Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/12622
DOI URL: http://dx.doi.org/10.21474/IJAR01/12622

RESEARCH ARTICLE

HYPOMAGNESEMIA AND PROLONGED HOSPITAL STAY: A CASE REPORT AND LITERATURE REVIEW

Ahmad Al-Shami, Jabri Aljabri and Shahad Al-Bloushi
Department of Internal Medicine at Al Jahra Hospital, Jahra and Kuwait.

Manuscript Info

Manuscript History
Received: 20 January 2021
Final Accepted: 24 February 2021
Published: March 2021

Abstract

Hypomagnesemia is a common finding in hospitalized patients mostly overlooked and rarely given as much attention as other electrolyte disturbances. This case report and literature review highlight how hypomagnesemia is common in patients who have a prolonged hospital stay. in addition, we highlight the multiple causes of hypomagnesemia and discuss them further with a literature review.

Introduction:-

The presentation starts with a 46-year-old Sudanese gentleman presenting to the emergency department after being treated by the family physician for throat infection for which he was given antibiotics and gargle medication. On the second day, he was not feeling well, even developing lower abdominal and left hip joint pain. This was not attributed to any recent trauma. With regards to his abdominal pain; no history of nausea, vomiting, fever nor changes in bowel habits. No change in his weight was documented. He had no contact with any sick person. Patient had not noticed any further complains. Past medical and surgical history were unremarkable.

The patient's family history shows he is a child of a consanguineous marriage with four other siblings in good health. No family history of any medical illness. As for his social history, he arrived in Kuwait and has been here for three years as a driver in an area known for farming. He is married to his cousin and has three children; one boy and two girls all healthy.

In the emergency department, Patient was afebrile and vitals within normal limits.

Examination was unremarkable except for Abdominal guarding and tenderness in left lower quadrant. Patient was admitted to surgical ward as a case of abdominal pain for investigation. The patient's initial labs shown in table 1.with regards to his serum Urea, Creatinine, electrolytes, liver enzymes, troponin I, coagulation profile, lipase, amylase, C- reactive protein and procalcitonin were normal. The abdominal x ray is seen in figure 1, a chest x ray and electrocardiogram were normal and a computerized tomography(CT) scan abdomen was done and showed fatty liver with few reactive bilateral inguinal lymph nodes, small hiatal hernia, and a normal appendix.

Corresponding Author:- Ahmad Al-Shami
Address:- Department of Internal Medicine at Al Jahra Hospital, Jahra and Kuwait.

