INTRODUCTION

In late December 2019, a newly identified member of coronaviridae family named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) originated in Wuhan, China, and has afterward spread to the rest of the world. Considering the highly contagious nature of the coronavirus disease 2019 (COVID-19), World Health Organization on March 11, 2020, announced it as a pandemic. Subgroups of patients, such as kidney transplant recipients, are at high risk because of immunosuppressive regimens. It seems that the clinical and laboratory manifestations and prognosis of COVID-19 pneumonia in kidney transplant recipients be different from those of the general population. So far, however, there have been scarce published studies. To our knowledge, the first report of COVID-19 in kidney transplant recipients is presented in this observational study.

METHODS

All kidney transplant recipients who referred to the Razi Hospital of Rasht with a diagnosis of SARS-CoV-2 infection from February 20 to 19th of April 2020 have been included in this observational study.

RESULTS

We present 22 cases of COVID-19 in kidney transplant recipients (median age 52 years [interquartile range 40.75-62.75 years]) and baseline eGFR 60 (mL/min/1.73 m²) (44.75-86.75). Patients complained of cough (72.7%), dyspnea (63.6%), fever (68.2%), and chill (72.7%) with greater prevalence. We decreased the dose of immunosuppression and started stress dose of intravenous hydrocortisone or equivalent oral prednisolone. Each patient received antiviral therapy based on the latest updated version of local protocol at the time of admission. CT scan findings in 90.9% of patients showed bilateral multifocal lesions. Acute kidney injury (AKI) was observed in 12 patients during hospitalization. Six patients died after a median of 12 days from admission (IQR, 1-21).

Conclusions: In this small observational study, we observed high AKI occurrence and mortality rate in kidney transplant recipients with COVID-19.

KEYWORDS

coronavirus, COVID-19, immunosuppression, kidney transplantation
infection in kidney transplant recipients is a 52-year-old male from Wuhan who improved 13 days after hospital admission. Our center as a referral hospital for patients with COVID-19 in North Iran admitted kidney transplant recipients. This essay is an observational study of clinical and laboratory characteristics, treatments, and outcome of COVID-19 in 22 kidney transplant recipients admitted in a teaching hospital in North of Iran.

2 | MATERIALS AND METHODS

All kidney transplant recipients who referred to the Razi Hospital of Rasht with diagnosis of SARS-CoV-2 infection from February 20 to 19th of April 2020 have been included in this observational study. Patients were categorized as probable if they had any acute respiratory and systemic signs and symptoms plus chest CT scan showing lower respiratory tract infection compatible with COVID-19. The diagnosis “confirmed” was used for cases with clinical presentation and chest CT scan compatible with COVID-19 who were laboratory-confirmed by RT-PCR. On admission, patients were classified based on the severity of infection to mild/moderate/severe/critically ill cases based on case definition by Chen et al.

All demographic data and considerable clinical and laboratory information on admission and during hospitalization were gathered. Also, clinical management of patients including immunosuppression changes and antiviral therapy based on local protocol in our country published by Ministry of Health, Treatment and Medical Training was documented. Oxygen requirements during hospitalization and occurrence of AKI according to the KDIGO criteria were recorded. In terms of short-term outcome of kidney function, we followed up patients during 2-8 weeks after discharge.

All lung CT scans available to us for this study were reviewed and evaluated by an expert radiologist. Findings including pure ground-glass opacity (GGO), crazy-paving, mixed GGO and consolidation, pure consolidation, reversed halo, intralesional vascular enlargement, linear opacities, traction bronchiectasis, mediastinal lymphadenopathies, pleural, and pericardial effusion were documented. There was a CT scan involvement score of zero to five for each lobe, with a total possible score of zero to 25. The total pulmonary involvement score was calculated.

The results are expressed as percentage for categorical variables or median (interquartile range; IQR) for continuous variables. The t test, chi-square, and Fisher’s exact tests were employed in analyses of variables. P-values of <.05 were considered as statistically significant.

The study protocol was approved by the local ethics committee of Guilan University of Medical Sciences.

