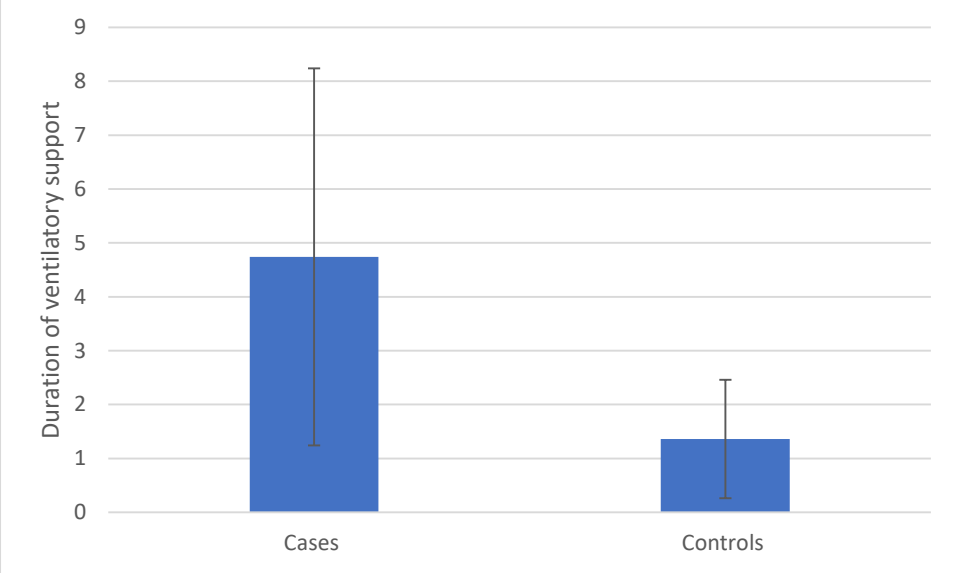

Figure-2: Duration of ventilatory support

The mean duration of ventilatory support in the case group was 4.74, while the mean duration of ventilatory support in the control group was 1.36, respectively. The output of the independent t- test showed that there was a statistically significant difference between the two

groups (cases and controls) with respect to the mean duration of ventilatory support in the i.e., t(df)= 5.782 (98) and p- value= 0.001, respectively.

Table-5: Need for Inotrope support (NIS)

			Group		Total	Chi- square	p-value
			Cases	Controls			
NIS	Yes	Count	37	15	52	19.391	0.001*
		Percent	74	30	52		
	No	Count	13	35	48		
		Percent	26	70	48		
Total		Count	50	50	100		
		Percent	100	100	100		

In the case group, 74% were in need for inotrope support while in the control group only 30% were in need for inotrope support, respectively. The output of the Chi- square test of association showed that there was a statistically significant association between the cases and controls, and the need for inotrope support, respectively (p= 0.001).

Table-6: Mortality rate between the cases and controls

			Group		**Total**	**Chi- square**	**p-value**
			Cases	Controls			
NIS	Yes	Count	24	8	32	11.765	0.001*
		Percent	48	16	32		
	No	Count	26	42	68		
		Percent	52	84	68		
Total		Count	50	50	100		
		Percent	100	100	100		

In the case group, 48% were died to the sepsis, while in the control group only 16% were died due to the sepsis, respectively. The output of the Chi-square test of association showed that there was a statistically significant difference between the cases and controls in relation to mortality. (p= 0.001).

Table 15 and Graph 13 shows the distribution of mean serum magnesium according to the mortality. The mean serum magnesium in the group of patients died was 1.13, while the mean serum magnesium in the group of patient's lives was 1.46, respectively. The output of the independent t- test showed that there was a statistically significant difference between the two groups with respect to the mean serum magnesium i.e., t(df)= -3.731 (98) and p- value= 0.001, respectively.

