ORIGINAL ARTICLE

JIACM 2024; 25 (3): 100-05

Serum Magnesium as a Prognostic Indicator in the Intensive Care Unit

Kolia Vaishnavi*, Jumana Hussain**, Mallikarjuna Shetty***, M Nageswara Rao****, Naval Chandra*****

Introduction

Magnesium is present in the intracellular fluid of all living cells and is the second most plentiful intra cellular cation after potassium. It is a co-enzyme for several enzymes and is essential for energy metabolism, regulation of cellular pathways and synthesis of DNA and RNA. So, magnesium abnormalities are likely to have an impact on morbidity and mortality in critically ill patients, but often go undiagnosed in the intensive care unit (ICU)[1-4].

Hypomagnesaemia is expected to develop in 20% to 65% of critically ill patients[3]. It is often associated with other electrolyte abnormalities such as hypokalaemia, hypocalcaemia and hypophosphataemia[2-5]. Factors contributing to magnesium deficiency in critical care settings are reduced absorption due to altered gastrointestinal activity, malnutrition, renal loss and diabetes[3,6-14].

Magnesium abnormalities in critically ill patients have been found to cause an increased requirement for ventilatory support because hypomagnesaemia causes muscle weakness and respiratory failure which leads to difficulty in weaning patients from the ventilator[1-14]. Hypomagnesaemia is found to be an important predictor of poor patient outcome in critically ill patients[15].

Hence, in an ICU set up, monitoring of serum magnesium levels along with other electrolytes could have an important prognostic as well as therapeutic implication[1,13-14,16].

Objectives

To determine serial values of serum magnesium in critically ill patients and correlate them with:-

a. Severity of illness as assessed by the Sequential Organ Failure Assessement (SOFA) score.

b. Outcome of the patient in terms of duration of ICU stay, need and duration of mechanical ventilation and mortality.

Material and Methods

A prospective observational study was carried-out in the medical ICU at Nizam's Institute of Medical Sciences over a period of one year from December 2021 to November 2022 after approval from the institutional ethics committee. A total of 83 patients in the age group 18 to 70 years were included in the study. After taking informed consent, the data of each patient was collected in a proforma which included age, gender, detailed history and examination.

Specifically, patients were assessed and followed-up for:-

1. SOFA Score (Table I)
2. Length of stay in ICU
3. Need for ventilatory support
4. Duration of ventilatory support
5. Outcome in terms of mortality

Serum magnesium levels were estimated by COBAS C501 clinical chemistry analyser. Other relevant investigations were carried-out based on the clinical condition of the patient.

Patients with renal failure with serum magnesium more than 4 mg/dL and patients on magnesium supplementation before admission into acute medical care unit were excluded from our study.

Statistical Analysis

Data was entered in MS excel and analysed using Stata 13 and Epi info. Data was analysed by mean, standard deviation, Chi-square test. A p value of <0.05 was considered statistically significant. In this study 95% confidence interval was employed.

Correlation between serum magnesium levels and mortality, mechanical ventilator support, duration of stay in ICU, and SOFA score were assessed by chi-square test. Receiver operating characteristic (ROC) curve analysis was done to assess diagnostic performance of serum magnesium levels in predicting requirement of mechanical ventilation and outcome of the patient in terms of mortality.

*Senior Resident, **Associate Professor, ***Additional Professor, ****Professor, *****Professor and Head, Department of General Medicine, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad - 500 084, Telangana.
Corresponding Author: Dr Jumana Hussain, Associate Professor, Department of General Medicine, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad - 500 084, Telangana. Phone: 7075168958, E-mail: jumana25@gmail.com.

Table I: Assessing the sequential organ failure assessment (SOFA) score of the patient[17].

	0	1	2	3	4
Glasgow Coma Scale Score	15	14 - 13	12 - 10	9 - 6	Less than 6
p02/fio2 mmHg	>400	<400	<300	<200	<100
Platelet Count (lac/mm)	>1.5	<1.5	<1	<0.5	<0.2
Serum Bilirubin (mg/dL)	<1.2	1.2 - 1.9	2 - 5.9	6 - 11.9	>12
Cardiovascular (vasopressor dosage in ug/kg/min)	MAP >70 mmHg	MAP <70 mmHg	Dopamine <5, or dobutamine (any dose)	Dopamine >5, or epinephrine < 0.1, Norepinephrine < 0.1	Dopamine >15, or epinephrine >0.1, or Norepinephrine >0.1
Serum creatinine	<1.2	1.2 - 1.9	2 - 3.4	3.5 - 4.9	>5
Urine output (mL/d)				<500	<200

Results

A total of 83 patients were included in the study. 47 (56.6%) were males and 36 (43.4%) were females. The mean age (Years) was 48.64 ± 16.40 years. Baseline characteristics are given in Table II.

