Original Article

Is there any link between Hyperphosphatemia, Hypoalbuminemia, and Hypocalcemia with Hospital Outcomes in COVID-19 Patients?

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Abstract

Background: Disturbed biochemical factors have been observed in viral infections including SARS, Ebola virus, and now COVID-19. This study aimed to evaluate the association between Calcium axis' derangements and hospital duration, ICU admission, mechanical ventilation, and death in patients with COVID-19. **Methods:** 428 hospitalized patients with COVID-19 were included in this study. On the first day of admission, the patients were extensively evaluated for biochemical and hormonal factors and followed up until discharge/death. The association between hyperphosphatemia, hypoalbuminemia, and hypocalcemia and major outcomes, including hospital duration, ICU admission, mechanical ventilation, and death, was investigated by logistic regression analysis. **Results:** Hyperphosphatemia and hypoalbuminemia were present in 27 (6.3%) and 59 (13.8%) cases, respectively in the study population. The results of the present study reveal the relation of these factors with worse outcomes in COVID-19 patients; such as hospital duration, ICU admission, mechanical ventilation, and death. On the other hand, high frequency of hypocalcemia (59.1%, 253 subject) has no significant influence on the mentioned outcomes (All *P* values were greater than 0.05). **Conclusions:** Poor outcomes were associated with hyperphosphatemia and hypoalbuminemia. It seems that we should evaluate the patients for derangements of phosphate, albumin, and calcium and try to treat them for all COVID-19 patients.

Keywords: *COVID-19, hyperphosphatemia, hypoalbuminemia, hypocalcemia*

Introduction

Viral infections have been seen to be accompanied by disturbance in various biochemical factors. In Ebola virus disease, hypoalbuminemia, hypokalemia, hyponatremia, hypocalcemia, and hypomagnesemia have been observed.[1] Patients with severe acute respiratory syndrome coronavirus (SARS-CoV) had hypocalcemia, hypokalemia, hypomagnesemia, and hypophosphatemia.[2] The same situation has been reported in COVID-19. Patients with COVID-19 have shown hypoalbuminemia[3,4] and hypocalcemia.[5,6] The relationship between the abnormal levels of these factors and clinical outcomes of the patients is of great interest. Hypoalbuminemia and hypocalcemia have been associated with worse outcomes in patients with COVID-19.[3,6] In the present study, we aimed to evaluate the association between hyperphosphatemia, hypoalbuminemia, and hypocalcemia and poor clinical outcomes and death in patients with COVID-19.

Methods

Setting and participants

This is a cross-sectional study conducted in Khorshid Hospital, Isfahan, Iran. The Hospital was designated for patients with COVID-19 in Isfahan from the beginning of the pandemic. Adult patients with clinical diagnosis of COVID-19 who were hospitalized there between April and July 2020 were included in this study. The study duration was from the time of admission to the hospital until discharge from the hospital or death. Clinically confirmed patients were diagnosed on the basis of the Centers for Disease Control and Prevention (CDC) clinical criteria.[7] The criteria for clinical diagnosis are as follows: (1) cases with radiological manifestations of COVID-19, especially Ground-glass opacity (GGO); or (2) cases with pneumonia who don't respond to treatment and their condition worsens rapidly and unexpectedly. Patients were

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included if they had a positive laboratory test and/or had radiological manifestations attributed to the COVID-19. Patients were excluded if they had any of the following: a history of parathyroid disease, chronic liver dysfunction, chronic kidney disease, malignancy, and recent calcium or vitamin D supplementation. Informed consents were obtained from the patients or their caregiver. The ethical committee of Isfahan University of medical science approved this study. The national ethical code for this study is IR.MUI.MED.REC.1399.085.

Data collection

All data were extracted from patients' records, including demographic data (e.g., age, education, employment, size of the family, housing type, and area); anthropometric measurements (height, weight, body mass index (BMI)); medical history (including comorbidities, surgeries, and immunodeficiency); medication history; COVID-19 exposure history; symptoms and signs (e.g., fever, dry cough, fatigue, shortness of breath, myalgia or arthralgia, sore throat, abdominal pain); vital signs at the time of admission (including blood pressure, pulse rate, respiratory rate, body temperature, O_2 saturation); and chest CT results.