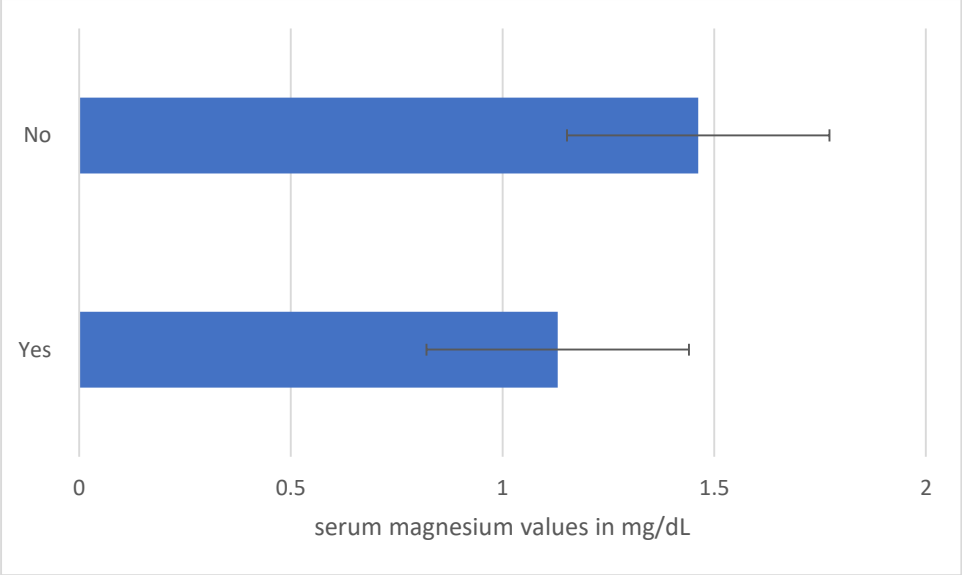

Figure-3: Mean serum magnesium according to mortality in cases

The mean Q-SOFA score in the group of patients died was 2.79, while the mean Q-SOFA score in the group of patient's lives was 1.92, respectively. The output of the independent t-test showed that there was a statistically significant difference between the two groups with respect to the mean Q-SOFA score i.e., t(df)= 5.038 (98) and p- value= 0.001, respectively.