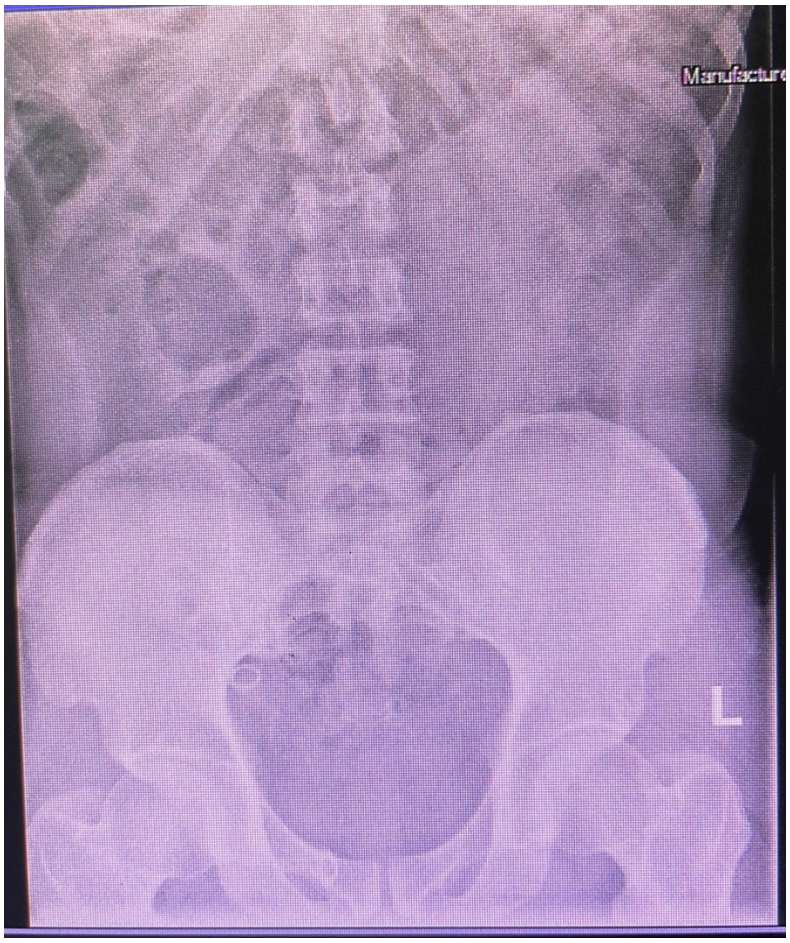

Figure 1 Abdominal X ray

Table 1:- Complete Blood count on admission.

LAB	RESULT	REFERENCE
Hemoglobin	16.6	13-17
Platelet	258	150-410
Neutrophil	17.2	2-7
Eosinophils	0	0.02-0.5
Lymphocytes	1.85	1-3
White blood cell	19	4-10

On the same day, Patient had an episode of seizure which was first witnessed in the hospital; claimed to be the first ever for the patient; lasted for less than 10 minutes with up-rolling of the eyes with tonic clonic movements and frothing. No urinary incontinence nor fever was documented yet a CT brain was done which shows no acute ischemic insult nor space occupying lesion and otherwise unremarkable. Patient was kept under observation and serum electrolytes and glucose werenormal. Next day, Patient developed rigidity in lower limbs then progressed to upper limbs associated with lock jaw and became febrile; temperature was 38 degrees Celsius.A preliminary impression of Tetanus was made and human tetanus Immunoglobulin (Ig) was given by the Neurology and infectious disease team. On the third day, he developed shortness of breath and decreased level of consciousness which was associated with generalized tonic – clonic seizure, so he was intubated and shifted to the Intensive care unit (ICU). He was started on inotropes, pulse steroids, broad spectrum antibiotics and broad-spectrum anti-epileptics. Lumbar puncture was done and the results in table 2. Creatinine Kinase was increased as expected reaching up to 5600 IU/ L; also, an EEG was abnormal showing low amplitude cerebral activity, delta waves were

seen in the left hemisphere.From that point onwards, no further episodes of seizures were witnessed. The patient was kept on Levetiracetam, sodium valproate and lacosamide.

Table 2:- Cerebrospinal fluid sample and culture.

CSF Investigations	Result	Reference
Colour	Colourless	colourless
Appearance	Clear	Clear
WBC	<5 cells/mm^3	0-5 cells/mm^3
RBC	<5 cells/mm^3	0-5 cells/mm^3
Protein	0.5	0.15-0.45 g/L
Glucose	6.37	2.2-3.9 mmol/L
Lactate	2.43	1.1-2.4 mmol/L
CSF c/s	No growth	No growth

During his ICU stay bronchoscopy was done and showed alveolar haemorrhage attributed to negative pressure pulmonary edema due to status epilepticus which prolonged his duration in the ICU. He developed deep vein thrombosis (DVT) in Left lower limb and was started on anticoagulation. At that point a full immunological and infectious disease panel was sent.The full virology panel was sent came back negative except for EBV which may explain his initial sore throat presentation alongside the abdominal pain. Also, HSV-1 was positive which could explain the seizure and disorientationand was treated for two weeks. Work up for HBV, HCV, HIV were negative; in addition, Leptospira, Brucella, and Malaria was negative. Moreover, the Tuberculosis work up was negative. Since the alveolar haemorrhage developed suddenly an immunology screen showed low complements yet the rest of the work up was negative. Shown in table 3.