Table II: Patient characteristics in the study.

Characteristics	
Age (mean)	48.64 ± 16.40 years
Gender	
Males	47 (56.6%)
Females	36 (43.4%)
Comorbid conditions	
Diabetes mellitus	29 (34.9%)
Hypertension	30 (36.1%)
Coronary artery disease	10 (12.0%)
Primary medical conditions	
Sepsis	45 (54.2%)
Heart failure	18 (21.7%)
Acute pancreatitis	5 (6%)
Diabetic ketoacidosis	8 (9.6%)
Pneumonia	10 (12%)
Duration of ICU stay	
Mean (SD)	9.81 (6.50) days
Median	7 days
Range	2 - 40 days
Mechanical ventilation (MV) requirement	39 (47%)
Duration of MV requirement	
Mean (SD)	7.90 (5.90) days
Median	6 days
Range	2 - 34 days
Outcome	
Discharge	55 (66.3%)
Mortality	28 (33.7%)

Hypomagnesaemia was present in 37 (44.6%) patients and hypermagnesaemia was present in 14 (16.9%) patients. Magnesium level was normal in 32 (38.6%) patients. 2 (2.5%) patients who had normal serum magnesium levels on day 1, developed dysmagnesaemia on day 3 and day 6 respectively. 18 (22.2%) patients, who had abnormal serum magnesium levels on day 1, were found to have normalisation of serum magnesium levels spontaneously.

Hypomagnesaemia was most commonly observed in the age group of 61 - 70 years with a female preponderance. Hypermagnesaemia was most commonly observed in the age group of 61 - 70 years and in male patients.

Among the patients with hypomagnesaemia and hypermagnesaemia on day 1, the mean (SD) SOFA scores were 8.76 (2.88) and 10.29 (3.20) respectively. Mean (SD) SOFA score in those with normal serum magnesium was 3.81 (2.78). This was found to be statistically significant with a p value <0.001 (See Fig. 1).

Among the study subjects with persistent hypomagnesaemia on day 3, the mean SOFA score was 8.28 and it was 10.31 in those with hypermagnesaemia. In contrast, in patients with normal magnesium levels on day 3, the mean SOFA score was 4.59, which was significantly lower. Similar results were seen in patients having persistent hypomagnesaemia and hypermagnesaemia on day 6, where the mean SOFA score was 9.30 and 10.50, respectively, as compared to 6.1 for patients with normomagnesaemia.

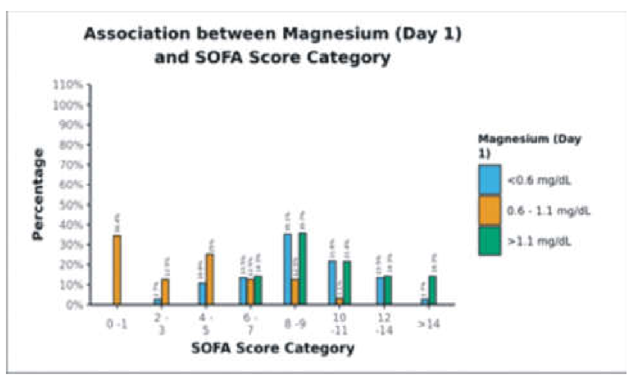

Fig. 1: Association between SOFA score and serum magnesium levels (day 1).

The mean duration of ICU stay in the hypomagnesaemia group was 12.30 days and in the hypermagnesaemia group was 11.14 days. The average length of stay for those with normal magnesium was 6.32 days. There was a statistically significant difference between the groups in terms of duration of ICU stay (P value is 0.016).