The extracted laboratory data including blood and urine analysis and real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR). For RT-PCR) test, nose and throat swab specimens were collected and assessed upon arrival or within the first 24 hours of the patients' admission. Blood analysis results included complete blood count, C-reactive protein, calcium, phosphorus, albumin, 25(OH) Vit D, PTH, magnesium, blood urea nitrogen (BUN), creatinine, erythrocyte sedimentation rate (ESR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), potassium, sodium, D-dimer, LDH, pH, HCO_3, PCO_2. The phosphate colorimetric assay Kit and bromocresol green albumin assay kit were used to measure phosphate and albumin, respectively. Calcium was measured using Arsenazo III Method. Serum calcium levels were corrected by serum albumin levels using the following formula:

Corrected calcium (mg/dL) = total Ca (mg/dL) + 0.8 (4.0 − serum albumin [g/dL]), where 4.0 represents the average albumin level.

Hyperphosphatemia was defined as serum phosphorous levels higher than 4.51 mg/dL.[8] The serum albumin levels lower than 3.5 g/dL were defined as hypoalbuminemia.[9] Patients were divided into two groups based on their corrected serum calcium levels, hypocalcemia (serum calcium levels below 8.5 mg/dL), and non-hypocalcemia (serum calcium levels ≥8.5 mg/dL).[10]

Outcomes

- Death or recovery and discharge from the hospital: Patients should have all the following criteria to be eligible for discharge: (1) no fever for 72 hours without antipyretic drugs, (2) SPO_2 >93% on room air without supplemental oxygen, and (3) improvement and stability of vital signs according to the attending/responsible physician.
- Hospital duration: the number of days the patients were hospitalized.
- ICU admission: whether the patients needed intensive care and how long they stayed in the ICU.
- Mechanical ventilation: Whether the patients needed mechanical ventilation.

Statistical methods

Statistical analyses were done using SPSS version 25 (SPSS, Inc., Chicago, IL, USA). Descriptive data are presented as mean ± 1SD and number (%), as appropriate. The continuous data were compared between two groups using the independent sample *t*-test and categorical data were compared by Chi-square test. A multiple binary logistic regression analysis was performed to identify potential risk of hyperphosphatemia, hypoalbuminemia, and hypocalcemia in COVID-19-related outcomes. The level of significance was considered less than 0.05.

Results

Baseline characteristics of the patients with COVID-19

Totally, 517 patients with confirmed diagnosis of COVID-19 were hospitalized in Khorshid Hospital between April and July 2020. Eighty-nine were excluded from the study for the following reasons: a history of CKD (n = 66), recent calcium supplementation (n = 13), incomplete records (n = 3), a history of chronic liver disease (n = 3), malignancy (n = 3), and age under 18 years old (n = 1). In total, 428 patients were included in the study. The age (mean ± SD) of the participants was 63.3 ± 16.7 years (range: 18–97), of whom 233 (54.4%) were male [Table 1]. The mean age was higher among those who suffered from worse outcomes, including being admitted to the ICU, needing mechanical ventilation, and dying [Table 2]. Regarding underlying conditions, hypertension had the highest prevalence (43.2%), followed by diabetes mellitus (DM) (28.3%), ischemic heart disease (IHD) (24.5%), chronic obstructive pulmonary disease (COPD) (9.6%), and history of cerebrovascular accident (CVA) (4%) [Table 1]. Further, history of CVA was associated with ICU admission, mechanical ventilation, and death [Table 2]. Cough (67.8%), dyspnea (66.4%), fever (65.4%), and weakness (57.2%) were among the most common symptoms at the time of admission [Table 1]. Of the patients hospitalized for COVID-19, 390 (91%) recovered and 38 (9%) died. Detailed demographic data and clinical features are presented in Table 1.

Laboratory finding

Serum phosphorous

Twenty-seven (6.3%) of patients had hyperphosphatemia, who were older than the patients without

Table l: Baseline demographic and clinical features of the studied population by gender