During the ICU stay he developed septicemia and an acute kidney injury. These factors prolonged his weaning process, yet he was discharged to the ward with a tracheostomy.He gradually improved and was feeding from nasogastric tube and later feeding per oral. Post ICU discharge Electromyography showed anaxonal motor involvement of lower limbs and ulnar nerves which is due to the prolonged stay in the ICU. The patient has continued to have a low serum magnesium for the duration of stay in the ward post discharge from the ICU. He was also found to have hypokalemia initially but was corrected upon replacement.The Hypomagnesemia has continued despite daily correction. Initially the omeprazole was stopped yet the patient continued to have hypomagnesemia. A daily correction with intravenous magnesium sulphate was given. The patient's urine electrolytes were sent alongside urine routine and microscopy attached table 4. This showed increase urinary magnesium losses in context of post-acute kidney injury. Acute tubular necrosis is mostly likely the cause of his acute kidney injury since he had a high creatinine kinase, high fractional excretion of sodium in urine and granular casts were present. The patient was given a high protein diet yet still no improvement in the magnesium was evident and he continued to be on oral magnesium tablet replacement. With continuous replacement of magnesium, physiotherapy, and supportive management he improved significantly. Later the patient was discharged with a follow up for further genetic testing. The literature review will discuss the significance of hypomagnesemia; its different causes and factors that are attributed to our case.

Table 3:- Immunological serological tests.

Investigation	Result	Reference
C3	0.65	0.8-1.52 g/L
C4	0.06	0.15-0.4 g/L
Anti-GBM	2	<20 U/mL
Anti-DsDNA	<1/10	<1/10
ANA	<1/80	<1/80
Anti-CCP	3	<18 U/ml
P-ANCA	<1/20	<1/20
C-ANCA	<1/20	<1/20

Table 4:- Urine electrolytes, urine microscopy and routine.

Urine Electrolytes	Result	Reference

Na	154 mmol/L	
K	33.9 mmol/L	
Cl	141 mmol/L	
Mg	**12.36 mmol/24h**	**3-5 mmol/24h**
Cr	74 mg/dl	
Phosphorous	8 mmol/L	
Glucose	2.12 mmol/L	

Urinalysis Post-AKI	Results
RBC	0-5
WBC	0-5
Casts	Granular casts present
Nitrites	Negative
Leukocytes	Negative

Literature Review:-

Magnesium is an important electrolyte a key part of many reactions such as cellular function and nerve conduction. The Normal serum magnesium levels are between 0.74 to 1.10 mmol/L. Hypomagnesemia is an electrolyte disturbance caused when there is a low level of serum magnesium less than 0.74 mmol/L. the strict hemostasis in the body is strictly regulated by uptake in the small intestine and excretion in the kidney. Hypomagnesemia can be attributed to chronic disease, alcohol use disorder, gastrointestinal losses, renal losses, and other conditions. Signs and symptoms of hypomagnesemia range from mild tremor to cardiac arrythmia. [1-4]

Hypomagnesemia gets less attention in medical literature compared to Hyponatremia, hypokalemia and hypocalcemia. This is evident by the amount of research of the aforementioned presentations. This is due to perhaps the lack of symptoms until the plasma levels are severely low; Clinical manifestations of hypomagnesemia that promptly lead to medical attention involve neuromuscular hyperexcitability that may range from tremors, fasciculation, tetany, to convulsions, and neuropsychiatric disturbances including apathy, delirium, and even coma. Hypomagnesemia's more serious complications are more associated with hypocalcemia and hypokalemia. [5-6]

As a daily requirement the Institute of Medicine recommends a daily magnesium intake of 310–420 mg per day in adults. The majority reaching up to 80% of dietary magnesium is absorbed in the intestines, where the absorption itself depends on both intake and body magnesium status and occurs via both passive and active pathways. Approximately two thirds of plasma magnesium in ionized or complexed forms is ultra-filterable in the kidneys. Once filtered, a quarter is reabsorbed passively with sodium and water in the proximal tubules; three quarters of the filtered magnesium load is reabsorbed paracellularly in the thick ascending limb of the loop of Henle. Finally, reabsorption at the Distal convoluted tubules DCT subsegment. this segment is essential to magnesium balance because it determines the final urinary Mg^{2+} loss. [7-8]

Causes of Hypomagnesemia can be attributed to several causes in the discussed case. Dividing them into different categories, gastrointestinal, renal and miscellaneous. First cause can be attributed to Proton pump inhibitors (PPI), usually with hypocalcemia found to be evident with chronic use of omeprazole. Several studies have showed than use of PPI a lower serum magnesium is evident. A study involving ICU patient demonstrated that concurrent use of diuretics also increased the prevalence of hypomagnesemia. [9-12] In the case discussed above the patient had been on PPI for at least 6 weeks which may have played a role in him developing hypomagnesemia. Prolonged NGT suction like vomiting could be a potential cause of hypomagnesemia this is also evident in patients with diarrhea, inflammatory bowel disease, intestinal and biliary fistulas and pancreatitis. This is similar to the concept in patients with inflammatory bowel disease [13-16]