In our study group, 39 (64.3%) patients required mechanical ventilation. Among these patients, 28 (71.8%) patients had hypomagneasemia, 9 (23%) patients had hypermagnesaemia and 2 (5.12%) patients had normomagnesaemia. There was significant association between Day 1 serum magnesium levels and requirement of mechanical ventilation with a p value of <0.001 (See Fig. 2).

The mean duration of mechanical ventilation requirement was 8.79 days in patients with hypomagnesaemia and 5.89 days in patients with hypermagnesaemia in our study. This was higher than patients with normomagnesaemia whose mean requirement was 4.5 days.

In our study, out of 37 patients with hypomagnesaemia (Day 1), 20 (54.1%) had mortality while 17 (45.9%) were discharged. In those with hypermagnesaemia (Day 1), 6 (42.9%) patients were discharged and 8 (57.1%) patients had mortality. All patients with normal magnesium levels on day 1 recovered. This was statistically significant with a p value of < 0.001 (See Fig. 3).

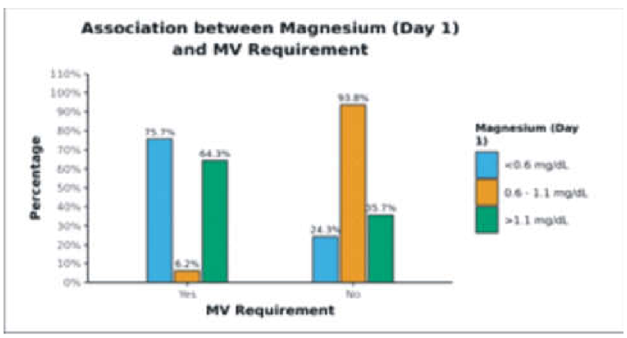

Fig. 2: *Association between serum magnesium levels (day 1) and mechanical ventilation requirement.*

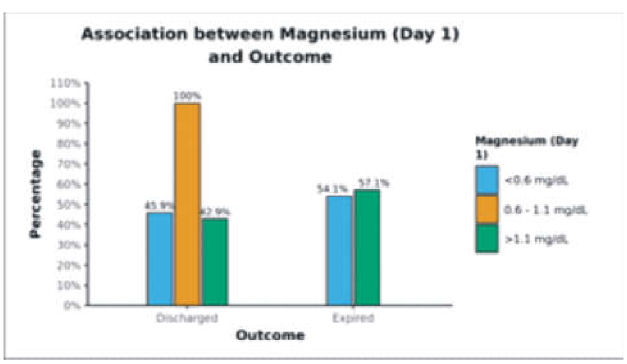

Fig. 3: *Association between day 1 serum magnesium level and outcome.*

We assessed association between trend of serum magnesium levels during ICU stay with outcome of study population in terms of mortality. 32 patients had persistent magnesium abnormalities throughout their stay. Mortality rate in this group was 68.8%. Among the 18 patients whose magnesium levels improved spontaneously, 13 (72.2%) improved and only 5 (27.8%) died. 2 (2.5%) patients who developed dysmagnesaemia on day 3 and day 6 during ICU stay improved. Serum magnesium levels remained normal in 29 (35.8%) patients during ICU stay and all of them were discharged. Thus, we observed a statistically significant association between the trend in serum magnesium levels and outcome in our study. (p value is <0.001) (See Fig. 4).

ROC curve analysis was done to assess diagnostic performance of serum magnesium levels in predicting mechanical ventilation requirement and outcome in terms of mortality. In our study we observed that serum magnesium levels on days 1, 3 and 6 at a cut-off values of </= 0.59 mg/dL, </= 0.61mg/dL and </= 0.59 mg/dL had sensitivity of 72%, 68% and 53% and specificity of 82%, 77% and 86% in predicting mechanical ventilation requirement. Day 1 and day 3 serum magnesium levels (<0.59 mg/dL and <0.61mg/dL respectively) significantly predicted mechanical ventilation requirement.

We observed that serum magnesium levels on days 1,3 and 6 at cut-off values of </= 0.57 mg/dL, </= 0.60 mg/dL and </= 0.6 mg/dL had sensitivity of 61%, 70% and 65% and specificity of 82% , 70% and 72 % in predicting mortality. Day 3 serum magnesium level was more sensitive than day 1 and day 6 serum magnesium levels in predicting the outcome in terms of mortality.