Characteristics	Total	Groups		*P*
		Male	Female	
Number	428	233	195	-
Age (year)*	63.30±16.75	62.12±16.18	64.67±17.34	0.117
BMI (kg/m^2)*	27.36±5.54	26.33±4.37	28.64±6.54	<0.0001
Positive PCR test†	228 (53.3)	122 (52.4)	106 (54.4)	0.680
Comorbidities				
Hypertension†	185 (43.2)	81 (34.8)	104 (53.6)	<0.0001
DM†	121 (28.3)	49 (21)	72 (37.1)	<0.0001
IHD†	105 (24.5)	45 (19.3)	60 (31.1)	0.005
Signs and symptoms				
Cough†	290 (67.8)	160 (68.7)	130 (66.7)	0.659
Dyspnea†	284 (66.4)	158 (67.8)	126 (64.6)	0.486
Fever†	280 (65.6)	139 (59.9)	141 (72.3)	0.007
Serum parameters				
Calcium (mg/dL)*	8.40±0.76	8.38±0.80	8.43±0.72	0.523
Albumin (g/dL)*	4.03±0.55	4.01±0.59	4.05±0.51	0.564
Phosphorus (mg/dL)*	2.93±1.04	2.90±1.08	2.97±1.00	0.443
PTH (pg/mL)*	73.68±64.79	73.51±64.72	73.89±65.03	0.953
D-dimer (ng/mL)*	2394.47±2119.25	2497.56±2284.68	2266.39±1921.03	0.664
CRP (mg/L)*	48.98±43.83	49.40±45.66	48.49±41.73	0.838
eGFR (mL/min/1.73 m^2)*	63.50±25.22	65.53±26.16	61.07±23.89	0.069
25(OH) VitD (ng/mL)*	30.86±17.65	27.32±14.80	35.07±19.75	<0.0001
Lung involvement				0.859
Bilateral lung†	363 (85.6)	198 (86.5)	165 (84.6)	---
Unilateral lung†	35 (8.3)	18 (7.9)	17 (8.7)	---

Data are presented as mean±SD, number, and number (percent). *P* values calculated using *Independent sample *t*-test, †Chi square test. BMI, body mass index; DM, diabetes mellitus; IHD, ischemic heart disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ICU, intensive care unit; PTH, parathyroid hormone; ALP, alkaline phosphatase; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; AST, aspartate transaminase; ALT, alanine transaminase

hyperphosphatemia (72.37 ± 15.20 vs. 62.70 ± 16.68 years, *P* value = 0.004). The rate of cough, myalgia, and dyspnea was lower in these patients compared to patients without hyperphosphatemia (*p* value < 0.05). Baseline underlying conditions were similar in both groups.

There were significant differences in serum parameters between the patients with or without hyperphosphatemia, including higher levels of creatinine, potassium, LDH, ALT, AST, ALP, BUN, PTH, and D-dimer (*p* value < 0.05), and lower level of estimated glomerular filtration rate (eGFR) (*p* value < 0.0001) in patients with hyperphosphatemia. Serum phosphorous had positive correlations with calcium (r = 0.142, *P* value = 0.004), LDH (r = 0.305, *P* value < 0.0001), BUN (r = 0.490, *P* value < 0.0001), creatinine (r = 0.414, *P* value < 0.0001), ALP (r = 0.130, *P* value = 0.008), ALT (r = 0.298, *P* value < 0.0001), AST (r = 0.272, *P* value < 0.0001), potassium (r = 0.296, *P* value < 0.0001), and D-dimer (r = 0.297, *P* value = 0.011).

The serum phosphorous was higher in patients who had worse outcomes. Hyperphosphatemia was significantly associated with a higher ICU admission, mechanical ventilation, and mortality. However, the hospital stay duration and ICU stay duration were not significantly different between the patients with or without hyperphosphatemia [Table 3]. Also, hyperphosphatemia significantly increased the risk of worse outcomes in both univariable and multivariable models [Table 4].

Serum albumin

In total, 59 (13.8%) of the patients with COVID-19 had hypoalbuminemia. The mean age of these patients (71.25 ± 14.34 years) was greater than that of patients without hypoalbuminemia (61.89 ± 16.73 years) (*p* value < 0.0001). The rate of cough, myalgia, and headache was lower in these patients compared to patients without hypoalbuminemia (*p* value < 0.05). There was no significant association between serum albumin level and baseline comorbidities. Serum creatinine, CRP, ESR, ALP, ALT, BUN, and D-dimer were significantly higher in patients with hypoalbuminemia (*p* value < 0.05). Serum albumin levels were also negatively correlated with creatinine (r = −0.245, *P* value < 0.0001), CRP (r = −0.312, *P* value < 0.0001), ESR (r = −0.132, *P* value = 0.007), Potassium (r = −0.195, *P* value < 0.0001), ALP (r = −0.143,