3 | RESULTS

Demographic and baseline clinical characteristics of included patients are shown in Table 1. Sixty-eight percent of the patients were men, and median age was 52 (IQR, 40.75-62.75). The median duration of hospitalization was 9 days (IQR, 5-15). Patients complained of a cough (72.7%), dyspnea (63.6%), fever (68.2%), and chills (72.7%) with greater prevalence among all reported symptoms.

Seventeen patients (77.27%) required oxygen therapy during hospitalization; five patients (22.72%) among them intubated. During the hospitalization period of the 22 patients, 6 patients died after a median of 12 days from admission (IQR, 1-21). Of those, one patient died of a massive gastrointestinal bleeding and 5 (22.72%) admitted in ICU due to complications of the SARS-CoV-2.

Sixteen patients were discharged from the hospital after a median of 8.5 days from admission (IQR, 5.25-13.5). Four of discharged patients required re-hospitalization because of recurrence of some symptoms. One of these patients finally expired. The total mortality rate was 6/22 (27.27%). Death incidence did not differ between patients in moderate and severe categories of infection (25% vs. 30%, respectively; P = .793). There was no significant difference in demographic characteristics, comorbidities, immunosuppressive regimen, vital signs on admission, blood parameters, type of diagnosis, lesion types and distribution, and score of CT findings between dead and recovered cases (P > .05).

While there was no significant difference in symptoms between died and recovered cases, a difference in death between patients who experienced chills symptom with who do not was observed (P = .023).

Changes in immunosuppression regimen and drug therapies of kidney transplant recipients on admission and patient outcomes are shown in Table 2. Mycophenolate was withdrawn in 21 patients. The low dose of glucocorticoids was replaced with a stress dose of intravenous hydrocortisone (60-300 mg/d) or equivalent oral prednisolone (Table 2). As the antiviral regimen used in our protocol has major interaction with calcineurin inhibitor (CNI) metabolism, the dose of tacrolimus or cyclosporine empirically decreased 20%-100% in 17 of the 22 patients. No correlation was found between mortality and variables, including changes in immunosuppression regimen and drug therapies of kidney transplant recipients on admission (P > .05) (Table 2).

There was no difference in mortality between cases with and without a history of ACEI/ARB use. There was no difference in mortality between cases whose statin was continued or discontinued during hospitalization (P = .083). Among 16 recovered patients, 12 (75%) were using statins before COVID-19 and prescribed to continue during hospitalization. Intravenous immunoglobulin (IVIG) was prescribed to four (18.18%) of the 22 patients, of these patients, one (25%) died (P > .05) (Tables 2. and S1).

