Increased Mortality Associated with Hypermagnesemia in Severe COVID-19 Illness

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Key Points

- Hypermagnesemia is common in patients admitted with coronavirus disease 2019.
- The development of hypermagnesemia in coronavirus disease 2019 is associated with renal failure and markers of high cell turnover.
- In adjusted models, patients who develop hypermagnesemia have an increased risk of mortality.

Abstract

Background Although electrolyte abnormalities are common among patients with COVID-19, very little has been reported on magnesium homeostasis in these patients. Here we report the incidence of hypermagnesemia, and its association with outcomes among patients admitted with COVID-19.

Methods We retrospectively identified all patients with a positive test result for SARS-CoV-2 who were admitted to a large quaternary care center in New York City in spring 2020. Details of the patients' demographics and hospital course were obtained retrospectively from medical records. Patients were defined as having hypermagnesemia if their median magnesium over the course of their hospitalization was >2.4 mg/dl.

Results A total of 1685 patients hospitalized with COVID-19 had their magnesium levels checked during their hospitalization, and were included in the final study cohort, among whom 355 (21%) had hypermagnesemia. Patients who were hypermagnesemic had a higher incidence of shock requiring pressors (35% vs 27%, $P<0.01$), respiratory failure requiring mechanical ventilation (28% vs 21%, $P=0.01$), AKI (65% vs 50%, $P<0.001$), and AKI severe enough to require renal replacement therapy (18% vs 5%, $P<0.001$). In an adjusted multivariable model, hypermagnesemia was observed more commonly with increasing age, male sex, AKI requiring RRT, hyperkalemia, and higher CPK. Survival probability at 30 days was 34% for the patients with hypermagnesemia, compared with 65% for patients without hypermagnesemia. An adjusted multivariable time to event analysis identified an increased risk of mortality with older age, need for vasopressors, higher C-reactive protein levels, and hypermagnesemia (HR, 2.03; 95% CI, 1.63 to 2.54, $P<0.001$).

Conclusions In conclusion, we identified an association between hypermagnesemia among patients hospitalized with COVID-19 and increased mortality. Although the exact mechanism of this relationship remains unclear, hypermagnesemia potentially represents increased cell turnover and higher severity of illness, which is frequently associated with more severe forms of AKI.

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Introduction

Magnesium is an often-overlooked electrolyte with diverse roles in critical physiologic processes, including blood pressure regulation, muscle and nerve function, and protein synthesis. Disordered magnesium homeostasis is common among both patients who are ambulatory and hospitalized (1). Despite extracellular magnesium (<1% of total body magnesium) being an insensitive marker for magnesium depletion, many chronic conditions or medications can predispose patients to depleted total body stores over time, resulting in hypomagnesemia (2). Conversely, in the absence of renal dysfunction, hypermagnesemia is uncommon due to the high capacity for renal clearance, and is usually only seen at a GFR <20 ml/min with concurrent exogenous magnesium (3).

Electrolyte abnormalities are common among patients with coronavirus disease 2019 (COVID-19)

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(particularly hyperkalemia), but very little has been reported on magnesium homeostasis in these patients. Although few reports include magnesium levels among patients with COVID-19 (4,5), anecdotal reports of severe hypermagnesemia among patients who were hospitalized at our institution prompted an investigation of magnesium homeostasis among patients with COVID-19. We report the incidence of hypermagnesemia and its association with outcomes among patients admitted with COVID-19 at a large quaternary care center in New York City.

Methods

Cohort Identification

We retrospectively identified all patients with a positive test result for severe acute respiratory syndrome coronavirus 2 from either a nasopharyngeal or oropharyngeal swab PCR who were admitted to Columbia University Irving Medical Center between March 1 and May 31, 2020, who had bloodwork during their hospitalization and were followed through June 10, 2020. This study protocol was approved by the Institutional Review Board of Columbia University Irving Medical Center and the requirement for informed consent was waived.

Clinical Characteristics and Outcomes

Details of the patients' hospital courses, demographics, clinical data, laboratory data, and clinical outcomes were obtained retrospectively from medical records. Comorbid conditions were determined by specific international classification of disease codes and are provided in Supplemental Table 1. The magnesium status was determined by the median magnesium level of each patient's entire hospitalization, with values above the upper limit of normal at our laboratory (>2.4 mg/dl) considered hypermagnesemic, and all others were categorized as not having hypermagnesemia. Specific laboratory value cutoffs are provided in each accompanying table and figure.