Renal causes include the urinary loss of magnesium. This is by far the most common category for hypomagnesemia; can be further divided into volume expansion, alcohol, uncontrolled diabetes mellitus, hypercalcemia, or familial renal magnesium wasting. With volume expansion basically there will be a decreased renal water and sodium reabsorption and hence passive magnesium reabsorption. Alcohol, diabetes mellitus and hypercalcemia as a cause of hypomagnesemia are not applicable to the case since the patient had no history of ethanol intake; nor is he having an uncontrolled blood glucose or hypercalcemia.

Familial renal magnesium wasting perhaps not as common as the other causes yet need to be kept as a possibility this includes Gitelman and Bartter syndrome. Gitelman is an autosomal recessive disease which is known to cause low serum magnesium alongside hypocalciuric and Metabolic Alkalosis. However, in the case the patient did not have metabolic alkalosis nor any evidence of hypercalciuria. With regards to barter syndrome a hypokalemia and metabolic alkalosis is expected to be seen, yet it was not clearly evident in the case discussed above yet cannot rule out a role out since a proper genetic testing is to be done to properly diagnose.

Other genetic disorders that cause renal loss of magnesium include familial hypomagnesemia with hypercalciuria and nephrocalcinosis, autosomal dominant isolated hypomagnesemia, autosomal recessive isolated hypomagnesemia, renal malformations and early onset diabetes mellitus. The patients' relative has been tested and showed a normal serum magnesium level. In the case the urinary calcium was normal and there was no history of renal stones nor any family history pointing towards a familial disorder. Genetic testing is needed to rule out genetic causes of hypomagnesemia.

Acute Kidney Injury is a common medical condition that happens in almost 5.7% of all hospitalized patients and reaching up to 15% in ICU patients [17]. In a study Published by Catalina Et Al., the Prevalence of Hypomagnesemia is found to be high in patients who develop acute kidney injury reaching up to 69% [18]. Low serum Magnesium is mostly observed in the recovery phase of AKI and being symptomatic in more than 70% of patients who had hypomagnesemia post AKI, and symptoms improved with correction of magnesium, which makes it important to monitor magnesium levels post AKI [17].

Medication such as Loop and thiazide diuretics are known to cause hypomagnesemia since it inhibits magnesium reabsorption. Usually the degree of hypomagnesemia is mild since the volume will be contracted promoting the kidney to reabsorb water, sodium and to a certain degree magnesium. In our case the patient had no received any form of diuresis, yet it has to be mentioned as among the most common medication to cause hypomagnesemia. Other medication are found to cause hypomagnesemia. Medication that's is known to cause hypomagnesemia includes thiazide and loop diuretics, Aminoglycosides, cisplatin, Calcineurin inhibitors, mycophenolate and Anti-EGF receptors.

Levetiracetam is among the medication in which have been demonstrated to cause hypomagnesemia. Levetiracetam is generally preferred since it has a few side effects. A case report which has shown a patient which was controlled Sodium Valproate later developed hypokalemia and hypomagnesemia after starting the levetiracetam; however, this has not been widely seen. In the case the patient was started on levetiracetam which may had a role in the development of hypomagnesemia. [19] Other medication that may cause hypomagnesemia and reported to cause a barter-like syndrome is colistin, which was given to our patient as he developed Ventilator acquired Pneumonia (VAP) [20].

Finally, it is important to understand that hypomagnesemia is common finding inpatients and usually multifactorial starting from medication induced to renal causes. It was evident multiple factors were attributed our case as the cause of the hypomagnesemia.The factors were medications such as omeprazole, levetiracetam, and colistin; moreover, acute kidney injury in the form of acute tubular necrosis(ATN), NGT suction, dietary deficiency and possibly any other genetic renal cause since there is strong family history of consanguinity.