On admission, serum creatinine was elevated in 40.9% of the patients. The median creatinine level at admission showed a 24.02% increase (IQR, 4.83%-106.56%; range 0%-375%) compared with the baseline, and the peak creatinine level showed 50.9% increment (IQR, 15.39%-131.22%; range 9.68%-511.11%) compared with the baseline. 12 of 22 patients experienced acute kidney injury, and six of them died. Table 3 shows details of changes in kidney function during hospitalization. In 16 patients at discharge,
| TABLE 1 | Baseline clinical and laboratory characteristics of 22 kidney transplant recipient infected with SARS-CoV-2 |
|---------|-------------------------------------------------------------------------------------------------------------|
| **Demographic characteristics** |                                                                                                             |
| Age (year) | 52 (40.75-62.75)                                                                                           |
| Sex (M/F) (n) | 15/7                                                                                                       |
| BMI | 26.17 (24.13-30.76)                                                                                         |
| **Comorbidities; n (%)** |                                                                                                             |
| Hypertension | 16 (72.7)                                                                                                    |
| Diabetes | 8 (36.4)                                                                                                     |
| Hyperthyroidism | 1 (4.5)                                                                                                    |
| Neurologic/ Psychiatric disorders | 3 (13.6)                                                                                                    |
| Ischemic heart disease | 1 (4.5)                                                                                                    |
| **Clinical data related to transplanted kidney** |                                                                                                             |
| Kidney transplantation age (year) | 8.5 (4.75-12)                                                                                               |
| **Baseline immunosuppressive regimen (n)** |                                                                                                             |
| Calcineurin inhibitors (CNIs) |                                                                                                             |
| Cyclosporine | 12/22                                                                                                       |
| Tacrolimus | 9/22                                                                                                        |
| Mycophenolate mofetil or sodium | 22/22                                                                                                       |
| Mammalian target of rapamycin inhibitor (mTORi) | 1/22                                                                                                        |
| Low dose of glucocorticoid | 22/22                                                                                                       |
| **Clinical characteristics of COVID-19 at disease onset; n (%)** |                                                                                                             |
| Cough | 16 (72.7)                                                                                                    |
| Chills | 16 (72.7)                                                                                                    |
| Fever | 15 (68.2)                                                                                                    |
| Dyspnea | 14 (63.6)                                                                                                   |
| Myalgia | 6 (27.3)                                                                                                    |
| Nausea & Vomiting | 5 (22.7)                                                                                                   |
| Headache | 4 (18.2)                                                                                                    |
| Fatigue | 4 (18.2)                                                                                                    |
| Diarrhea | 4 (18.2)                                                                                                   |
| Sore throat | 3 (13.6)                                                                                                   |
| Anorexia | 2 (9.1)                                                                                                     |
| Sputum production | 2 (9.1)                                                                                                   |
| Dizziness | 1 (4.5)                                                                                                    |
| Abdominal pain | 1 (4.5)                                                                                                   |
| **Vital signs on admission** |                                                                                                             |
| Systolic blood pressure (mm Hg) | 110 (110-120)                                                                                               |
| Heart rate (beat per minute) | 83 (78-86)                                                                                                  |
| Respiratory rate (breaths per minute) | 20 (18-20)                                                                                                 |
| Percutaneous oxygen saturation (%) | 94 (88.75-96.25)                                                                                           |
| Temperature (°C) | 37.1 (37-37.22)                                                                                             |
| **Blood parameters at hospital admission** |                                                                                                             |
| Platelets (/mL) | 131 500 (110 250-182 000)                                                                                   |
| Hemoglobin | 10.97 (10.1-12.97)                                                                                           |
| Hematocrit | 35.9 (31.25-41.55)                                                                                            |
| Mean corpuscular volume (fL) | 87.6 (81.37-92.5)                                                                                           |
| WBCs (cell/mL) | 5450 (3975-6450)                                                                                             |

(Continues)
Creatinine level compared with the baseline increased by 10.55% (IQR, 0.83%-27.46%; range 10%-150%). During the follow-up period, serum creatinine was measured in 12 of 16 patients (Table 3). In terms of electrolyte abnormalities, there is a difference in hypokalemia occurrence between the died and recovered cases (Table 4).

| Characteristics of lung lesions on CT |  |
|-------------------------------------|--|
| Total CT score of the pulmonary involvement; n = 19 | 8 (6-14) |
| Lesion distribution; n = 21 |  |
| Multifocal bilateral | 20 (90.9) |
| Multifocal unilateral | 1 (4.5) |
| Lesion type; n = 21 |  |
| Ground-glass opacity and consolidation | 4 (18.2) |
| Only ground-glass opacity | 5 (22.7) |
| Only consolidation | 12 (54.5) |
| Other findings; n = 21 |  |
| Linear opacity | 4 (18.2) |
| Reversed halo sign | 1 (4.5) |
| Bronchiectasis | 4 (18.2) |

(Continues)
DISCUSSION

This paper presented the clinical and laboratory characteristics and outcome of the first 22 kidney transplant recipients who infected with COVID-19 in Razi hospital, Rasht, Iran. This ongoing COVID-19 pandemic has been proposed to cause high mortality rate in patients with comorbidities such as cardiovascular diseases, diabetes, chronic respiratory diseases, and hypertension.\(^1\)\(^2\)\(^11\)\(^14\) In this study, hypertension was the most common comorbidity and five of died patients had hypertension.