AKI was defined based according to AKI Network (AKIN) definitions (6), interpreted as an absolute increase in creatinine of >0.3 mg/dl or >50% increase from baseline, and staged as follows:

AKIN stage 1: ≥0.3 mg/dl increase in creatinine within a 48-hour window or a 1.5- to 2-fold increase in creatinine compared with baseline.
AKIN stage 2: >2- to 3-fold increase in creatinine compared with baseline.
AKIN stage 3: ≥0.5 mg/dl increase in creatinine within a 48-hour window when creatinine ≥4.0 mg/dl, or >3-fold increase in creatinine compared with baseline.

Because urine output was not available for the majority of our cohort, loss of excretory function was determined solely by creatinine kinetics. Determination of baseline creatinine was made using the following hierarchy:

1. median creatinine from 365 to 7 days before presentation; if none available, then:
2. minimum creatinine from 7 days before presentation to the day of presentation; if none available, then:
3. minimum creatinine from presentation to discharge.

4. If no creatinine or only a single creatinine was measured during the index hospitalization without prior measurements, these patients were labeled as having an unknown baseline creatinine.

Statistical Analysis

Results are presented as a percent of the cohort, means and standard deviations, or median and interquartile range. Chi-squared or Fisher's exact test were used to compare magnesium status groups on categorical variables, and t tests or Wilcoxon signed-rank test for continuous variables. Logistic regression models were used to evaluate for factors associated with the development of hypermagnesemia. Kaplan–Meier survival analysis was used to estimate and display survival stratified by hypermagnesemia status. Cox proportional hazards models were used to assess the hazard ratios for death as the outcome. Due to significant concordance between clinical illness severity as measured by the need for vasopressors, mechanical ventilation, and AKI requiring RRT (Supplemental Table 2), only AKI requiring RRT was used for the multivariable hypermagnesemia model and only vasopressor status was used in the Cox multivariable model for death. Odds ratios (OR) and hazard ratios are presented with 95% confidence intervals (95% CIs). Two sensitivity analyses were performed for both the logistic regression and Cox proportional hazard models, excluding patients who experienced any hypermagnesemia in one analysis, and excluding patients whose median magnesium level was below the lower limit of normal to evaluate for bias, by grouping patients who were normomagnesemic and hypomagnesemic together. Missing laboratory data are presented in Supplemental Table 3. No missing data were imputed. Statistical analyses were performed using Stata 16 (College Station TX).

Results

A total of 1685 patients hospitalized with COVID-19 had their magnesium levels checked during their hospital course, and were included in the final study cohort, among whom 355 (21%) had hypermagnesemia (Table 1 and Figure 1). The mean of the median magnesium levels for the group classified as not hypermagnesemic was 2.1±0.2 versus 2.8±0.5 in the hypermagnesemic group (P<0.0001; Table 2). The maximum magnesium levels were significantly higher among patients with hypermagnesemia (3.0±0.6 vs 2.3±0.5 mg/dl, P<0.001; Table 2). Time from admission to the peak serum magnesium levels was not different between the groups (4.4±5.7 days vs 4.7±5.4 days; P=0.30). Importantly, the incidence of any hypomagnesemia was low, with only 9% of patients experiencing at least one serum magnesium level below the lower limit of the normal range, and only 0.3% of patients in the hypermagnesemia group (Table 2).

Patients with hypermagnesemia had similar age, race, and body mass index compared with those without hypermagnesemia. However, they were less likely to be female (29% vs 43%, P<0.001), or have comorbid hypertension (58% vs 65%, P=0.01) or diabetes (38% vs 44%, P=0.03) (Table 1). Additionally, patients who experienced hypermagnesemia were noted to have higher peak phosphorus concentrations,

