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An exploratory study of selenium status in healthy individuals and in patients with COVID-19 in a south Indian population: The case for adequate selenium status

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ABSTRACT

The acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic has affected millions of individuals, causing major health and economic disruptions worldwide. The pandemic is still raging, with a second and third wave in a few countries, while new infections steadily rise in India. Nutrition and immune status are two critical aspects of fighting the virus successfully. Recently, selenium status was reported to positively correlate with the survival of patients with COVID-19 compared with non-survivors. We analyzed the blood serum levels in 30 apparently healthy individuals and in 30 patients with confirmed COVID-19 infection in the southern part of India. The patients showed significantly lower selenium levels of 69.2 ± 8.7 ng/mL than controls 79.1 ± 10.9 ng/mL. The difference was statistically significant (P = 0.0003). Interestingly, the control group showed a borderline level of selenium, suggesting that the level of this micronutrient is not optimum in the population studied. The results of this exploratory study pave the way for further research in a larger population and suggest that selenium supplementation may be helpful in reducing the effects of the virus.

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection (COVID-19) pandemic has led to devastating effects on the health and economy worldwide. Age and presence of comorbidities such as obesity, diabetes, cardiovascular diseases, hypertension, and pulmonary diseases are associated with disease severity [1]. More than 80% of the cases are reported to be mild, whereas the rest are associated with severe pulmonary distress, shock, myocardial injury, heart failure, dysfunctional coagulation, and renal failure. The severity of the disease is associated with an overreaction of the immune system, leading to a release of several cytokines and chemokines, also known as cytokine storm [2].

There is no specific therapeutic drug recommended for the treatment of COVID-19. Anti-flu drugs and corticosteroids are being used in clinical settings. Other therapeutic strategies include convalescent sera from recovered individuals, interferon, anti-inflammatory therapies, and ventilator support. The search for vaccines and other pharmacologic agents to prevent viral infection is underway to fight the pandemic.

Selenium is an essential trace element incorporated into 25 selenoproteins having selenocysteine in their active center. Some of these selenoproteins are essential for defense against viral infections, control of thyroid hormone signaling, protection against oxidative stress, protein folding, and mitochondrial health [3]. Glutathione peroxidases and thioredoxin reductase are selenoproteins critical for antiviral defense through their redox signaling and homeostatic activities [3]. Viral infection causes oxidative stress, enhancing the replication and accumulation of mutations in the viral RNA genome, leading to increased virulence and damage to host [4].

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Selenium deficiency contributes to mutations in the viral genome to highly virulent forms, and is associated with increased susceptibility and pathogenicity of viral infections, which can be alleviated by adequate levels [4]. Selenoproteins are essential for an effective immune response to infections. Selenium supplementation has been reported to reduce allergic asthma, augment vaccine responses, and reduce the progression of tuberculosis or HIV-1 [5]. India is now reporting increased incidences of COVID-19 infection. To our knowledge, there are very few reports on the average serum selenium levels in Indians. Interestingly, an association was reported between the cure rate from COVID-19 and the basal selenium status in different regions of China [6]. Strengthening this observation, a deficiency of elemental selenium, and its transporter protein levels were reported in patients with COVID-19 in Germany [7]. Based on these reports, in the present exploratory study, we assessed the serum

Table 1
Summary statistics of participant demographics*

Parameter	Controls (n = 30)	COVID-19 patients (n = 30)	*P*-value
Age (y)*	33.5 (26–37)	40.5 (37.5–43)	<0.001
Sex, n (%)			
Male	14 (46.7)	24 (80)	<0.001
Female	16 (53.3)	6 (20)	
BMI (kg/m^2)	25.4 ± 2.6	24.5 ± 2.5	NS
SBP (mm Hg)	121.9 ± 6.4	123.3 ± 7.9	NS
DBP (mm Hg)	77.9 ± 5.2	76. 7 ± 7.5	NS
SpO_2 (%)	96.9 ± 1.6	91.9 ± 1.1	<0.0001
Pulse rate (BPM)	81.4 ± 4.5	84.5 ± 4.5	<0.01

BMI, body mass index; BPM, beats per minute; DBP, diastolic blood pressure; NS, non-significant; SBP, systolic blood pressure; SpO_2, oxygen saturation
*Age represented as median (IQR); sex represented as n (%). All other data represented as mean ± SD.