In our study we evaluated the association between serum magnesium abnormalities and co-morbid conditions in the study population. The prevalence of hypomagnesaemia was 48% and 46.6% in study subjects with diabetes mellitus and hypertension, respectively. Whereas the prevalence of hypermagnesaemia was 10% and 16% in study subjects

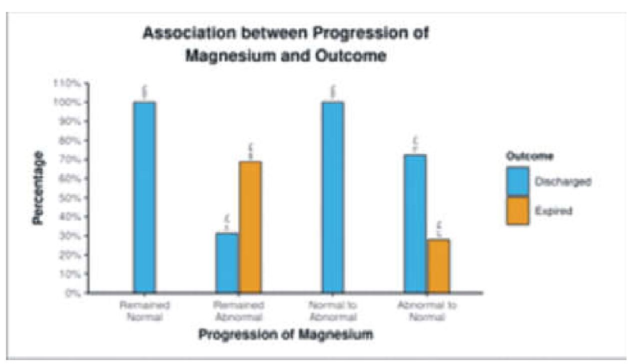

Fig. 4: *Association between trend of serum magnesium levels during ICU stay and outcome of study population.*

Table III: Comparison of present study with similar studies.

Study	Mortality Rate			Mean Duration of stay (Days)			Mechanical ventilation requirement			Mean SOFA Score		
	HypoMg	HyperMg	NormoMg	HypoMg	HyperMg	NormoMg	HypoMg	HyperMg	NormoMg	HypoMg	HyperMg	NormoMg
Present Study	54.1%	57.1%	25%	12.3	11.4	6.34	71.7%	23.2%	5.1%	8.76	10.29	3.81
R Sudha *et al*[19]	39%	-	25%	-	-	-	60%	-	43%	-	-	-
Safavi *et al*[13]	55%	-	35%	9.16	-	5.71	58.6%	-	41.4%	10.8	10.8	7.58
Tasnuva Saiful *et al*[18]	37.5%	25%	20%	7.45	8.67	6.83	-	-	-	-	-	-
Gonuguntla *et al*[20]	51.3%	23.1%	29.3%	Did not vary	Did not vary	Did not vary	High	Low	High	High	Low	High

Note: HypoMg - Hypomagnesaemia; HyperMg - Hypermagnesaemia; NormoMg - Normomagnesaemia; SOFA - Sequential Organ Failure Assessment.

with diabetes mellitus and hypertension. This was found to be higher than patients with other co-morbidities but was not statistically significant.

We observed that hypomagnesaemia was more common than hypermagnesaemia in the presence of other electrolyte abnormalities. The prevalence of hypomagnesaemia was higher in patients with hyponatraemia, hypokalaemia, hypercalcaemia and hypophosphataemia. Whereas the prevalence of hypermagnesaemia was higher in the study subjects with hyperkalaemia, hyperphosphataemia and hypocalcaemia.

Discussion

In our study, out of 83 patients admitted in ICU, hypomagnesaemia was present in 44.6% patients, hypermagnesaemia was present in 16.9% patients and in 38.6% of the patients the serum magnesium levels were normal. Similarly, in studies done by Saiful *et al*[18] and Sudha *et al*[19], the prevalence of hypomagnesaemia was 53.33% and 45%, respectively. Prevalence of hypermagnesaemia was 13.33% and 6%, respectively. Normomagnesaemia was seen in 33.33% and 49% of the patients, respectively.

Hypomagnesaemia was most commonly observed in the age group of 61 - 70 years with a female preponderance. Hypermagnesaemia was most commonly observed in the age group of 61 - 70 years and in male patients in our study. These findings were in contrast to those in a study by Saiful *et al*[18], where hypomagnesaemia and hypermagnesaemia were mostly observed in patients above 70 years of age and more commonly in males. In a study by Sudha *et al*[19] hypomagnesaemia was prevalent mostly in age group of 51 - 60 years.