Table 1. Demographics and baseline outpatient characteristics of the cohort

| Characteristics	Total		Not Hypermagnesemic		Hypermagnesemic[a]		P value
	n	%	n	%	n	%	
N	1685	100	1330	79	355	21	
Age	65.2	16.30	64.9	16.42	66.3	15.79	0.17
Sex (female)	679	40	577	43	102	29	<0.001
Race and ethnicity							0.14
Black	365	22	288	22	77	22	
White nonHispanic/Latino	180	11	154	12	26	7	
White Hispanic/Latino	210	12	167	13	43	12	
Other Hispanic/Latino	557	33	438	33	119	34	
Other race or not reported	373	22	283	21	90	25	
BMI							0.40
<20	108	6	88	6	20	6	
20–25	385	23	316	22	69	19	
25–30	515	31	515	36	120	34	
30–35	308	18	237	16	71	20	
≥35	242	14	193	13	49	14	
Missing	127	8	101	7	26	7	
Medical history							
Hypertension	1073	64	867	65	206	58	0.01
Diabetes mellitus	720	43	586	44	134	38	0.03
Pulmonary disease	299	18	244	18	55	15	0.21
CKD	252	15	204	15	48	14	0.39
ESKD	72	4	56	4	16	5	0.81
Liver disease	96	6	83	6	13	4	0.06

BMI, body mass index.
[a]Defined as median admission (Mg) > upper limit of normal (2.4 mg/dl).

higher serum potassium levels, and more commonly had creatine phosphokinase >5000 U/L, and no differences were observed in peak alkaline phosphatase levels or incidence of hypercalcemia (Table 2). Several markers of inflammation that were being measured routinely on patients with COVID-19 early in the pandemic were higher among patients with hypermagnesemia, including lactate dehydrogenase, erythrocyte sedimentation rate, and C-reactive protein (CRP) (Table 2).

During their COVID-19 hospitalization, patients with hypermagnesemia also had a higher incidence of shock requiring pressors (35% vs 27%, $P<0.01$), respiratory failure requiring mechanical ventilation (28% vs 21%, $P=0.01$), AKI (65% vs 50%, $P<0.001$), and AKI severe enough to require
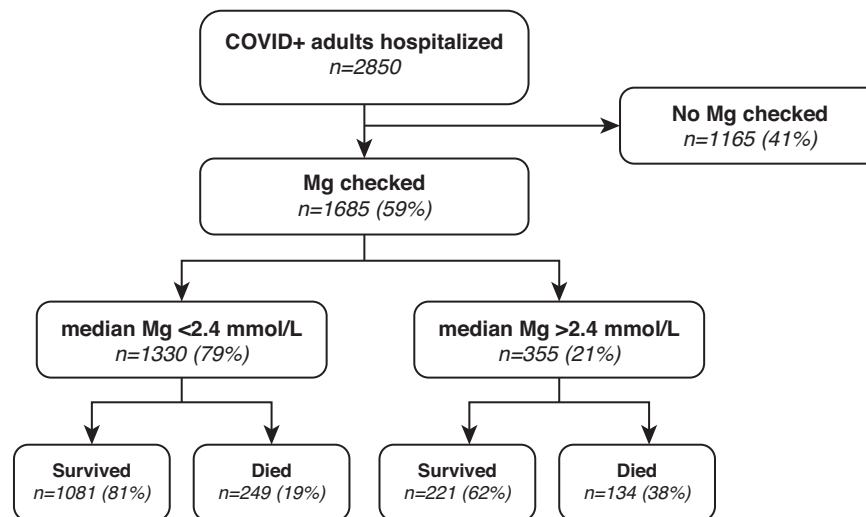
Figure 1. | Incidence and outcomes of patients who are hypermagnesemic. Of the 1685 (59%) of patients with COVID-19 admitted who had magnesium levels checked, 21% had a median magnesium level >2.4 mg/dl. In total, 38% of patients with hypermagnesemia died during their hospitalization, compared with only 19% of patients without hypermagnesemia. Mg, magnesium; COVID-19, coronavirus disease 2019.

Table 2. Clinical outcomes, illness severity, and mortality by hypermagnesemia status: Magnesium characterization, COVID illness severity, and clinical outcomes