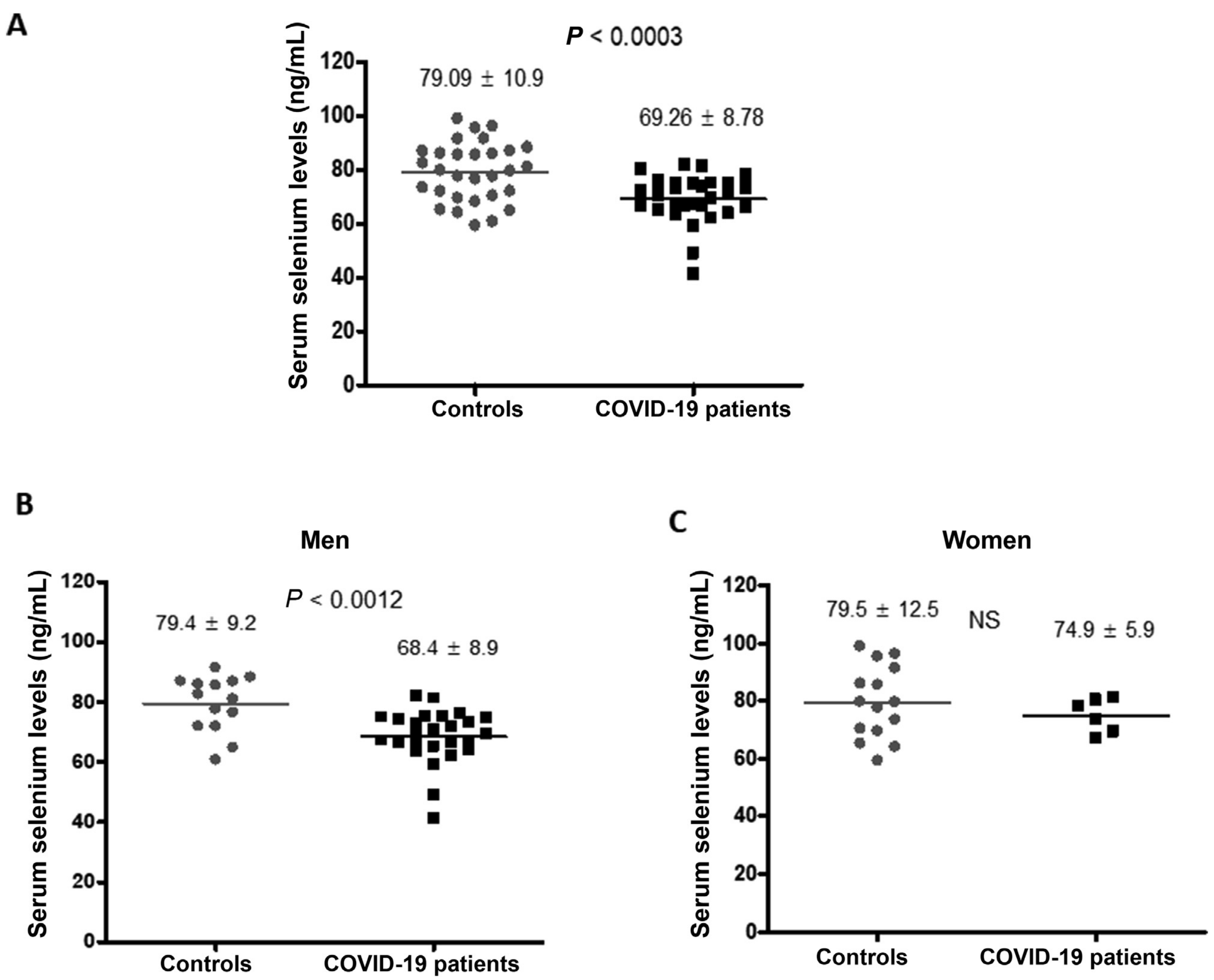

Fig. 1. Selenium levels in controls and COVID-19 patients. (**A**) Distribution of selenium levels in controls and COVID-19 patients. (**B**) Selenium levels in men. (**C**) Selenium levels in women.

selenium levels in patients with COVID-19 and control individuals to understand the correlation between these levels and viral infection and recovery.

Methods

The study was conducted with 30 COVID-19–positive individuals and 30 apparently healthy controls in the 18 to 45 y age group. Controls did not present with signs or symptoms of viral/bacterial infection, had body temperature between 96°F to 99°F, and had >90% oxygen saturation. SARS-CoV-2 infection in patients was confirmed by the nasopharyngeal swab reverse transcription polymerase chain reaction test. The patients were in stable condition with fever and dyspnea without hypoxemia. Asymptomatic patients, those requiring tube feeding or parenteral nutrition, patients on ventilator support or in unstable condition, and those admitted to the isolation ward for >24 h of confirmed COVID-19–positive test were excluded from the study. Individuals participating in any other study, including any form of dietary supplements/multivitamins or disease-specific oral nutrition supplements, also were excluded from the study. Informed consent was given by all participants. The study was conducted in accordance with the regulatory requirements as per ICMR Guidelines 2017, and the Declaration of Helsinki, Fortaleza, 2013 & the ICH (Step V), Guidance on Good Clinical Practice and applicable regulatory requirements. This clinical trial was registered prospectively with Clinical Trials Registry– India.