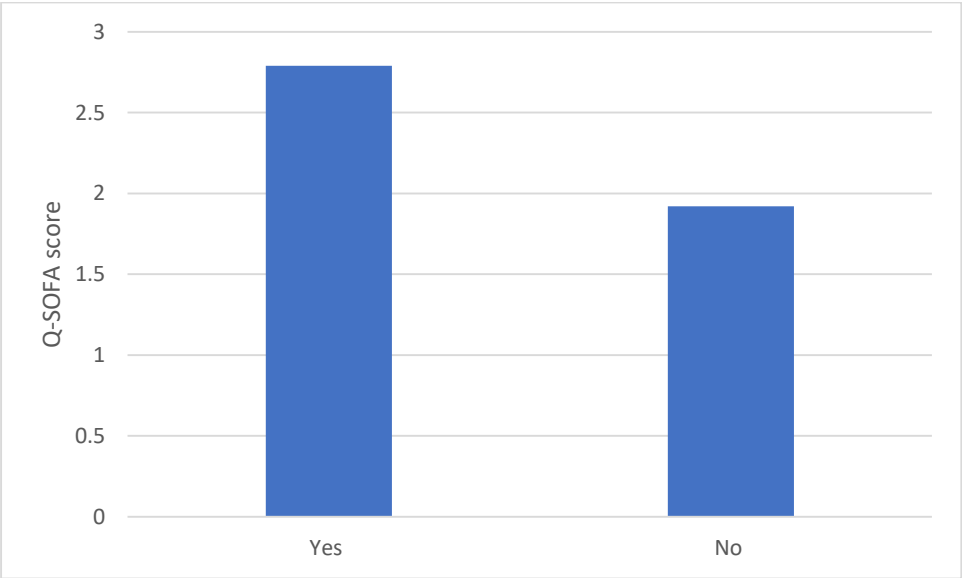

Figure-4: Mean Q-SOFA according to mortality in cases

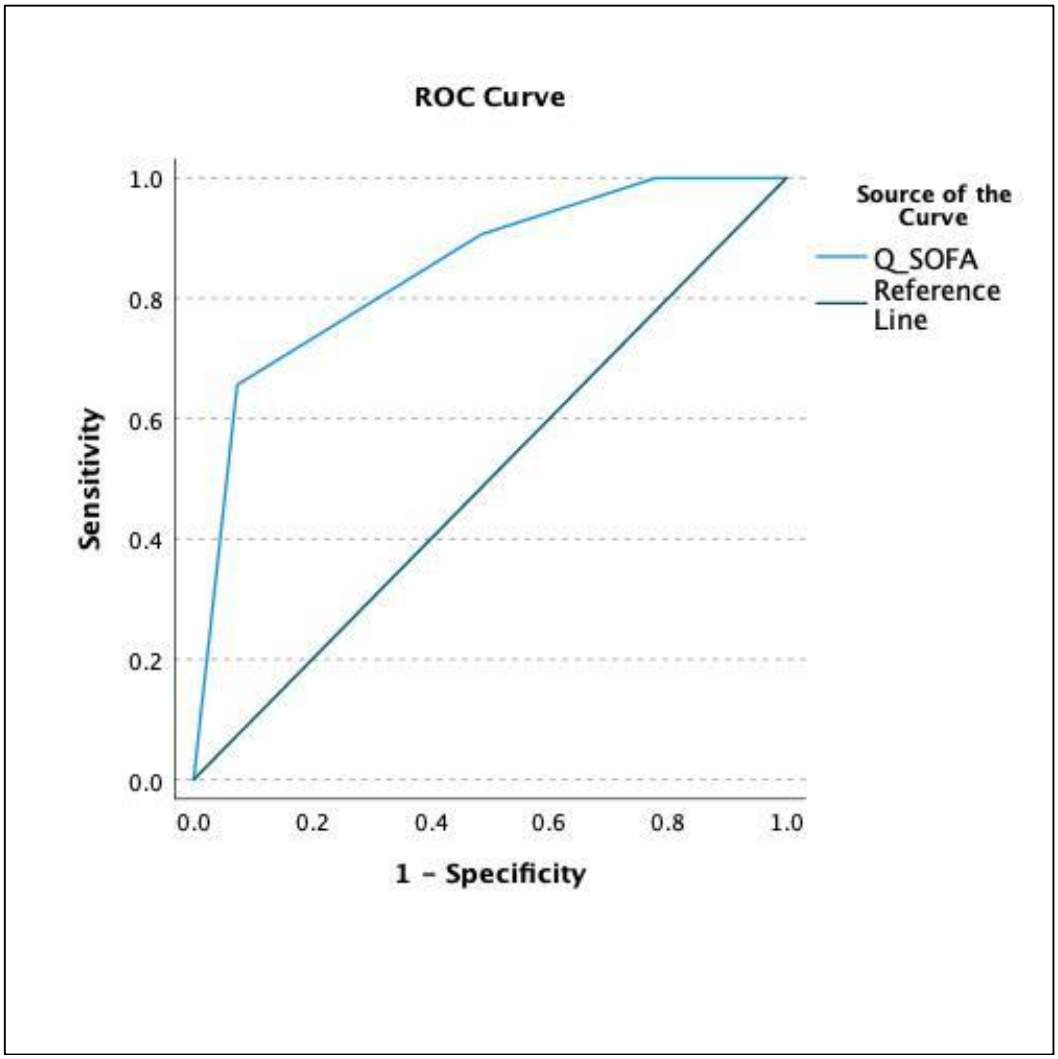

Figure-5: The receiver operating characteristics curve used to predict mortality

It demonstrates the receiver operating characteristics curves of the qSOFA scores for predicting the mortality in the sepsis patients with normal and low magnesium levels. The area under the ROC curve (AUROC) of the qSOFA was 0.847 (p= 0.009) with 95% confidence interval ranging between 0.765 to 0.929, respectively.

Table-7: Two-by-two contingency tables to test the diagnostic performance of qSOFA in predicting the mortality

			Mortality		Total	Chi- square	p-value
			Yes	No			
qSOFA cut- off	>2	Count	29	33	62	16.367	0.001*
		Percent	90.6	48.5	62		
	<2	Count	3	35	38		
		Percent	9.4	51.5	38		
Total		Count	32	68	100		
		Percent	100	100	100		

*Statistically significant (p<0.05)

It was found that in 90.6% patients who died, their qSOFA scores were higher than >2, and in 9.4% patients qSOFA scores were lower than <2, respectively. On the other hand, 48.5% patients who were alive had their qSOFA scores were higher than >2, and in 51.5% patients

qSOFA scores were lower than <2, respectively. The output of the Chi-square test of association showed that there was a statistically significant association between the qSOFA cut-off score >2, and mortality, respectively (p= 0.001).

