Frequency of Hypomagnesemia among Hospitalized Patients in a Nigerian Tertiary Hospital

***Abdullahi M[1], Ibrahim MB[2]**

ABSTRACT

Magnesium deficiency is associated with increased morbidity and mortality among hospitalized patients and yet it was reported to be one of the most under-diagnosed electrolyte disturbances, as plasma magnesium is not part of the routine electrolyte panel in most hospitals in our setting. Previous studies reported varied prevalence of magnesium deficiency among hospitalized patients. We aimed have to determine the frequency of hypomagnesemia, and the underlying clinical conditions associated with it, among hospitalized patients at a tertiary hospital in north eastern Nigeria. Across-sectional study carried out among one hundred and eighty (180) hospitalized patients. Clinical details of study subjects were obtained from hospital case notes. Plasma magnesium was measured using colorimetric method and frequency of hypomagnesemia determined. Frequency of hypomagnesemia was 18.3%. 81.7%had normal plasma magnesium levels and none of the subjects had hypermagnesemia. Proportion of subjects with hypomagnesemia was higher in subjects aged ≥ 50 years compared to the younger subjects aged <50 years (59.1% vs. 12.7%, p < 0.05). Hypomagnesemia was common among type 2 diabetic patients and those on diuretic therapy (proportion of 20% and 29.4% respectively). Hypomagnesemia is common among hospitalized patients in our setting, with type 2 diabetic patients and those on diuretics therapy frequently affected. We recommend routine estimation of magnesium status among hospitalized patients at risk of low magnesium status.We also recommend further studies that will investigate the role of magnesium deficiency in the outcome (morbidity and mortality) of hospitalized patients in our setting.

Keywords: Magnesium, Hospitalization, Nigeria

INTRODUCTION

Magnesium is the fourth most abundant cation and second most abundant intracellular divalent cation.[1,2] It plays an essential physiological role in over 300 intracellular biochemical reactions. Magnesium is required for a number of cellular functions including cellular energy production, protein synthesis and degradation, regulation of intracellular free calcium ion concentration, release of neurotransmitters and maintenance of neuromuscular excitability.[1,2]

Alterations in plasma magnesium levels, especially hypomagnesemia, are associated with increased morbidity and mortality rates in hospitalized patients.[3-6] Different organ systems are affected by magnesium deficiency, mainly, because of disturbances in the function of excitable membranes of neuromuscular and cardiac conducting system.[2] It is also known that hypomagnesemia can induce electrolytes imbalances including hypocalcemia, hypokalemia and hypophosphatemia which might further aggravate neuromuscular and cardiovascular functions.[2] Other consequences of magnesium deficiency include depressed immune response, arrhythmias, seizures, depression, osteoporosis and sudden cardiac death.[3,4] Previous clinical studies have shown that hypomagnesemia is relatively common in hospitalized patients.[5,6,9-11]

Routine measurement of plasma magnesium as part of the electrolyte panel, for hospitalized patients, is not done in most hospitals in our setting, and because signs and symptoms of hypomagnesemia are non specific nor do they constitute a syndrome that is easily detectable clinically,[12] hypomagnesemia and its associated complications often will go undetected. The aim of this study was to determine the need for recommending routine measurement of plasma magnesium for patients on admission at a tertiary hospital in north eastern Nigeria. We also aimed to identify the underlying primary medical conditions as well as other predisposing factors associated with magnesium balance.

Department of Chemical Pathology,[1] Gombe State University, Gombe, Nigeria
Department of Internal Medicine,[2] Federal Teaching Hospital, Gombe, Nigeria

*Corresponding author: drgombe@gmail.com

PATIENTS/MATERIALS AND METHOD

This is a cross sectional analytical study conducted at the medical, surgical and emergency wards of a Federal Teaching Hospital in Gombe, north eastern Nigeria. The study protocol was approved by the Health Research Ethics Committee of the Federal Teaching Hospital Gombe, Nigeria. We used non-probability sampling method in which consecutive adult (aged > 18 years) patients, were enrolled as they were admitted in to the hospital for various clinical conditions. We screened 340 hospital admissions, and 180 subjects fulfilled the selection criteria.

All study subjects were enrolled in the study after an informed consent was sought and obtained. All study subjects are Nigerians of African descent and living in Gombe State. We excluded from the study, patients receiving magnesium containing antacids and/or any form of magnesium supplementation prior to and/or during admission in the hospital. Cigarette smoking and/or alcohol ingestion were also part of the exclusion criteria.

Detailed history and physical examination findings of each study subject were recorded at the time of blood sample collection. The study did not interfere with the management of the study subjects throughout their hospital stay in any way.