The immunosuppressive regimen increases susceptibility of transplant recipients for respiratory viral infection and causes poor prognosis in this population,\(^15\) but there are no data on the association between immunosuppressive therapy in solid organ transplant recipients and risk of SARS-CoV-2 infection. Although there are not strong recommendations on the approach to the immunosuppressive regimen in kidney transplant recipients with COVID-19, some studies suggest that antimetabolite agents (mycophenolate and azathioprine)\(^7\)\(^9\)\(^15\) should be stopped at the time of admission to hospital, dose of prednisolone should be either unchanged or increased, and CNI dose should be reduced.\(^7\)\(^15\) Another knowledge gap is the consensus on the percentage of CNI dose reduction in comparison with baseline dose in these patients, as it may threaten patients with organ rejection. It is interesting that in vitro studies have shown that some agents used in immunosuppression regimens inhibit coronavirus families. It is reported that treatment of cells with rapamycin inhibits MERS-CoV infection.\(^16\) Cyclosporine is thought to inhibit the replication of a different type of coronaviruses.\(^7\) Further investigations are needed to be done to establish these findings in clinical studies. Tacrolimus can prevent the growth of the human coronaviruses SARS-CoV, HCoV-NL63, and HCoV-229E in cell culture. Based on these data, it makes sense to study the effect of keeping low doses of tacrolimus in COVID-19–infected transplant patients.\(^17\)

Despite immunosuppression dose reduction nearly similar to recommendations, 27.27% of our patients died after a median of 12 days from admission (IQR, 1-21). This finding nearly is consistent with that of Alberici et al\(^8\) who found 25% death among their patients after a

### TABLE 1 (Continued)

| Blood gas characteristics (normal range); n = 10 |
|-----------------------------------------------|
| Median (IQR) pH (7.35-7.45)                   | 7.29 (7.23-7.39) |
| Median (IQR) partial pressure of carbon dioxide, mm Hg (35-45) | 35.5 (28.5-39.3) |
| Median (IQR) actual bicarbonate, mEq/L (21.0-28.0) | 17.7 (13.07-20.6) |

| Acid/Base disturbance                          |
|-----------------------------------------------|
| Normal blood gas                               | 2/10 |
| Acute metabolic acidosis                       | 2/10 |
| Partially compensated metabolic acidosis       | 3/10 |
| Compensated metabolic acidosis                 | 1/10 |
| Compensated respiratory alkalosis              | 1/10 |
| Mixed respiratory and metabolic acidosis       | 1/10 |

| COVID-19 diagnosis                             |
|-----------------------------------------------|
| Probable cases                                 | 17/22 |
| Confirmed cases                                | 5/22  |

| COVID-19 severity on admission                  |
|-----------------------------------------------|
| Mild                                          | 0    |
| Moderate                                      | 12 (54.5) |
| Severe                                        | 10 (45.5) |
| Critically ill                                 | 0    |

| Ventilation requirement during hospitalization  |
|-----------------------------------------------|
| Room air                                      | 5 (22.7) |
| Oxygen nasal cannula                          | 8 (36.4) |
| Oxygen mask reservoir bag                     | 4 (18.2) |
| Invasive mechanical ventilation               | 5 (22.7) |

Note: Data are reported as number and percentages or median (interquartile range) unless otherwise indicated. Unless specified, counts are from the total cohort (N = 22).

Abbreviations: BMI, body mass index; BS, blood sugar; BUN, blood urea nitrogen; CK-MB, creatine kinase-MB; CPK, creatine phosphokinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; PTT, partial thromboplastin time; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SCr, serum creatinine; WBC, white blood cell.

aPrednisolone 5-10 mg/d.
TABLE 2 Changes in immunosuppression regimen and drug therapies of kidney transplant recipients on admission and outcome

| IS changes                                                                 | Total (22) | Deaths (6) |
|----------------------------------------------------------------------------|------------|------------|
| Mycophenolate withdrawn                                                   | 21         | 6          |
| Low dose of glucocorticoids withdrawn and hydrocortisone 60-300 mg/d or equivalent dose of prednisolone started | 22         | 6          |
| Routine dose of CNI continued                                             | 5          | 2          |
| 20%-25% decrease in dose of CNI                                           | 2          | 0          |
| 26%-50% decrease in dos of CNI                                             | 10         | 2          |
| More than 50% decrease in dose of CNI                                     | 1          | 1          |
| CNI hold                                                                  | 3          | 1          |
| mTORI was changed to CNI                                                  | 1          | 0          |