Table-8: Diagnostic performance of qSOFA score for mortality

Measures	qSOFA>2
Sensitivity	90.62 (74.9%- 98.02%)
Specificity	51.47 (39.03%- 63.78%)
Positive likelihood ratio	1.87 (1.43- 2.44)
Negative likelihood ratio	0.18 (0.06- 0.55)
Positive predictive value	46.77 (40.18%- 53.49%)
Negative predictive value	92.11 (79.5%- 97.23%)
Accuracy	64 (53.79%- 73.36%)

. The sensitivity of the cut-off value >2 was 90.62% with 95% CI ranging between 74.9% and 98.02%), sensitivity of 51.47% with 95% CI ranging between 39.03% and 63.78%), positive and negative likelihood ratios of 1.87 and 0.18, positive and negative predictive values of 46.77% (40.18% and 53.49%) and 92.11% (79.5% and 97.23%), and accuracy of 64% (53.79% and 73.36%), respectively.

DISCUSSION

Hypomagnesemia is a common finding in ICU patients. One of the main reasons for this increased interest among clinicians, especially those working in intensive care units (ICUs), is the reports about a high incidence of hypomagnesemia in patients admitted to an ICU. Because the role of Mg is primarily that of a cofactor in intracellular biochemical reactions, and almost 99% of the total body Mg can be found intracellularly, the benefit of the measurement of total Mg concentration in serum has been questioned. After potassium, Mg is the second most prevalent intra- cellular cation, and it has an important role as a cofactor in various enzymatic reactions, including those involving adenosine triphosphatase. Mg is therefore an important element for providing energy and regulating various processes in the cell and cell membrane. It also has a role in protein and DNA synthesis, DNA and RNA transcription, translation of messenger RNA, and the regulation of mitochondrial function. So, recognition and treatment of hypomagnesemia in patients entering the ICU may be important and has been discussed several times. Moreover, it is comprehensible that hypomagnesemia is associated with severity of illness or increased mortality.[8]

The incidence of hypomagnesemia varies from 20% to 65% in intensive care unit (ICU) patients. Hypomagnesemia may present as tetany, vertigo, reversible psychiatric aberrations, seizures, cardiac arrhythmias, hypertension, muscular weakness, acute cerebral ischemia and asthma. The pathology of magnesium deficiencies is multifactorial including gastrointestinal disorders, renal loss, renal diseases, drug-induced loss, metabolic acidosis, and other causes. In addition, critically ill patients have several potential risks of magnesium dysregulation. It was significantly associated with increased and prolonged need for mechanical ventilation, difficulty to wean, prolonged ICU stay and increased mortality in critically ill patients.

Many studies found that only hypomagnesemia, but not hypermagnesemia is linked with increased mortality. However, reports of mortality due to magnesium dysregulation in the critical care setting are controversial. Also, it is unknown whether comorbidities of the study population have any effect on this association. Whether hypomagnesemia directly contributes

to cellular alterations leading to increased mortality, morbidity and poor patient outcome in critically ill patients or it is just a marker of critical illness, is not clear. Hypomagnesemia and sepsis have an important role in increased mortality and morbidity, especially in the aged people. Hypomagnesemia is associated with increased release of endothelin and proinflammatory cytokines. This was strongly associated with increased mortality in experimental sepsis, and Mg replacement provided significant protection against endo- toxin challenge. This effect was due to the downregulation of the release of inflammatory cytokines (tumor necrosis factor-alpha and interleukin-6). Sepsis was an independent risk factor for developing hypomagnesemia during ICU stay.[9] In the study by Limaye et al[10] the incidence of sepsis was twice as common in hypomagnesemic patients than in normomagnesemic patients. Hypomagnesemia is also associated with diabetes mellitus, which may be due to increased renal losses of Mg that accompany glycosuria.Hypomagnesemia also leads to muscle weakness and respiratory failure, causing difficulty in weaning the patient from the ventilator. Prolonged ventilation is not just due to muscle weak- ness causing difficulty in weaning.

In the present study, an attempt was made to study serum magnesium levels in patients with sepsis in critical care unit on admission in ICU and its correlation with patient's duration of ICU stay, Q-SOFA score, need for mechanical ventilation, need for ionotropic support and mortality. One hundred patients were enrolled in the present study and serum total magnesium levels were evaluated on admission. Patients were divided into two groups; case group in which patients with sepsis and low serum magnesium levels were seen i.e., hypomagnesemic group (<1.7 mg/dL) and control group in which patients with sepsis and normal serum magnesium levels were seen i.e., normomagnesemic group (1.7-2.4 mg/ dL). The serum magnesium levels in patients with sepsis in critical care unit on admission in ICU and its correlation with patient's duration of ICU stay, Q-SOFA score, need for mechanical ventilation, need for ionotropic support and mortality. Our findings showed that hypomagnesemia was significantly associated with increased duration of ICU stay, higher Q-SOFA score, longer duration of ventilator support, need for ionotropic support and mortality.