Table 2: Clinical and laboratory features of the studied population by outcomes

	ICU			Mechanical ventilation			Death		
	Yes	No	*P*	Yes	No	*P*	Yes	No	*P*
Age (year)*	68.34±15.97	62.08±16.73	0.002	70.40±16.17	62.25±16.66	0.001	72.84±15.18	62.35±16.62	<0.0001
BMI (kg/m^2)*	27.34±6.63	27.36±5.26	0.984	27.21±6.74	27.30±5.25	0.934	26.25±6.19	27.45±5.49	0.331
Hypertension †	34 (42)	151 (43.6)	0.785	22 (43.1)	162 (43.4)	0.968	16 (43.2)	169 (43.3)	0.992
DM†	18 (22)	103 (29.9)	0.153	15 (28.8)	104 (28)	0.894	14 (36.8)	107 (27.5)	0.223
IHD†	22 (26.8)	83 (24.1)	0.610	16 (30.8)	88 (23.7)	0.269	12 (31.6)	93 (24)	0.299
COPD†	10 (12.2)	31 (9)	0.375	4 (7.7)	36 (9.7)	0.646	4 (10.5)	37 (9.5)	0.839
CVA†	7 (8.5)	10 (2.9)	0.019	6 (11.5%)	11 (3)	0.003	6 (15.8)	11 (2.8)	<0.0001
Calcium (mg/dL)*	8.46±0.97	8.38±0.71	0.415	8.46±1.06	8.39±0.72	0.565	8.55±1.14	8.38±0.71	0.203
Albumin (g/dL)*	3.78±0.66	4.09±0.51	<0.0001	3.68±0.66	4.08±0.52	<0.0001	3.60±0.70	4.07±0.52	<0.0001
Phosphorus (mg/dL)*	3.40±1.62	2.82±0.82	<0.0001	3.44±1.74	2.85±0.88	<0.0001	3.65±1.71	2.86±0.93	<0.0001
Magnesium (mg/dL)*	2.01±0.31	1.93±0.29	0.027	2.04±031	1.94±0.29	0.019	2.02±0.31	1.94±0.29	0.101
PTH (pg/mL)*	105.13±92.06	66.36±54.20	<0.0001	94.24±66.75	70.77±64.28	0.016	93.06±71.29	71.86±63.94	0.060
D-dimer (ng/mL)*	3408.38±2643.18	1965.51±1709.03	0.007	3911.27±2920.91	2008.85±1687.33	0.001	3716.51±3538.02	2277.82±19.46.52	0.111
ALP (U/L)*	205.57±153.31	189.26±104.83	0.253	221.92±184.72	188.71±102.52	0.053	237.21±210.66	188.00±101.19	0.012
CRP (mg/L)*	60.67±45.23	46.24±43.11	0.010	62.26±45.93	47.37±43.32	0.026	60.87±40.50	47.82±44.02	0.093
Creatinine (mg/dL)*	1.75±1.94	1.25±0.83	<0.0001	1.79±1.47	1.29±1.08	0.003	1.94±1.63	1.29±1.07	0.001
eGFR (mL/min/1.73 m^2)*	56.28±27.48	65.21±24.39	0.004	51.19±25.47	65.04±24.74	<0.0001	48.84±26.22	64.93±24.70	<0.0001
AST (U/L)*	134.42±591.75	43.39±37.23	0.005	74.65±119.48	59.37±278.60	0.697	52.28±31.20	61.80±275.73	0.832
ALT (U/L)*	114.70±414.89	41.46±70.32	0.002	59.62±133.32	55.22±201.07	0.880	35.64±25.59	57.34±202.15	0.515
25(OH) VitD (ng/mL)*	31.68±19.06	30.67±17.33	0.646	31.68±20.54	30.67±17.29	0.703	29.85±17.69	30.96±17.66	0.715

Data are presented as mean±SD, number (%). *P* values calculated using *independent sample *t*-test, †Chi square test. BMI, body mass index; DM, diabetes mellitus; IHD, ischemic heart disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ICU, intensive care unit; MV, mechanical ventilation ; PTH, parathyroid hormone; ALP, alkaline phosphatase; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; AST, aspartate transaminase; ALT, alanine transaminase

Table 3: Observed outcomes of the studied population by hypocalcemia, hyperphosphatemia, and hypoalbuminemia