Finding	Total		Not Hypermagnesemic		Hypermagnesemic[a]		P value
	n	%	n	%	n	%	
N	1685	100	1330	79	355	21	
Characterization of magnesium							
Mean of median magnesium levels, mg/dL	2.2	0.4	2.1	0.2	2.8	0.5	<0.001
Any hypomagenesemia,%[b]	159	9	154	9	5	0.3	<0.001
Peak magnesium, mmol/L	2.5	0.6	2.3	0.5	3.0	0.6	<0.001
Time to peak magnesium (days)	4.4	5.7	4.4	5.7	4.7	5.4	0.30
Outpatient magnesium supplementation	36	2	29	2	7	2	0.81
Inpatient magnesium supplementation	53	3	47	4	6	2	0.08
Loop or Thiazide diuretic use	48	3	41	3	7	2	0.26
Additional laboratory values							
Hypercalcemia (any),%[c]	224	13	171	13	53	15	0.31
Phosphate (peak), mg/dl	4.9	2.3	4.6	2.0	6.0	3.0	<0.001
Potassium (peak), mmol/L	5.4	1.1	5.3	1.0	5.7	1.1	<0.001
Lactate dehydrogenase (peak), U/L	329	414	304	340	419	609	<0.001
Low haptoglobin,%[d]	25	1	20	2	5	1	0.99
Erythrocyte sedimentation rate (peak), mm/h	89	34	87	35	96	30	<0.001
C-reactive protein (peak), mg/L	183	105	175	106	213	97	<0.001
Alkaline phosphatase (peak), U/L	139	139	137	135	147	135	0.25
Creatine phosphokinase, % >5000 U/L	49	3	28	2	21	6	<0.001
Illness severity and clinical outcomes							
Pressors or inotropic support	475	28	352	27	123	35	<0.01
Mechanical ventilation	377	22	278	21	99	28	0.01
AKI[e]							<0.001
Unknown	62	4	50	4	12	4	
No AKI	697	43	589	46	108	32	
Any AKI	854	53	635	50	219	65	
Stage 1	322	20	248	19	74	22	
Stage 2	184	11	155	12	29	9	
Stage 3	348	22	232	18	116	34	
Stage 3 + renal replacement therapy	125	8	63	5	62	18	<0.001
Mortality							<0.001
In-hospital death	383	23	249	19	134	38	
Survived to discharge or end of observation	1302	77	1081	81	221	62	

[a]Defined as median admission (Mg) > upper limit of normal (2.4 mg/dl).
[b]Defined as median admission (Mg) < upper limit of normal (1.7 mg/dl).
[c]Defined as any (calcium) > upper limit of normal (>10.3 mg/dl).
[d]Defined as any (haptoglobin) < 20 U/L.
[e]n=1613, excluding ESKD n=72.

renal replacement therapy (18% vs 5%; Table 2). There were no differences in the use of either outpatient (before hospitalization) or inpatient magnesium supplementation between the two groups.

Univariate logistic regression identified factors associated with hypermagnesemia (n=1371; Table 3). Hypermagnesemia was more common among men (OR, 1.90; 95% CI, 1.47 to 2.45, P<0.001) in addition to being associated with more severe infections as evidenced by the need for vasopressors (OR, 1.47; 95% CI, 1.15 to 1.89, P<0.01), mechanical ventilation (OR, 1.46; 95% CI, 1.12 to 1.91, P=0.01) and the development of developing AKI requiring RRT (OR, 4.26; 95% CI, 2.93 to 6.18, P<0.001). Several markers of cell turnover and illness severity (including hyperkalemia, creatine phosphokinase (CPK), lactate dehydrogenase [LDH], and CRP) were also associated with hypermagnesemia. In a multivariable model, hypermagnesemia was observed more commonly with increasing age, male sex, AKI requiring RRT, hyperkalemia,

and higher CPK, whereas LDH and CRP were no longer significantly associated with hypermagnesemia. Interestingly, patients who were hypermagnesemic had lower odds of having either hypertension or diabetes, both in univariate and multivariate models (Table 3). Sensitivity analysis excluding patients with any hypomagnesemia showed small differences in race, history of diabetes, and CPK; however, subsequent analysis only excluding patients with a median magnesium <1.7 mg/dl provided results more similar to the primary multivariable model (Supplemental Table 4).

Survival probability at 30 days was 34% for the patients with hypermagnesemia, compared with 65% for patients without hypermagnesemia. By the end of follow-up, a greater proportion of patients with hypermagnesemia had died (38% vs 19%, P<0.001; Table 2). Time to event analyses identified an increased risk of mortality with older age, hypertension, diabetes, need for vasopressors, higher CRP levels, and hypermagnesemia. Hypermagnesemia was

Table 3. Logistic regression analysis of characteristics and outcomes associated with hypermagnesemia (n=1371)