Blood samples and 24-h urine samples were collected from all participants. Selenium status was analyzed by quantitative inductively coupled plasma-mass spectrometry (ICP-MS). All necessary precautions were taken in handling the specimens collected as per standard laboratory guidelines considering COVID-19 complications.

Statistical analysis was performed for all participants with STATA version 15 (StataCorp, College Station, TX, USA). Descriptive statistics are presented for continuous variables, whereas categorical variables are described as their respective percentages. The difference in serum selenium levels between the groups was analyzed using the Welch *t* test. A statistical significance of $P < 0.05$ was considered significant.

Results

The demographic data of the participants are presented in Table 1. The median age was 40.5 y (26–37) in patients with COVID-19 and 33.5 y (37.5–43; $P < 0.001$) in the control group. The male-to-female ratio was 24:6 and 14:16 in patient and control groups, respectively. Oxygen saturation (SpO_2) was significantly lower in patients (91.9 ± 1.15) than in controls (96.9 ± 1.6; $P < 0.0001$). SpO_2 was <95% in all patients, whereas 28 of the 30 control participants had ≥95%. Two control individuals had a saturation of 94%.

The mean serum selenium levels are represented in Figure 1. The mean levels were 69.3 ± 8.8 ng/mL in the patients and was 79.1 ± 10.9 ng/mL in the control group. The difference of 9.8 ng/mL was highly significant ($P < 0.0003$; Fig. 1). The difference in selenium levels showed a similar trend in men (79.4 ± 9.2 versus 68.4 ± 8.2 ng/mL, $P < 0.001$ in the control and COVID-19 groups, respectively). In women, although the levels were lower in the patient group, the difference was not significant (79.4 ± 12.5 versus 74.9 ± 5.9 ng/mL). We observed that 43.3% of patients with