Sample collection and preparation

Each patient was properly identified and the antecubital fossa was cleaned with a methylated spirit-soaked swab and allowed to air dry. A tourniquet was applied to the upper arm, for a maximum of 1-2 minutes, to visualize the superficial veins. The most prominent vein was then identified and punctured with a sterilized 5-ml syringe and 21-G needle. Blood sample (5 ml) was collected and the needle gently withdrawn and hemostasis secured by applying pressure with a clean dry cotton wool. The blood collected was transferred to a lithium heparin bottle and transported immediately to the laboratory at room temperature, where it was centrifuged at 4000 rpm for 10 min. The supernatant plasma was pipette into another plain bottle and kept at -20^{0}C until analyzed for plasma total magnesium. Arms with indwelling intravenous lines were avoided. Prolonged application of tourniquet was also avoided.

Laboratory analysis

During analysis, the plasma samples were thawed, and aliquots were taken and assayed for plasma total magnesium level using a colorimetric assay kit (Agappe Diagnostics Limited, Kerala, India). Magnesium reacts with Xylidyl Blue to form a colored compound in alkaline solution. The intensity of the colour formed is proportional to the concentration of magnesium in the sample. Hypomagnesemia was defined as plasma magnesium levels less than 0.75 mmol/L.[13] Hemolyzed samples were excluded and delayed separation of plasma from cells was avoided. All blood samples were treated the same throughout the process of blood collection, transport and analysis. All laboratory analyses were conducted at the Chemical Pathology Laboratory of Gombe State University/Federal Teaching Hospital, Gombe.

Statistical analysis

Statistical package for social sciences (SPSS) version 20.0 was used for statistical analysis. Data are summarized using frequencies and proportions and presented using tables and figures. Mean differences between groups were determined using t-test. We compare proportion differences between groups using chi-square test. All p-values were two-sided and considered significant if less than 0.05.

RESULTS

We screened 340 hospital admissions, and 180 subjects fulfilled the selection criteria. Clinical and biochemical characteristics of the selected study subjects are summarized in Tables 1 and 2.The mean age of the study subjects, which were predominantly females (n=101, 56.1%), was 51.0±5.2 years. Majority of the subjects were overweight, BMI > 25kg/m^2 (n=96, 53.3%).When the study subjects were categorized in to two age groups (< 50 years and ≥ 50 years); most of the subjects were less than fifty years of age (n=158, 87.8%).

The frequency distribution of plasma magnesium of the study subjects is shown in Figure 1. Frequency of hypomagnesemia was 18.3% (33/180). About 81.7% (147/180) had normal magnesium levels and none of the subjects had hypermagnesemia. It was also observed that subjects aged ≥50 years had higher

incidence of hypomagnesemia compared to the younger subjects aged < 50 years (59.1% vs. 12.7%, $p < 0.05$).

The underlying clinical conditions that are known to cause magnesium deficiency identified in subjects with hypomagnesemia were summarized in Table 3. The clinical conditions included; type 2 diabetes mellitus (7 out of 35), diuretics therapy (5 out of 17), enterocutaneous fistulae (2 out of 3), gentamicin therapy (1 out of 2), proton pump inhibitors (PPIs) therapy (1 out of 4), malignancy (4 out of 31), chronic diarrhoea (1 out of 5) and nasogastric suction. In some of the subjects, more than one condition might have contributed to the development of the hypomagnesemia.

Table 1. Clinical characteristics of the study subjects by plasma magnesium category

	All patients	Hypomagnesemia (m ± SD)	Normomagnesemia (m ± SD)	*p-value*
Number	180	33	147	-
Age (years)	51.0 ± 5.2	57.4 ± 4.6	49.2 ± 6.0	*< 0.05**
Sex ratio (M/F)	79/101	12/21	67/80	-
BMI (kg/m^2)	26.6 ± 2.1	28.2 ± 2.5	26.0 ± 1.9	*< 0.05**
Plasma Mg (mmol/L)	0.79 ± 0.03	0.63 ± 0.02	0.82 ± 0.02	*< 0.05**

Mg, magnesium, BP, blood pressure, BMI, body mass index, m, mean, SD, standard deviation
* *statistically significant*

Table 2. Frequency of Hypomagnesaemia in study subjects according to relevant demographic characteristics

Variables	Number of subjects	Hypomagnesemia Proportion	Percentage	*p-value*
Age				
<50 years (n=158)	20	20/158	12.7%	
≥50 years (n=22)	13	13/22	59.1%	*≥ 0.05*
Sex				
Males (n=79)	12	12/79	15.2%	
Females (n=101)	21	21/101	20.8%	*< 0.05**
Body mass index				
<25kg/m^2 (n=84)	15	15/84	17.9%	
≥25kg/m^2 (n=96)	18	18/96	18.8%	*< 0.05*