References:-

1. Andreozzi F, Cuminetti G, Karmali R, Kamgang P. Electrolyte Disorders as Triggers for Takotsubo Cardiomyopathy. Eur J Case Rep Intern Med. 2018;5(4):000760. [PMC free article] [PubMed]
2. Kurstjens S, Bouras H, Overmars-Bos C, Kebieche M, Bindels RJM, Hoenderop JGJ, de Baaij JHF. Diabetes-induced hypomagnesemia is not modulated by metformin treatment in mice. Sci Rep. 2019 Feb 11;9(1):1770. [PMC free article] [PubMed]
3. Ranathunge TA, Karunaratne DGGP, Rajapakse RMG, Watkins DL. Doxorubicin Loaded Magnesium Oxide Nanoflakes as pH Dependent Carriers for Simultaneous Treatment of Cancer and Hypomagnesemia. Nanomaterials (Basel). 2019 Feb 06;9(2) [PMC free article] [PubMed]
4. Brophy C, Woods R, Murphy MS, Sheahan P. Perioperative magnesium levels in total thyroidectomy and relationship to hypocalcemia. Head Neck. 2019 Jun;41(6):1713-1718. [PubMed]

5. J. H. F. de Baaij, J. G. J. Hoenderop, and R. J. M. Bindels, "Magnesium in man: implications for health and disease," *Physiological Reviews*, vol. 95, no. 1, pp. 1–46, 2015.
6. Schwartz R, Spencer H, Welsh JJ. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable 26 Mg. Am J Clin Nutr. 1984;39(4):571–576. [PubMed] [Google Scholar]
7. Fine KD, Santa Ana CA, Porter JL, Fordtran JS. Intestinal absorption of magnesium from food and supplements. J Clin Invest. 1991;88(2):396–402.[PMC free article] [PubMed] [Google Scholar]
8. Quamme GA. Recent developments in intestinal magnesium absorption. Cur Opin Gastroenterol. 2008;24(2):230–235. [PubMed] [Google Scholar]
9. Quamme GA, Dirks JH. The physiology of renal magnesium handling. Ren Physiol. 1986;9(5):257–269.[PubMed] [Google Scholar]
10. Danziger J, William JH, Scott DJ, et al. Proton-pump inhibitor use is associated with low serum magnesium concentrations. Kidney Int 2013; 83:692.
11. Koulouridis I, Alfayez M, Tighiouart H, et al. Out-of-hospital use of proton pump inhibitors and hypomagnesemia at hospital admission: a nested case-control study. Am J Kidney Dis 2013; 62:730.
12. Park CH, Kim EH, Roh YH, et al. The association between the use of proton pump inhibitors and the risk of hypomagnesemia: a systematic review and meta-analysis. PLoS One 2014; 9:e112558.
13. Zipursky J, Macdonald EM, Hollands S, et al. Proton pump inhibitors and hospitalization with hypomagnesemia: a population-based case-control study. PLoS Med 2014; 11:e1001736.
14. LaSala MA, Lifshitz F, Silverberg M, Wapnir RA, Carrera E. Magnesium metabolism studies in children with chronic inflammatory disease of the bowel. J Pediatr Gastroenterol Nutr. 1985;4:75–81. [PubMed] [Google Scholar]
15. 42. Nyhlin H, Dyckner T, Ek B, Wester PO. Plasma and skeletal muscle electrolytes in patients with Crohn's disease. J Am Coll Nutr. 1985;4:531–538. [PubMed] [Google Scholar]
16. 43. Hanna S. Plasma magnesium in health and disease. J Clin Pathol. 1961;14:410–414. [PMC free article][PubMed] [Google Scholar]
17. 44. Smith GA, Tompkins RK. Biliary magnesium loss in the postoperative patient. Arch Surg. 1974;109:77–79. [PubMed] [Google Scholar]
18. Satish R, Gokulnath G. Serum magnesium in recovering acute renal failure. J Indian Journal of Nephrology. 2008
19. Ventakarakesh C. Role of Hypomagnesaemia in acute kidney injury. J of clinical and diagnostic research. 2018 Mar, vol 12(3): OC08- OC10
20. Aksoy D, Cevik B, Kurt S, Pekdas E, Solmaz V. Hypokalemia and hypomagnesaemia related to levetiracetam use. J Clin Neurosci. 2014;21(11):1989–1990. [PubMed]
21. Mohammed T, Manjit M, Animesh R, Naval K. Colistin-induced acquired vartter-like syndrome : an unusual cause of meltdown. Unexpected outcome (positive or negative) including adverse drug reactions case report. BMJ case reports volume 13 issue 2.