Antiviral therapy

| Hydroxychloroquine                                                        | 2          | 1          |
| Hydroxychloroquine + Oseltamivir                                          | 1          | 1          |
| Hydroxychloroquine + Lopinavir/ritonavir                                   | 1          | 0          |
| Hydroxychloroquine + Lopinavir/ritonavir + Oseltamivir                    | 16         | 2          |
| Hydroxychloroquine + Lopinavir/ritonavir + Ribavirin                      | 2          | 2          |
| IVIG                                                                      | 4          | 1          |
| Other ABs                                                                 | 21         | 6          |
| LABA or SABA                                                              | 5          | 3          |
| Anticholinergic                                                           | 5          | 3          |
| Vitamin D                                                                 | 11         | 5          |
| DH of ACEI/ARBs                                                           | 6          | 2          |
| Continued use of ACEI/ARBs during hospitalization                         | 6          | 2          |
| DH of Statin use                                                          | 18         | 6          |
| Continued use of Statins during hospitalization                           | 14         | 3          |

median period of 15 days from symptom onset. While we found AKI in near 54% of patients in our study, six of 20 patients (30%) were developed acute kidney injury in another study. Notably, their approaches to immunosuppression regimen management at admission were somewhat different and more homogenous in comparison with the approach of our center. In another preliminary study on seven cases of kidney transplant recipients the mortality rate was 14%. Recently, a very high early mortality, 28% in 3 weeks, among kidney transplant recipient has been reported that is consistent with our results.

In terms of laboratory tests, lymphopenia was observed in 10 of 11 patients with an available lymphocyte count. Other studies showed lymphopenia as a laboratory feature in these patients. It has been suggested that as immunosuppressed patients are likely to have baseline lymphopenia, a further decrease in lymphocyte count is likely to be of prognostic value and it should be part of routine testing in kidney transplant patients requiring hospital admission for COVID-19 infection. Among our patients, five were confirmed cases with virological examination. During this epidemic situation in our region, most of the cases (17 patients) were probable cases of SARS-CoV-2 infection. There was no virological diagnosis for them because of a shortage of RT-PCR kits, or it was waived due to the rapid spread, highly contagious nature of this disease and highly suspicion to SARS-CoV-2 infection.

All of the patients in this study were prescribed hydroxychloroquine, and 86% of them received lopinavir/ritonavir. Although the local guidelines were suggesting the use of lopinavir/ritonavir and hydroxychloroquine in COVID-19 treatment in the first weeks of this pandemic, their efficacy is questionable. Newer guidelines recommend against the use of lopinavir/ritonavir; except in the context of a clinical trial, because of unfavorable pharmacodynamics and negative clinical trial data. Furthermore, there are insufficient clinical data to recommend either for or against using hydroxychloroquine for the treatment of COVID-19.

AKI on admission or AKI developed during hospitalization occurred in over half of kidney transplant patients with COVID-19, of them 50% of died. The prevalence of kidney disease on admission and the development of AKI during hospitalization in patients with COVID-19 are high and are associated with in-hospital mortality. Given that the occurrence of AKI in another case series was 57%, it seems that transplant patients are more susceptible for AKI with COVID-19 in comparison with other populations.

This study encountered several limitations, including limited sample size and short-term period of follow-up. Another limitation of our study is the heterogeneity in the approach to change or the dose of CNI in patients. Thus, this is an introductory study for designing research with more homogeneity in implementing guideline of immunosuppression dose reduction. Moreover, we missed some laboratory data (eg, lymphocyte count, lactate dehydrogenase, creatine phosphokinase, arterial blood gas, blood concentration of CNIs) because those were not performed in some patients. This defect, along with the small sample size, results in misinterpretation and the inability to draw conclusion.

In this study, high AKI occurrence and mortality rate in kidney transplant recipients with COVID-19 show the urgent need for discovering treatment drugs and modalities with higher efficacy. Also, further researches might explore the long-term outcome and complications of COVID-19 infection in patients who underwent kidney transplantation.