Our study showed that patients in ICU with hypomagnesaemia at admission had a mean SOFA score of 8.76 and those with hypermagnesaemia had a mean SOFA score of 10.29. These findings, when compared to patients with normal magnesium levels at admission, in whom the mean SOFA score was 3.81, were found to be significantly higher (p value <0.05). In our study we found that patients who had hypomagnesaemia and hypermagnesaemia at admission in ICU , as well as persistent dysmagnesaemia on day 3 and 6, had higher SOFA scores when compared with patients with normal magnesium levels, thus predicting a higher mortality rate in patients with serum magnesium abnormalities. This is in accordance with the study by Safavi *et al*[13] which showed higher mean SOFA score (10.8) in both hypomagnesaemia and hypermagnesaemia group when compared with patients with normal magnesium levels (7.58). A study in the Indian scenario by Gonuguntla *et al*[20], found that patients with hypomagnesaemia had higher SOFA scores than those with normal magnesium levels. However, in contrast with our study, they found that mean SOFA scores in patients with hypermagnesaemia were lower than those with normomagnesaemia.

Our study showed that mortality rate was higher in patients with hypomagnesaemia and hypermagnesaemia, that is 54.1% and 57.1%, respectively. Gonuguntla *et al*[20] had similar mortality (51.3%) in their patients with hypomagnesaemia but had lower mortality (23.1%) in their patients with hypermagnesaemia.

Unique to our study is the serial measurement of serum magnesium levels on days 3 and 6. Thirty-two patients had persistent magnesium abnormalities throughout their stay. Mortality rate in this group was high (68.8%). Among the 18 patients whose magnesium levels improved, 13 (72.2%) recovered and only 5 (27.8%) died. This was statistically significant with a p value of less than 0.001. These results suggest the importance of frequent monitoring of serum magnesium levels to assess the prognosis of patients admitted in ICU and the necessity to correct abnormal serum magnesium levels in these patients, however further intervention studies on magnesium correction in ICU patients are required.

In our study , the mean duration of ICU stay was 12.30 days and 11.14 days in study subjects with hypomagnesaemia and hypermagnesaemia, respectively, which was significantly higher when compared to patients with normal magnesium levels, in whom, the mean duration of ICU stay was 6.34 days. This was in concordance with the results of a study done by Saiful *et al*[18] and Safavi *et al*[13]. Gonuguntla *et al*[20] had similar results with hypomagnesaemia patients requiring a longer ICU stay but not with hypermagnesaemia patients.

Patients with serum magnesium abnormalities – hypomagnesaemia and hypermagnesaemia had higher requirement of mechanical ventilation support as well as longer duration of mechanical ventilation. This observation could be due to respiratory muscle weakness and respiratory failure[1-14]. These results were in line with the results of a study done by Sudha *et al*[19] Safavi *et al*[13].

Our study showed that patients with hypomagnesaemia and hypermagnesaemia had a mean duration of mechanical ventilation requirement for 8.79 days and 5.89 days, respectively. The mean duration of mechanical ventilation requirement was 4.5 days in patients with normal serum magnesium levels, which was significantly lower when compared to patients with dysmagnesaemia. These results were consistent with the results of similar studies done by Safavi *et al*[13] and Munoz *et al*[21] which showed a longer duration of mechanical ventilation support in study population with hypomagnesaemia. In a study done by Sudha *et al*[19] patients with hypomagnesaemia and hypermagnesaemia had longer duration of mechanical ventilation requirement (See Table III).

In our study, we found day 1 serum magnesium level had more sensitivity and was the best parameter in terms of diagnostic accuracy in predicting mechanical ventilation requirement when compared to day 3 and 6 serum magnesium levels. Day 1 serum magnesium level was the best parameter in terms of diagnostic accuracy in predicting mortality. Day 3 serum magnesium level was more sensitive than day 1 and day 6 serum magnesium levels in predicting mortality.

Our study showed a higher prevalence of serum magnesium abnormalities in patients with diabetes mellitus, hypertension and sepsis but this was not statistically significant.

We also observed that magnesium abnormalities were associated with other electrolytes disturbances especially potassium. Thus, these electrolyte abnormalities should prompt investigation of serum magnesium and correction as required.

Conclusion

Serum magnesium abnormalities are frequently encountered in ICU patients. Both hypomagnesaemia and hypermagnesaemia are associated with higher mortality and morbidity in terms of longer duration of ICU stay and requirement of mechanical ventilation. This is substantiated by the association between dysmagnesaemia and higher SOFA score, which is a known prognostic indicator in ICU patients. Hence, serum magnesium is a simple, economical and accessible investigation that can be used for prognostication in ICU patients.