Variable	Univariate			Multivariable		
	Odds Ratio	95% Confidence Interval	P value	Odds Ratio	95% Confidence Interval	P value
Demographics						
Age (per 10 years)	1.05	0.98 to 1.13	0.17	1.17	1.06 to 1.29	<0.01
Sex (reference: female)	1.90	1.47 to 2.45	<0.001	2.11	1.56 to 2.87	<0.001
Race (reference: White)[a]	1.32	0.99 to 1.76	0.06	1.32	0.95 to 1.85	0.10
PMHx						
HTN	0.74	0.58 to 0.94	0.01	0.71	0.51 to 0.98	<0.05
DM	0.77	0.61 to 0.98	0.03	0.73	0.53 to 0.99	<0.05
ESKD	1.07	0.61 to 1.90	0.81	1.64	0.87 to 3.10	0.13
Illness severity						
Pressors	1.47	1.15 to 1.89	<0.01			
Mechanical ventilation	1.46	1.12 to 1.91	0.01			
AKI requiring RRT	4.26	2.93 to 6.18	<0.001	3.08	1.97 to 4.81	<0.001
Labs						
Any hypercalcemia, mg/dl [b]	1.19	0.85 to 1.66	0.31	0.88	0.59 to 1.31	0.52
Any hyperkalemia, mmol/L [c]	2.19	1.72 to 2.80	<0.001	1.59	1.17 to 2.16	<0.05
Creatine phosphokinase (per 1000 U/L)	1.05	1.02 to 1.08	<0.01	1.03	1.00 to 1.06	<0.05
Lactate dehydrogenase (per 100 U/L)	1.06	1.03 to 1.08	<0.001	1.03	1.00 to 1.06	0.08
Alkaline phosphatase (per 10 U/L)	1.00	1.00 to 1.01	0.25	1.00	0.99 to 1.01	0.43
C-reactive protein (per 10 mg/L)	1.03	1.02 to 1.05	<0.001	1.01	0.99 to 1.02	0.39

PMHx, Past medical history; HTN, hypertension; DM, diabetes.
[a]Reference group White non-Hispanic/Latino and White Hispanic/Latino.
[b]Hypercalcemia defined as corrected calcium >ULN (10.3 mg/dl).
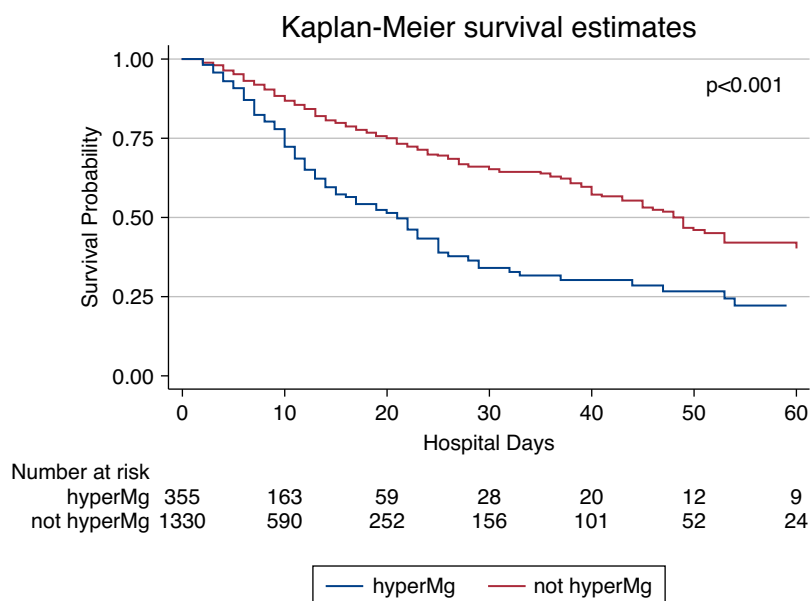[c]Hyperkalemia defined as potassium >ULN (5.1 mmol/L).

associated with a two-fold increase in mortality (Figure 2), an effect size that was similar even after adjusting for age, sex, race, comorbidities, and illness severity (n=1594; hazard ratio, 2.03; 95% CI, 1.63 to 2.54, P<0.001; Table 4). Additional time-to-event analyses were performed grouping patients by tertiles of their median magnesium levels during their hospitalization, which revealed significant lower survival probability for patients across tertiles (P<0.001; Supplemental Figure 1). Finally, sensitivity analysis excluding patients with any hypomagnesemia showed only slight differences and subsequent analysis only excluding patients with a median magnesium <1.7 mg/dl did not show any significant differences from the primary multivariable model (Supplemental Table 5).