* *statistically significant*

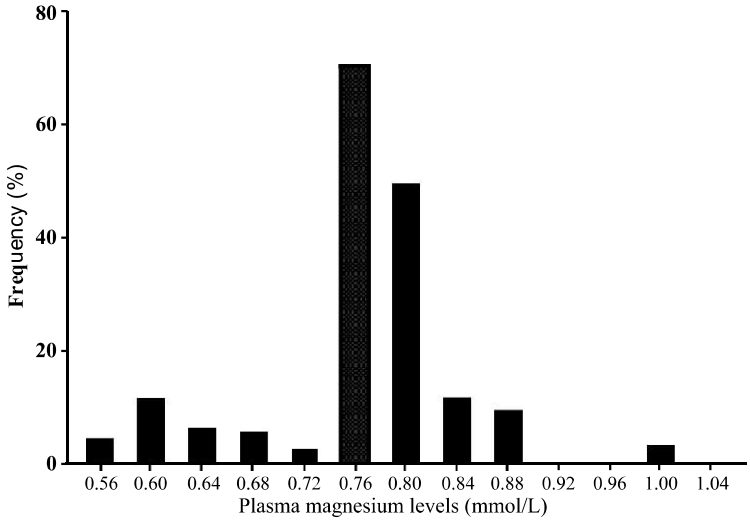

Figure 1. Frequency distribution of plasma magnesium levels among study subjects

Table 3. Summary of clinical conditions of patients with hypomagnesemia

Clinical condition	Frequency	Number of subjects with hypomagnesemia (%)
Type 2 diabetes mellitus	35	7 (20.0)
Diuretics therapy	17	5(29.4)
Malignancy	31	4(12.9)
Chronic diarrhoea	5	1(20.0)
Aminoglycoside therapy	2	1(50.0)
Enterocutaneous fistulae	3	2(66.7)
Nasogastric suction	1	1(100.0)
Proton pump inhibitors therapy	4	1(25.0)
Multiple conditions	28	6(21.4)
Others	54	5(9.2)
Total (overall prevalence)	180	33(18.3)

DISCUSSION

We studied the prevalence of hypomagnesemia and the clinical conditions associated with it in a cohort of hospitalized patients at a tertiary hospital in north eastern Nigeria. The prevalence of hypomagnesemia in the present study was 18.3%. It was also observed in this study that hypomagnesemia is frequently associated with diuretics therapy and type 2 diabetes mellitus.

Several studies have investigated the incidence of hypomagnesemia in hospitalized patients ranging from 14% -70%.[5-9,10] The wide range might be explained by the differences in the type of patient populations in the various studies and also the definition of hypomagnesemia used by the different authors and whether total or ionized magnesium was measured. The prevalence rate was generally observed to be higher in studies where total magnesium was measured rather than ionized magnesium and in those whom the study subjects were predominantly critically ill patients.

Kagima JW, in a prospective observational study done among critically ill patients in a tertiary hospital in Kenya, reported an incidence of admission hypomagnesemia of 16.7% which was comparable to our findings.[14] Our study subjects were predominantly chronically ill patients from the medical and surgical wards, and therefore were more likely to have had factors known to predispose to the development of magnesium deficiency, such as prolonged loop diuretics therapy and losses of magnesium in gastrointestinal fluids via vomiting, diarrhoea or nasogastric suction.

In the present study, about 20% (7 of 35) of the subjects with type 2 diabetes mellitus had hypomagnesemia. Type 2 diabetes mellitus has long been known to be associated frequently with magnesium deficiency. The pathogenesis of hypomagnesemia in type 2 diabetes is related to the increased urinary excretion of magnesium associated with hyperglycemia and osmotic diuresis in poorly controlled diabetes.[15] Also, a high proportion (29.4%) of patients on loop diuretics therapy were found to have hypomagnesemia. Loop diuretics therapy also may cause renal wasting of magnesium. Magnesium reabsorption at the thick ascending limb (TAL) of the loop of Henle is inhibited by loop diuretics, causing an increased urinary excretion of magnesium.[16,17] There was no clear explanation for the hypomagnesemia seen in some cases among the study subjects.

LIMITATIONS

The small sample size could be a limitation for the analysis of data and the measurement of magnesium was limited to the plasma compartment. Magnesium deficiency can exist even when plasma magnesium is normal, and therefore, there is possibility of misclassification of subjects.

CONCLUSIONS

Magnesium deficiency, as measured by plasma magnesium level, has been shown to be common among hospitalized patients in our setting. Magnesium deficiency may be associated with serious clinical consequences, but because the associated clinical signs and symptoms are often non specific, its presence is not readily detected clinically. In none of all the cases of hypomagnesemia in this study was there an indication that the team responsible for care of the patients suspected the presence of the hypomagnesemia. This suggests the need to consider including a routine measurement of plasma magnesium in patients at risk of developing magnesium deficiency, and possibly as part of the baseline investigations done for newly admitted patients in our setting.

We recommend further studies that will investigate the role of magnesium deficiency in the outcome (morbidity and mortality) of hospitalized patients and the benefits of routine plasma magnesium determination on patient care in our setting.

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Conflict of interest: Nil

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