Furthermore, improving trend of serum magnesium levels is associated with better outcomes suggesting a therapeutic implication.

Limitations

Our study has a limitation of smaller sample size. In this study we measured total serum magnesium levels. Ionized magnesium is a more sensitive test that could have strengthened this study. This study included patients admitted only in medical intensive care unit but not trauma and post-operative patients. This is only an observational study and not an interventional study as serum magnesium levels were not corrected in patients with dysmagnesaemia.

References

1. Long S, Romani AM. Role of Cellular Magnesium in Human Diseases. *Austin J Nutr Food Sci* 2014; 2 (10): 1051.
2. Dhaval K, Krishnaswami V, Sahil K *et al*. Role of Magnesium in Cardiovascular Diseases. *Cardiology in Review* 2014; 22 (4):182-92.
3. Chakraborti S, Chakraborti T, Mandal M *et al.* Protective role of magnesium in cardiovascular diseases: A review. *MOLL CE* 2002; 238: 163-79.
4. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *British J Anaesthesia* 1999; 83 (2).
5. Wacker WE, Parisi AF. Magnesium metabolism. *N Engl J Med* 1968; 278 (13): 712-7.
6. Reinhart RA. Magnesium metabolism: a review with special reference to the relationship between intracellular content and serum levels. *Archives of Inter Med* 1988; 148 (11): 2415-20.
7. Reinhart RA. Magnesium deficiency: Recognition and treatment in the emergency medicine setting. *Amer J Emer Med* 1992; 10 (1): 78-83.
8. Reinhart RA. Magnesium metabolism. *Wisconsin Med J* 1990; 89 (10) :579-83.
9. Barbagallo M, Dominguez LJ. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. *Archives Biochemist Biophysi* 2007; 458 (1): 40-7.
10. Sales CH, Pedrosa LD. Magnesium and diabetes mellitus: their relation. *Clinical Nutrition* 2006; 25 (4): 554-62.
11. Iseri LT, Allen BJ, Brodsky MA. Magnesium therapy of cardiac arrhythmias in critical-care medicine. *Magnesium* 1989; 8 (5-6): 299-306.
12. Noronha JL, Matuschak GM. Magnesium in critical illness: metabolism, assessment, and treatment. *Applied Physiolo Intensi Care Med* 2006; 1:57-69.

13. Safavi M, Honarmand A. Admission hypomagnesaemia – impact on mortality or morbidity in critically ill patients. *Middle East J Anaesthesiolo* 2007 October.
14. Limaye CS, Londhey VA, Nadkart MY, Borges NE. Hypomagnesaemia in critically ill medical patients. *JAPI* 2011; 59: 19-22.
15. Velissaris D, Karamouzos V, Pierrakos C *et al*. Hypomagnesaemia in Critically Ill Sepsis Patients. *J Clin Med Res* 2015; 7 (12): 911-8. Epub 2015 Oct 23.
16. Guerrero-Romero F, Rodríguez-Morán M. Low serum magnesium levels and metabolic syndrome. *Acta Diabetol* 2002; 39: 209-13.
17. Moreno R, Vincent JL, Matos R *et al*. The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. Working Group on Sepsis related Problems of the ESICM. *Intensive Care Med* 1999; 25 (7): 686-96.
18. Saiful, Tasnuva, Mostafi *et al*. Experience with Serum Magnesium Estimations in Critically Ill Patients Admitted in High Dependency Unit of A Tertiary Care Hospital. *Bangladesh J Med* 2019; 29: 69-74.
19. Sudha R, Bharanidharan S. Serum Magnesium in Relation to APACHE IV Score and Outcome in Critically Ill Patients. *Inter J Current Res Review* 7 (13): 58-61.
20. Gonuguntla V, Talwar V, Krishna B, Srinivasan G. Correlation of Serum Magnesium Levels with Clinical Outcome: A Prospective Observational Study in Critically Ill Patients Admitted to a Tertiary Care ICU in India. *Ind J Crit Care Med* 2023; 27 (5): 342-7.
21. Muñoz-Castañeda JR, Pendón-Ruiz de Mier MV, Rodríguez M *et al*. Magnesium replacement to protect cardiovascular and kidney damage? Lack of prospective clinical trials. *Inter J Molecular Sci* 2018; 19 (3): 664.