In the present study, mean Q-SOFA score ± SD in case group i.e., patients with sepsis low magnesium (hypomagnesemic group) and in control group i.e., patients with sepsis and normal magnesium were 2.34 ± 0.74 and 1.12 ± 0.87, respectively. Mean Q-SOFA score was significantly higher in sepsis patients who had hypomagnesemia compared to patients with normal magnesium levels. A prospective comparative study by Rezk et al.[11] conducted on 100 patients with sepsis and evidence of Multi-Organ Failure (MOF) with clinical suspicion of infection. They aimed to test the usefulness of Q-SOFA as a useful predictor of sepsis and evidence of multiorgan failure in critically ill patients in and comparing the predictive value of qSOFA score with that of SOFA score and APACHE II in sepsis and outcome in critically ill patients. They observed that there was a highly significant increase in baseline APACH-II, SOFA-1, qSOFA-0 scores, in non-survivors' group; compared to survivors' group, respectively.

Serum magnesium and need for mechanical ventilation. In the present study, of 50 sepsis cases that had hypomagnesemia, 38 (76%) needed mechanical ventilation. The percentage of patients, who required ventilator support, was significantly higher among hypomagnesemic group as compared to normomagnesemic group. These findings were similar to the findings of Solanki et al.[14] in which they reported that 51.7% (45/87) of the patients with hypomagnesemia were in need for mechanical ventilation which is higher than the patients with normomagnesemia. Kiran HS et al.[12] observed that the patients with hypomagnesemia

compared to patients with normomagnesemia needed ventilator support more frequently (35% vs. 17%). Similarly, Khare et al.[13] and Limaye et al.[10] in their studies also reported a longer duration of mechanical ventilation in the hypomagnesemic patients which falls in line with the findings of the present study.

In the present study, the mean duration of ventilatory support in the case group (hypomagnesemia) was 4.74 + 3.5 days, while the mean duration of ventilatory support in the control group (normomagnesemia) was 1.36 + 2.19 days, respectively.
These findings were similar to the findings of Solanki et al.[14] in which they reported that the mean duration of ventilator support in hypomagnesemic group, and normal magnesium group was 4.9 ± 1.8 days, and 3.9 ± 1.7 days, respectively. These findings indicate that the mean duration of ventilator support was significantly higher among patients who had hypomagnesemia /hypermagnesemia compared to patients with normal magnesium levels.

In another study by Sunil et al.[9] they reported that fifty-nine (57.84%) patients with hypomagnesemia needed mechanical ventilatory support, while 43 (42.15%) patients did not require this support; the difference was not statistically significant (p=0.18). The mean duration of ventilatory assistance for the hypomagnesemic group was 3.07 ± 5.05 days and that for the normomagnesemic group was 2.15 ± 3.46 days; the difference was not statistically significant. Hypomagnesaemia is known to produce muscle weakness and respiratory failure; hence, hypomagnesaemia causes difficulty in weaning off the ventilator, and thus the duration of ventilator support is prolonged.

In our study, the mean duration ± SD of ICU stay was 6.64 ± 3.04 days, and 3.88 ± 2.8 days in hypomagnesemic, and normal magnesium group respectively. The mean duration of ICU stay was significantly higher in hypomagnesemic group of patients as compared to normomagnesemic group of patients. These findings were similar to the findings of Solanki et al.[14] in which they reported the mean duration ± SD of ICU stay was 6.2 ± 2.3days and 4.5 ± 1.7 days in hypomagnesemic, and normal magnesium groups respectively.

Similarly, Khare et al.[13] in their study reported the mean duration of ICU stay was higher in hypomagnesemia group than in hypermagnesemia group, this difference was not statistically significant. On the contrary to the present study findings, Limaye et al.[10] they did not find any statistically significant correlation between length of ICU stay and magnesium levels. In another study by Sunil et al.[9] the mean duration of stay in the MICU was 5.61 ± 5.55 days in patients with a normal magnesium level and 5.57 ± 6. 10 days in patients with hypomagnesemia, while the total duration of stay was 5.59 ± 5.87 days (p= 0.5).