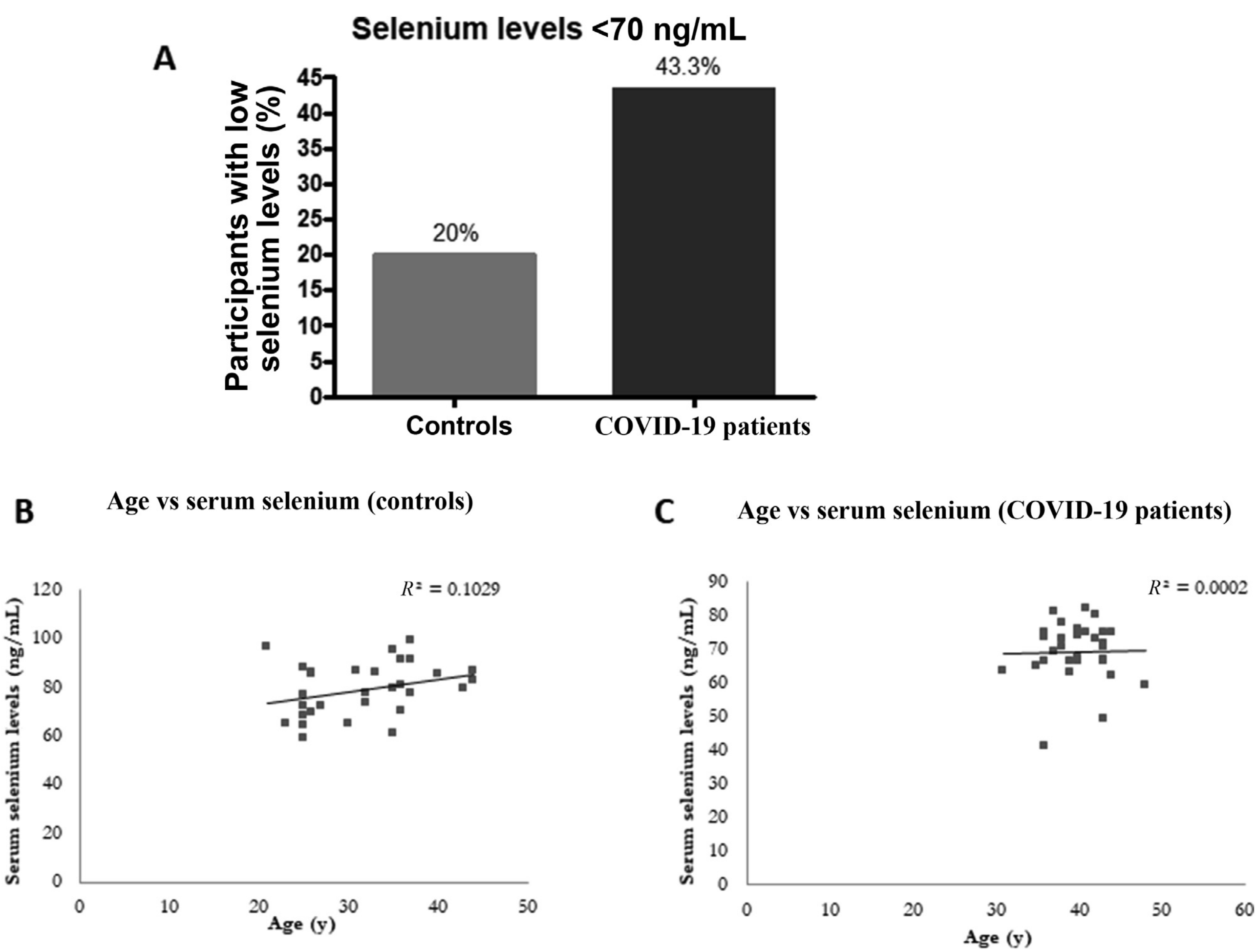

Fig. 2. (**A**) Percentage of participants with <70 ng/mL of serum selenium levels in control and COVID-19 patient groups. Correlation of age with serum selenium levels in (**B**) controls and (**C**) patients with COVID-19.

COVID-19 had lower selenium levels compared with 20% of the control group (Fig. 2A). Because the age of controls and patients were not matched in the two groups, we performed a correlation analysis of age and serum selenium levels. The R^2 values were 0.103 for controls and 0.002 for patients (P = not significant for both) suggesting that the difference in age may not have contributed to the difference in serum selenium levels (Fig. 2B and C).

Discussion

Selenium status varies widely in different parts of the world. Although the normal range in the blood is fixed at 70 to 150 ng/mL, a minimum level of 98.7 ng/mL of serum selenium was required to optimize glutathione peroxidase activity based on 48 European studies and 44 in the Middle East [8,9]. Furthermore, in the National Nutrition Examination Survey, serum selenium levels (1.51 μmol/L or 118.8 ng/mL) was independently associated with anemia in older adults [10]. In the Nutritional Prevention of Cancer (NPI), serum selenium concentrations at 1.34 to 1.54 μmol/l (106−121 ng/mL) showed a protective effect against cancer in clinical studies [11−13].

Serum selenium concentrations <70 ng/mL are correlated with limiting supplies of the micronutrient as per the Food and Nutrition Board of the Institute of Medicine [14]. We observed that the mean levels in control individuals were only 79.1 ± 10.9 ng/mL, which is much lower than the optimum required levels, suggesting a general deficiency of this micronutrient in the population studied. Urine samples did not show detectable values of selenium.

Nutrition and diet influence the competence of the immune system and influence the risk for and severity of an infection [15]. Micronutrients such as iron, selenium, and zinc provide antioxidant and anti-inflammatory support and are essential for optimal functioning of the immune system [16]. The nutritional status of an individual is associated with the risk for, severity, and outcome of SARS-CoV-2 infection, thus stressing the importance of maintaining macro- and micronutrient status as a preventive measure for COVID-19 [17].

Selenium deficiency is reported to affect 500 million to 1 billion people worldwide, mainly due to inadequate dietary intake. Dietary selenium availability, in turn, is controlled by soil−plant interactions. Loss of selenium-rich soil has reduced the dietary availability of this micronutrient, thus increasing the deficiency of selenium worldwide [18]. India is a vast country with wide geographic soil status. In one study, the northern part of India was reported to have normal levels of soil selenium [19]. Similar data is not available for southern part of the country, where the present study was conducted. One study with 201 adults in Mumbai, reported an average concentration of 100 ng/mL [20]. In contrast, the present results show a borderline low level in the control individuals, suggesting that selenium deficiency may be more widespread than reported.

Conclusion

This exploratory study demonstrates that selenium status is lower in patients with COVID-19 than in healthy controls, in corroboration with two recently published studies. In the present study, relatively young patients with mild symptoms with slight hypoxia were analyzed, unlike in the German study, wherein patients were older and had severe symptoms. The observational nature of the study precluded any conclusion on the casual relationship between selenium status and COVID-19. Future studies in a larger population would be valuable. Improving the selenium status by nutritional measures or supplementation may be helpful in reducing the devastation caused by this virus in India.

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