Discussion

Our observational study demonstrates that hypermagnesemia in patients hospitalized with COVID-19 is common, with nearly one in five patients having an elevated median serum magnesium level. The presence of hypermagnesemia was associated with greater illness severity, and patients who develop hypermagnesemia experience twice the mortality rate seen in patients with normal magnesium concentrations, suggesting hypermagnesemia may serve as a useful prognostic marker in patients hospitalized with COVID-19.

Given magnesium's role as a primarily intracellular ion, hypermagnesemia may either reflect elevated total body stores (resulting from exogenous administration, decreased clearance, or both), or a shift in magnesium between compartments. In our cohort, markers of inflammation and high cell turnover (such as potassium, phosphate, LDH, erythrocyte sedimentation rate, CRP, CPK) were all higher in the hypermagnesemia group, suggesting the elevated magnesium level may simply reflect increased cell turnover, rather than a true total body excess. The high rate of lymphocyte death and lymphocyte cell turnover combined with the underrecognized complication of rhabdomyolysis may explain the high serum magnesium observed, particularly in individuals with severe COVID-19. Although bone serves as a large magnesium reservoir, markers of elevated bone turnover, such as alkaline phosphate, were not associated with the development of hypermagnesemia, making bone an unlikely source of the elevated serum magnesium in our cohort. We did not observe any differences in either the outpatient magnesium medications that patients were receiving before hospitalization or inpatient magnesium supplementation between the two groups, making excess administration an unlikely cause. Another consideration is that these patients developed hypermagnesemia secondary to decreased renal clearance (i.e., AKI). Although this certainly remains a possibility, it is worth noting the hypermagnesemia group did have higher incidences of AKI, but it was disproportionately skewed toward higher severity AKI and, accordingly, this group also had higher rates of renal replacement therapy. Therefore, although high rates of AKI leading to decreased native renal magnesium clearance might have been an explanation for the development of hypermagnesemia in this group, the higher rates of extracorporeal magnesium clearance must also be considered. Further, the high incidence of hypermagnesemia appears to be much higher than would be traditionally encountered among patients

Kaplan-Meier survival estimates

p<0.001

Number at risk

	0	10	20	30	40	50	60
hyperMg	355	163	59	28	20	12	9
not hyperMg	1330	590	252	156	101	52	24

— hyperMg — not hyperMg

Figure 2. | Patient survival curves by hypermagnesemia status. Kaplan–Meier curve for patient survival over time from admission for all patients stratified by those who had a median magnesium less than the upper limit of normal (red) and those who had a median magnesium greater than the upper limit of normal (>2.4 mg/dl; blue), $P<0.001$. HyperMg, hypermagnesemia.

hospitalized for other reasons who develop severe AKI. As a result, the high incidence of hypermagnesemia among patients hospitalized with COVID-19 appears to be secondary to a combination of increased cell turnover and decreased renal clearance. Other smaller cohorts have also reported a higher incidence of both rhabdomyolysis and hypermagnesemia in COVID-19 nonsurvivors compared with survivors (4). Another smaller study of 20 patients reported a 25% incidence of hypermagnesemia in their cohort, but also noted that 50% of their patients developed hypomagnesemia (5).

Whether the hypermagnesemia is merely evidence of severe illness or is in the contributory pathway for the poor prognosis cannot be determined from our analysis. Although there are many papers touting the protective effect magnesium supplementation may have in outcomes of patients with COVID-19 (putting forth magnesium's anti-inflammatory, antioxidative, antispasmodic, vasodilatory, and neuroprotective effects), these are purely speculative (7–11). Few studies have attempted to investigate whether magnesium plays a role in outcomes in COVID-19, but all

Table 4. Survival analysis showing hazard ratios for death (n=1594)