Returning to the question posed at the beginning of this study, it is now probable to state that kidney transplant recipients may have poor outcomes and prognosis when infected with COVID-19 and require hospitalization and more medical cares.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

AUTHORS’ CONTRIBUTION
Simin Dashti-Khavidaki conceived and designed the presented idea; worked on literature search and helped shape the research
and in interpreting the results; and contributed to the final manu-
script preparation, editing, and review. Ali Monfared helped shape
the research; collected data; aided in interpreting the results; and
contributed to the manuscript preparation, editing, and review.
Ramezan Jafari was involved in interpretation of CT scan of pa-
tients and aided in the final manuscript preparation, editing, and
review. Atefeh Jafari designed and directed the study and was
involved in data collection, data analysis/interpretation, manu-
script preparation, editing, and review and final approval of ar-
ticle. Elham Ramezanzade collected data, discussed the results,
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| TABLE 3 | Changes in kidney function of kidney transplant patients with COVID-19 during hospitalization and after discharge |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Characteristics**             | **Total (22)**                  | **Deaths (6)**                  | **Recovered patients (16)**     | **P-value**                     |
| Baseline SCr (mg/dL)            | 1.15 (0.9-1.72)                 | 1.15 (0.8-1.55)                 | 1.15 (0.9-1.77)                 | .654                            |
| Baseline eGFR (mL/min/1.73 m²)¶  | 60 (44.75-86.75)                | 59.5 (43.75-84.75)              | 63 (44.25-88.25)                | .9                              |
| SCr on admission                | 1.69 (1.1-3.29)                 | 1.61 (1.25-3.07)                | 1.73 (1.1-3.29)                 | .965                            |
| Peak serum creatinine           | 2.19 (1.33-3.67)                | 2.54 (1.74-4.69)                | 1.74 (1.24-3.55)                | .398                            |

Proteinuria; n = 11
- Negative: 4/11 (36.36)
- 1+: 2/11 (18.18)
- 2+ to 3+: 5/11 (45.45)

Hematuria; n = 11
- Negative: 8/11 (72.72)
- 1+: 2/11 (18.18)
- 2+ to 3+: 1/11 (9.09)

Scr at discharge or death: 1.63 (1.06-2.72)

Acute kidney injury<sup>b</sup>: 12/22 (54.54)

AKI Stage
- Stage 1: 3/22 (16.7)
- Stage 2: 4/22 (50)
- Stage 3: 5/22 (22.7)

Scr at follow-up; n = 13: 1.36 (1.07-2.1)

Note: Data are reported as percentages or median (interquartile range) unless otherwise indicated. Unless specified, counts are from the total cohort (N = 22).

Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; SCr, serum creatinine.

<sup>¶</sup>Determined with the CKD Epidemiology Collaboration’s CKD-EPI equation

<sup>b</sup>AKI definition: an increase in serum creatinine by 0.3 mg/dL within 48 h or a 50% increase in serum creatinine from baseline within 7 d. When the AKI was detected, the peak serum creatinine level increase of 1.5 to 1.9, 2.0 to 2.9, and more than or equal with 3 times baseline is defined as AKI stage 1, 2, and 3, respectively.

| TABLE 4 | Electrolyte abnormalities of kidney transplant recipients with COVID-19 who died and recovered |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Abnormality**                 | **Total (22)**                  | **Deaths (6)**                  | **Recovered patients (16)**     | **P-value**                     |
| Hyperkalemia<sup>a</sup>        | 3 (13.6)                        | 3 (50)                          | 0                               | .013                            |
| Hypokalemia<sup>a</sup>         | 5 (22.7)                        | 1 (16.7)                        | 4 (25)                          | 1                               |
| Hyponatremia<sup>b</sup>        | 11 (50)                         | 5 (83.3)                        | 6 (37.5)                        | .149                            |
| Hypernatremia<sup>b</sup>       | 1 (4.5)                         | 1 (16.7)                        | 0                               | .273                            |
| Hypomagnesemia<sup>c</sup><br>n = 21 | 13 (59.1)                      | 3 (50)                          | 10 (62.5)                       | .631                            |

Note: Unless specified, counts are from the total cohort (N = 22)

Values are numbers (percentages).

<sup>a</sup>Hyperkalemia: potassium levels below 3.5 mEq/L or above 5 mEq/L defined as hypokalemia or hyperkalemia, respectively.

<sup>b</sup>Hyponatremia: sodium levels below 135 mEq/L or above 145 mEq/L defined as hyponatremia or hypernatremia, respectively.

<sup>c</sup>Hypomagnesemia: magnesium levels below 1.8 mg/dL defined as hypomagnesemia.
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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

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