



Contributing Factors for Calcium Changes During Hospitalization in COVID-19: A Longitudinal Study

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Abstract

Background: Hypocalcemia is highly prevalent in Coronavirus disease 2019 (COVID-19). There is limited evidence about the course and roles of different parameters in the occurrence of new or worsening hypocalcemia.

Objectives: This prospective longitudinal study was conducted on hospitalized COVID-19 patients in Qazvin, Iran, in 2021.

Methods: Serum levels of calcium, albumin, parathormone (PTH), 25(OH)D (vitamin D), magnesium, and phosphate were assessed on the first day (time one), as well as fourth to sixth days (time two) of hospitalization. Paired t-test, McNemar's test, and multivariate logistic regression test were used to compare data at two times and evaluating the independent roles of different variables in the occurrence or worsening of hypocalcemia.

Results: Out of a total of 123 participants, 102 patients completed the study. The mean serum calcium level significantly decreased from 8.32 ± 0.52 mg/dL to 8.02 ± 0.55 mg/dL at time two compared to time one ($P < 0.001$). Also, we witnessed new or worsening hypocalcemia at time two in 44 (55%) patients with normal serum calcium or mild hypocalcemia at time one ($P < 0.001$). The PTH level decreased from 42.17 ± 27.20 pg/mL to 31.28 ± 23.42 pg/mL ($P < 0.001$). The decrease in albumin and PTH levels was an independent significant factor in the occurrence or worsening of hypocalcemia at time two (OR = 1.27; 95% CI: 1.10 - 1.46; $P = 0.001$ for each 1 g/L decrement albumin and OR = 1.29; 95% CI: 1.03 - 1.62; $P = 0.026$ for each 10 pg/mL decrement PTH). Vitamin D deficiency or changes during hospitalization did not have a significant role in new or worsening hypocalcemia.

Conclusions: Decreased PTH secretion and hypoalbuminemia have significant roles in the occurrence of new or worsening hypocalcemia during hospitalization due to COVID-19.

Keywords: Hypocalcemia, COVID-19, Parathormone, Vitamin D

1. Background

Hypocalcemia of critical illnesses has been introduced since decades ago (1, 2). Association of this disorder with severe infectious disease, especially septicemia, is stronger than in other critical situations (3, 4).

Since the epidemic of coronavirus disease 2019 (COVID-19), many studies have reported high prevalence of hypocalcemia in this disease (5-7). The reported prevalence of hypocalcemia in the hospitalized COVID-19 patients varies from about 60% to 80% in different studies (8-10). Higher degrees of inflammation have been reported in more severe hypocalcemic patients (9). Moreover, in a meta-analysis, Martha et al. showed the association between poor prognosis and mortality of COVID-19 with hypocalcemia (11).

Several mechanisms have been mentioned as the involving factors in the hypocalcemia of critical illnesses. Hypoalbuminemia (12), functional hypoparathyroidism due to suppressive effects of inflammatory markers or hypomagnesemia (13), resistance to parathyroid hormone (PTH) (14), decreased vitamin D level due to redistribution and renal wasting (15), and calcium precipitation by high levels of free fatty acids (16) have been mentioned as the main causes of hypocalcemia in these situations.

Hypocalcemia of COVID-19 may be somehow different from that of other critical illnesses. Based on limited studies, the prevalence of hypocalcemia in COVID-19 is possibly higher than other critical illnesses (7) and is even reported in about two-thirds of non-severe cases (17).

Despite the high prevalence, impact on mortality, and possible differences with usual hypocalcemia of critical ill-