	Univariate			Multivariable		
Variable	Hazard Ratio	95% Confidence Interval	P value	Hazard Ratio	95% Confidence Interval	P value
Demographics						
Age (per 10 years)	1.67	1.53 to 1.81	<0.001	1.86	1.68 to 2.06	<0.001
Sex (reference: female)	1.17	0.94 to 1.44	0.16	1.24	0.99 to 1.55	0.06
Race (reference: White)	0.89	0.71 to 1.12	0.33	1.01	0.80 to 1.28	0.92
PMHx						
HTN	1.69	1.35 to 2.11	<0.001	1.07	0.83 to 1.38	0.60
DM	1.45	1.18 to 1.77	<0.001	1.22	0.97 to 1.52	0.08
ESRD	0.97	0.55 to 1.68	0.90	1.36	0.78 to 2.40	0.28
Illness severity						
Pressors	1.81	1.44 to 2.26	<0.001	1.98	1.53 to 2.55	<0.001
Mechanical Ventilation	1.24	0.99 to 1.55	0.06			
AKI requiring RRT	1.27	0.98 to 1.64	0.07			
Labs						
C-reactive protein (per 10 mg/L)	1.03	1.02 to 1.04	<0.001	1.01	1.00 to 1.03	0.03
Hypermagnesemia[a]	2.14	1.73 to 2.64	<0.001	2.03	1.63 to 2.54	<0.001

PMHx, Past medical history; HTN, hypertension; DM, xx.
[a]Defined as median (Mg) > upper limit of normal (2.4 mg/dl).

have methodological limitations (*e.g.*, small sample size, not randomized, selection bias, and confounding) (12,13). There are also conflicting reports of the role magnesium homeostasis plays in the expression of IL-6 and other cytokines in non–COVID-19 critical illness, with some studies reporting the proinflammatory effect of hypomagnesemia leading to increased production of IL-1β, IL-6, and TNF-α and PAI-1 (11,14,15), whereas one study reported patients treated with magnesium had lower levels of TNF-α, but higher levels of IL-6, IL-4, and IL-10 (16). Unfortunately, there were too few patients in our cohort with available cytokine levels (in particular IL-6) to make any meaningful conclusions about the association with magnesium. One alternative explanation for the high incidence and poor outcomes associated with hypermagnesemia is from transcellular shift of magnesium from the intracellular to extracellular space in response to stress hormones (11), which is plausible given the association between vasopressor use and the development of hypermagnesemia in our cohort. Finally, one compelling physiologic explanation for the worse outcomes seen in hypermagnesemia is magnesium's known vasoplegic effect on vascular smooth muscle (17). Magnesium has important antagonistic effects to calcium and functions as a physiologic calcium channel blocker, leading to a reduction of blood pressure (*e.g.*, the standard of care in the treatment of pre-eclampsia). As a result, in the absence of additional data, our findings would argue against the use of magnesium supplementation in patients with COVID-19 as some have proposed.

Although this is the largest and most granular description of magnesium homeostasis in patients with COVID-19, it is not without limitations. First, the observational nature of the study introduces the possibility of residual confounders that were not identified. Second, because the categorization of groups in our analysis was defined by their median magnesium level, there is a possibility for temporal bias because the sequence of the event of hypermagnesemia with other clinical outcomes was not necessarily uniform. Finally, our study design precludes any determination of whether treating hypermagnesemia confers any clinical benefit by altering the clinical trajectory of these patients. Despite these limitations, the novelty of the question, large sample size, detailed description, and extensive laboratory data are strengths of this study.

In conclusion, we identified an association between hypermagnesemia among patients hospitalized with COVID-19 and increased mortality. Although the exact mechanism of this relationship remains unclear, this finding potentially represents increased cell turnover and severity of illness, which is frequently associated with more severe forms of AKI. Additional prospective studies are needed to understand: (*1*) the mechanisms that underlie this association, (*2*) the potential role of magnesium concentrations as a prognostic marker, and (*3*) whether correction of hypermagnesemia alters the prognosis of patients with serious severe acute respiratory syndrome coronavirus 2 infections.

Supplemental Material

This article contains the following supplemental material online at http://kidney360.asnjournals.org/lookup/suppl/doi: 10.34067/KID.0002592021/-/DCSupplemental

Supplemental Table 1. International classification of disease codes used for determining medical history.

Supplemental Table 2. Illness severity concordance.

Supplemental Table 3. Missing data.

Supplemental Table 4. Sensitivity analysis of the logistic regression analysis of characteristics and outcomes associated with developing hypermagnesemia, excluding patients with hypomagnesemia.

Supplemental Table 5. Sensitivity analysis of the survival analysis showing hazard ratios for death excluding patients with hypomagnesemia.

Supplemental Figure 1. Patient survival curves by median magnesium tertiles. Kaplan–Meier curve for patient survival over time from admission for all patients stratified by tertiles of median magnesium (lowest values = tertile 1 (blue) whereas highest values = tertile 3 (green); $P<0.001$).

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