In the present study, the incidence of mortality was significantly higher in hypomagnesemia patients compared with normal magnesium levels patients. Our study showed hypomagnesemia is the independent and statistically significant determinant of increase in ICU mortality. The rate of mortality was 48% in hypomagnesemia group than the normal magnesium group which is 16%. It was found that the mean serum magnesium in the group of patients died was 1.13 + 0.3, while the mean serum magnesium in the group of patient's lives was 1.46 + 0.3, respectively. It was also found that the mean Q-SOFA score in the group of patients died was 2.79 + 0.4, while the Q-SOFA score in the group of survivors was 1.92 + 0.7, respectively. These findings were similar to the findings of Solanki et al[14]. in which they reported the incidence of mortality was significantly higher in hypomagnesemia patients compared with normal magnesium levels patients. However, they reported that there was no association found between hypermagnesemia and ICU mortality.

In another study by Murali et al.[15] the authors studied the impact of serum magnesium on mortality. They reported that the mean serum magnesium among survivors and non survivors were 2.07 ± 0.4 and 1.3 ± 0.3 respectively and this association was statistically significant. They observed the majority of deaths occurred in the hypomagnesaemic group in comparison to normomagnesemia and hypermagnesemia, a fact that is also endorsed by studies conducted by other researchers. Limaye et al[10] observed that the death rate among hypomagnesaemic patients were significantly higher than (31%) normomagnesaemic and (43%)hypermagnesaemic patients. Significant association between mortality and hypomagnesaemia was found ($p<0.05$). Jiang Pan et al.[16] performed a systematic review and meta-analysis to evaluate the association of serum magnesium level with prognosis of critically ill patients upon admission to the ICU. The total sample size from the studies comprised of 1,122 cases and 630 controls. They found that the patients with hypomagnesemia had higher mortality rate (risk ratio [RR] 1.76; 95% Confidence Interval [CI] 1.54-2.00; $p<0.001$). Sunil et al.[9] reported that mortality rate in the hypomagnesemic group was 39.21% (40), whereas that in the normomagnesemic group was 28.57%. The cure/discharge rates were 50 (71.42%) for patients with normal magnesium and 62 (60.78%) for those with low magnesium, and the difference was not statistically significant.

According to the literature, it was found that qSOFA had good prognostic value for mortality in septic patients in resource limited countries and supports using it as a triage tool to identify the patients at risk of poor outcome in resource limited countries.

In the present study, we evaluated whether the qSOFA score would be useful to predict in hospital mortality in a group of sepsis patients who were presented with normal and low levels of serum magnesium. ROC curve analysis of the qSOFA scores for predicting the mortality in the sepsis patients with normal and low magnesium levels. The area under the ROC curve (AUROC) of the qSOFA was 0.847 ($p= 0.009$) with 95% confidence interval ranging between 0.765 to 0.929, respectively.

When the diagnostic performance of the cut-off value Q-SOFA score >2 was tested to predict the mortality in patients with sepsis, it resulted in the sensitivity of 90.62% with 95% CI ranging between 74.9% and 98.02%), sensitivity of 51.47% with 95% CI ranging between 39.03% and 63.78%), positive and negative likelihood ratios of 1.87 and 0.18, positive and negative predictive values of 46.77% (40.18% and 53.49%) and 92.11% (79.5% and 97.23%), and accuracy of 64% (53.79% and 73.36%), respectively. In a study by Shahsavarinia K et al.[17]the authors evaluated the validity of Q-SOFA for early detection and risk stratification of septic patients in emergency department. Q-SOFA was calculated for each patient and correlated with sepsis grades and mortality. Their findings showed that ROC curve for prediction of outcome with qSOFA showed an area under curve of 0.59. (p value: 0.04). The sensitivity of qSOFA for detection of sepsis was 66.3% with a specificity of 60.6%. Negative predictive value and positive predictive value for qSOFA in sepsis detection was 35.7% and 84.5%, respectively based on the clinical diagnostic statement by surviving sepsis campaign. Time spent to sepsis detection was 16 minutes shorter with qSOFA score compared to SIRS criteria in this study. They concluded that Q-SOFA has acceptable value for risk stratification of severity, multi organ failure and mortality. However, it is not a good diagnostic marker for sepsis detection.