Outcome	HypoCa	non-HypoCa	*P*	HyperP	non-HyperP	*P*	HypoAlb	Non-HypoAlb	*P*
ICU admission†	52 (20)	30 (17)	0.425	15 (55.6)	65 (16.4)	<0.0001	25 (42.4)	57 (15.6)	<0.0001
Mechanical ventilation†	33 (13)	19 (11)	0.532	10 (38.5)	40 (10.2)	<0.0001	18 (30.5)	34 (9.4)	<0.0001
Death†	23 (9)	15 (8)	0.895	10 (37)	27 (6.8)	<0.0001	15 (25.4)	23 (6.3)	0.001
Hospital duration (days)*	7.448±8.12	6.564±6.07	0.225	7.25±8.47	7.06±7.32	0.896	8.91±7.97	6.79±7.23	0.040
ICU duration (days)*	7.94±8.65	7.17±5.53	0.664	4.36±3.62	8.45±8.06	0.068	7.47±5.98	7.74±8.17	0.080

Data are presented as mean±SD, number (%). *P* values calculated using *independent sample *t*-test, †Chi square test. HypoCa, hypocalcemia; HyperP, hyperphosphatemia; HypoAlb, hypoalbuminemia.

Table 4: Univariate and multivariate association of Hyperphosphatemia and Hypocalcaemia with outcomes (death, MV, and ICU admission)

Characteristics	Outcome					
	ICU admission		Mechanical Ventilation		Death	
	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate
Hyperphosphatemia	6.133 (2.745-13.704); <0.0001	6.244 (2.275-17.133); <0.0001	5.516 (2.346-12.970); <0.0001	4.495 (1.519-13.296); 0.007	8.017 (3.348-19.202); <0.0001	6.298 (2.095-18.935); 0.001
Hypoalbuminemia	3.264 (1.778-5.990); <0.0001	2.362 (1.158-4.818); 0.018	4.248 (2.202-8.196); <0.0001	2.732 (1.285-5.809); 0.009	5.084 (2.469-10.468); <0.0001	3.265 (1.438-7.411); 0.005
Hypocalcaemia	1.412 (0.834-2.391); 0.199	1.533 (0.846-2.778); 0.159	1.211 (0.664-2.209); 0.533	1.399 (0.720-2.717); 0.322	1.047 (0.530-2.069); 0.896	1.145 (0.545-2.405); 0.721

Data presented as OR (CI 95%); *P* value. Multivariate analyses adjusted for severity factors at admission, including O2Sat, CRP, eGFR, and Lymphopenia

P value = 0.003), ALT ($r = -0.123$, *P* value = 0.011), BUN ($r = -0.307$, *P* value < 0.0001), ferritin ($r = -0.307$, *P* value = 0.006), PTH ($r = -0.125$, *P* value = 0.011), and D-dimer ($r = -0.284$, *P* value = 0.014).

The serum albumin was lower in patients with worse outcomes. Further, patients with hypoalbuminemia had a higher risk of ICU admission, mechanical ventilation, and death. The hospital stay was longer in patients with hypoalbuminemia (8.91 ± 7.97 days) than it was in patients without hypoalbuminemia (6.79 ± 7.23 days) (*p* value = 0.04) [Table 3].

Serum calcium

Regarding the calcium axis, 253 (59%) had hypocalcemia on admission, who were older than patients without hypocalcemia (65.26 ± 16.59 vs. 61.79 ± 16.70 years, *P* value = 0.035). Patients with DM were less likely to have hypocalcemia (*p* value = 0.005). However, patients with or without hypocalcemia did not differ in other baseline underlying conditions (hypertension, CVA, COPD). Moreover, these two groups were not different in gender, COVID-19 signs and symptoms, CT findings, and BMI. Serum PTH level was significantly higher in patients with hypocalcemia (79.59 ± 72.60 vs. 65.33 ± 51.06, *P* value = 0.028). Serum calcium was negatively correlated with PTH ($r = -0.103$, *P* value = 0.035). eGFR was higher (*p* value = 0.027) and phosphorous was lower (*p* value = 0.041) in the group with hypocalcemia. Other laboratory parameters did not have any significant difference between these two groups.

Serum calcium at the time of admission was not different in patients with and without worse outcomes [Table 2]. Furthermore, the presence of hypocalcemia at the time of admission was not associated with increased ICU admission, mechanical ventilation, death incidence, and hospital and ICU duration [Table 3]. Also, the risk of these worse outcomes was not increased in hypocalcemia in univariate and multivariate analysis [Table 4]. However, when hypocalcemia was defined by total calcium, there was a significant association between total hypocalcemia and worse outcomes.

Discussion

This study is one of the few studies exploring the association of clinical outcomes including hospital duration, ICU admission, needing mechanical ventilation, and death in patients with COVID-19 with hyperphosphatemia, hypoalbuminemia,[11,12] and hypocalcemia.[5,6,13]

We observed that hyperphosphatemia and hypoalbuminemia were significantly associated with death and other poor outcomes. One explanation could be renal insufficiency or sepsis. A study by Uribarri *et al*. showed that renal failure on admission is prevalent in patients with COVID-19 and associates with a higher mortality rate.[14] Although we excluded patients who had a known history of renal disease

from the study, we observed that the mean phosphorus and creatinine were higher and eGFR and albumin were lower in the patients who had worse outcomes.

To explore whether hyperphosphatemia is an independent factor in worse outcomes, or it is related to other underlying complications, such as renal insufficiency or sepsis, we adjusted lymphopenia, elevated CRP, low O_2 saturation, and low eGFR by univariate and multivariate analysis. The results showed that even after eliminating the confounding factors, hyperphosphatemia remained as an independent factor for ICU admission, mechanical ventilation, and death.

In our study, albumin had a negative correlation with inflammatory indicators, including CRP, ESR, LDH, and D-dimer. Other studies have had similar observations.[3,12] As the severity of inflammation is a known risk factor of mortality and morbidity in COVID-19, these findings can explain the correlation between hypoalbuminemia and poor outcomes in our study and others' studies. We observed an association between lower serum albumin levels and more incidences of ICU admissions, needing mechanical ventilation, and death. Similarly, other studies have reported the same results.[11,12]

Our study showed that hypocalcemia is considerably prevalent in patients with COVID-19, and 59% of them had hypocalcemia at the time of admission. Other studies have shown similar results. Liu *et al*.[6] and Di Filippo *et al*. reported that, respectively, 62.6% and 74.7% of their patients with COVID-19 had hypocalcemia.[5] Moreover, hypocalcemia has previously been reported in other viral infections such as SARS and Ebola.[1,2] Various mechanisms could be suggested for the high prevalence of hypocalcemia including vitamin D deficiency, a decline in serum albumin, functional hypoparathyroidism, hypomagnesemia, nutritional insufficiency, and hyperphosphatemia.[15] None of these can explain the high prevalence of hypocalcemia in our study. In our study, hypocalcemia did not have a significant association with major outcomes like hospital duration, ICU admission, mechanical ventilation, and death. This unexpected observation may be due to an early treatment of the hypocalcemic patients, as all of them were treated by the supplemental calcium and vitamin D. Our results were inconsistent with other studies. Sun *et al*.[13] found that lower serum calcium values were associated with higher mortality rates and needing mechanical ventilation. Further, Liu *et al*.[6] reported that patients with hypocalcemia had more incidence of poor outcomes. This inconsistency can be due to small differences between our studies. Sun *et al*. had performed their analysis based on total calcium, while our results are based on corrected calcium (corrected with albumin). Similar to Sun *et al*., when we used total hypocalcemia, we observed a significant association between this hypocalcemia and worse outcomes. Another difference between our studies was that Liu *et al*.[6] had only included severe COVID-19 patients, while our study population consisted of both mild and severe cases. Di Filippo *et al*.[5] reported that hypocalcemia increased the odds of death and ICU admission. However, according to our multivariate regression model, hypocalcemia did not increase the odds of death significantly.

Limitations

One of the limitations of our study is that it was performed in a single center. However, Khorshid Hospital was the referring center for COVID-19 patients, and patients from all around the city and adjacent towns were referred to it. Another limitation was that not all the included patients have a positive PCR test for COVID-19. Patients with a negative PCR but COVID-19-related lung involvement were also included. A considerable part of patients with COVID-19 consists of clinically confirmed cases.

Conclusions

At the time of admission to the hospital, hyperphosphatemia, hypoalbuminemia, and hypocalcemia were prevalent in hospitalized patients with COVID-19. Poor outcomes were associated with hyperphosphatemia, hypoalbuminemia, and possibly hypocalcemia. It seems that we should evaluate the patients for derangements of calcium axis and try to treat them.

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Other forms of presentation

This work has been presented as a poster presentation at the virtual national conference on COVID-19 researches at Isfahan University of Medical Sciences on December 15, 2020.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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