In another study by Yu et al.[18] the authors confirmed that the Q-SOFA score is superior in mortality prediction compared with SIRS in terms of discrimination, model fit,

reclassification, and calibration statistics. Q-SOFA alone has the best specificity (87.0%) and can subsequently serve as a quick confirmation tool to aid in the decision to pursue more invasive treatment. They reported the sensitivity of a Q-SOFA score ≥2 to be low at 55%, albeit with a high specificity (84%). A screening tool requires high sensitivity, whereas a confirmation tool requires high specificity. They confirmed that Q- SOFA has low sensitivity and high specificity in predicting sepsis mortality.

Kim KS et al.[19] evaluated the predictive value of Q-SOFA scores derived from vital signs taken during triage for 28-day mortality in ED patients with sepsis. Among the 928 patients diagnosed with severe sepsis or septic shock using the old definition, 231 (24.9%) died within 28 days. More than half of the sepsis patients (493/928, 53.1%) and more than one-third of the mortality cases (88/231, 38.1%) had a qSOFA score <2. The sensitivity of a qSOFA score ≥2 was 61.9%, while the specificity, positive predictive value, and negative predictive value of a qSOFA score ≥2 for 28-day mortality were 58.1%, 32.9%, and 82.2%, respectively. They concluded that clinical criteria of the Q-SOFA are less sensitive than the SIRS assessment and SOFA to predict 28-day mortality in ED patients with sepsis. Baig et al.[20] compared Q-SOFA score and SOFA score when applied to severe sepsis & septic shock patients in the Emergency Department (ED) for prediction of in-hospital mortality in the setting of a tertiary care hospital ED in a low-middle income country. They found that in patients with severe sepsis, the AUROC of Q-SOFA for predicting mortality in subjects was 0.92 (95% CI; 0.89–0.94) with 96% sensitivity and 87% specificity. In patients with septic shock, the AUROC of qSOFA for predicting mortality in subjects was 0.89 (95% CI; 0.85–0.92) with 92% sensitivity and 85% specificity. They concluded that Q-SOFA score is an effective tool at predicting in hospital mortality in comparison to SOFA score when applied to severe sepsis and septic shock patients. In another study by Koch et al.[21] the authors examined the ability of SOFA and qSOFA scores to predict suspected infection and mortality in IMCU patients. Regarding mortality prediction, the Q-SOFA score performed sufficiently within the IMCU cohort (AUCROC SIRS 0.72 [0.71–0.72]; SOFA 0.52 [0.51–0.53]; Q-SOFA 0.82 [0.79–0.84]). They concluded that Q-SOFA score is appropriate for mortality prediction in IMCU patients, SOFA score prediction quality is increased in critically ill patients.

Perman et al[22] in their retrospective observational study, we explored the performance of triage Q-SOFA (tqSOFA), maximum Q-SOFA, and first initial serum lactate (> 3 mmol/L) at predicting in-hospital mortality and compared these results to those for the initial SIRS criteria obtained in triage. A total of 2859 sepsis cases were included and the in-hospital mortality rate was 14.4%. The sensitivity of tqSOFA ≥ 2 and maximum Q-SOFA ≥ 2 to predict in-hospital mortality were 33% and 69%, respectively. They demonstrated that that in a large ED sepsis database the earliest measurement of end organ impairment, tqSOFA, performed poorly at identifying patients at increased risk of mortality and maximum Q-SOFA did not significantly outperform initial serum lactate levels.

LIMITATIONS:

The present study has some limitations which are as follows:

- The major limitation was small number of patients studied.
- Apart from serum magnesium, confounding factors such as presence of other electrolyte imbalance like serum sodium, potassium, calcium and phosphorus, which are known to occur in critically ill patients can impact prolonged ICU stay, need of mechanical ventilation, increased ventilatory days, arrythmias and mortality. The effect of these confounding factors was not taken into consideration.

- We did not study the effects of the changes in the magnesium levels during the course of ICU stay on the outcome.

CONCLUSION:

Based on the findings of the present study, the following conclusions can be made;
Hypomagnesemia is common in hospitalised patients, especially critically ill. It has a high morbidity and mortality among these patients. The assessment of serum magnesium concentration is inexpensive and easy to employ and provides important information about magnesium status in patients. Hypomagnesemia, when detected, may require correction for the management of those with critical illness for better outcomes.

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