



ORIGINAL ARTICLE

A Hospital-based Electronic Information Approach: Analyzing the association between nCOVID-19 and 25-(OH)-D

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Abstract:

Background: nCOVID-19 is portrayed by obvious fluctuations in terms of symptomatic severity. Recently, 25-(OH)-D has been suggested as a potential factor in determining nCOVID-19 severity. This survey aimed to study the relationship between serum level of 25-hydroxyvitamin-D (25-(OH)-D) and nCOVID-19 severity. **Methodology:** A hospital-based electronic information approach was utilized at Najran Hospitals for ten months. Participants were nCOVID-19 diagnosed patients. Subjects' demographic characteristics and clinical outcomes were obtained from the hospitals' electronic records. **Results:** 134 subjects' electronic data were obtained and used in the current survey. The mean age of the sample was 41.6 ± 13.9 ; among them, 71(53%) were males. 91(67.9%) of the studied subjects were either asymptomatic or had mild symptoms that refer to the group (1). At the same time, 43(32.1%) were nCOVID-19 severely ill cases and had been admitted to ICUs who were group (2). Prevalence of serum 25-(OH)-D Deficiency, Insufficiently, and Adequate according to gender (females vs. males) was (32% vs. 16%), (42% vs. 22%) and (25% vs. 62%) respectively. A statistically significant difference was observed in gender and mean age regarding nCOVID-19 severity. Moreover, a significant difference was noticed between the mean \pm SD of serum 25-[OH]-D levels among the two groups were 38.66 ± 12.9 vs. 32.09 ± 9.57) in favor of group 1. **Conclusion:** Our findings revealed that sera 25-(OH)-D is potentially correlated with the severity of the nCOVID-19 pandemic.

Keywords: nCOVID-19; ICU patients; level of 25-(OH)-D

BACKGROUND

Since December 2020, news and social media have announced a new variant of coronavirus which causes nCOVID-19, and since then, other variants have been reported, and some are under investigation^{1,2}.

nCOVID-19 pandemic continues to have negative effects on people's lives. Recently, heavily mutated versions of coronavirus were emerging globally^{3,4,5}. Accordingly, scientists keep trying to find effective methods for controlling this disease.

nCOVID-19 pandemic is portrayed by marked fluctuation in terms of clinical severity. Patients may face various clinical manifestations that range from no symptoms to critical illness or even death. Internationally COVID-19 mortality rate is estimated to be around 3%^{6,7,8}.

The determination of the nCOVID-19 pandemic's severity depends on pneumonia, respiratory distress syndrome, venous thrombosis, and/or other physiological disorders^{9,10}.

It has been documented that many factors may enhance the severity of COVID-19; among these factors is vitamin D deficiency. It has been noticed that the most nCOVID-19 related deaths occur in countries where vitamin D is deficit^{11,12}.

Deficiency in vitamin-D in humans has been defined as sera 25-[OH]-D is below 20ng/ml (less than 50mmol/L.)^{13,14}

Individuals who are most susceptible to developing acute episodes of nCOVID-19 infection need more protection by strengthening their immune system. The main defense mechanism against inflammation and infections, in general, is provided by T-regulatory lymphocytes (T-

regs) that had been reported to be elevated by 25-(OH)-D supplementation^{15,16}. Multiple studies documented that vitamin D has protection properties against pathogens by enhancing adaptive and innate immunity, improving human immunity^{17,18}.

Some scientists emphasized the vital role of 25-(OH)-D in maintaining the skeleton and calcium-phosphorus metabolic process, and thus it has additional skeletal activities that have recently been hypothesized. For instance, it modulates the immune response; besides, it has anti-inflammatory properties for both infectious and autoimmune diseases that may help humans recover from serious COVID-19-related complications. Numerous researchers have concluded that deficiency in 25-(OH)-D is considered one of the elements associated with an elevation of inflammatory cytokines, increasing the possibility of developing viral respiratory tract infections (VRTI) and increasing the thrombotic episodes which had been detected in COVID-19 cases^{19,20,21}.

Scientists highlight the effectiveness of vitamin D on human immunity; they believe that a sufficient level of 25-(OH)-D will enhance and promote human immunity and, therefore, protect from serious diseases and/or help reduce serious complications such as COVID-19's complications²².

These facts raised our interest regarding the potential of 25-(OH)-D. Therefore, this survey was conveyed to study the 25-(OH)-D deficiency role in enhancing nCOVID-19 severity among patients by utilizing the hospitals' electronic records approach.

The serum level of the circulating 25-(OH)D is considered the best indicator for determining the status of 25-(OH)-D, which reflects the level of 25-(OH)-D that comes from the synthesis in the human skin and/or dietary intake²³.

METHODOLOGY

For eight months, a hospital-based electronic approach study and a purposive sampling technique were adopted to extract 134 patients' information at King Khalid and Najran East hospitals in Najran city.

Ethical approval was obtained from Najran University Deanship of Research and hospitals' management boards.

According to the existing electronic data, cases' had been categorized into two groups as follows:

Group(1): Those cases with PCR-positive test for nCOVID-19 and who were symptoms free and therefore had been treated as out-patients.

Group(2): Those were seriously ill cases with PCR-positive tests for nCOVID-19 and accordingly had been admitted into ICUs based on the hospitals' criteria for ICU admissions.

Collecting data process

Data about the participants' demographics, clinical features, and outcome of nCOVID-19 were obtained from hospitals' computerized database records.

Results of 25-(OH)-D levels had been categorized according to standard measures that the USA institute approved of medicine²⁴, as follows:

≥ 30 ng/ml is considered an adequate value
 $< 30 - 20$ ng/ml is labeled as Insufficiency and deficiency is below 20 ng/ml.

Statistical Analysis

For statistical analysis, IBM- SPSS-Inc. Version 24- Chicago, IL had been utilized. Sera levels of 25(OH)D had been presented as continuous variables.

Quantitative data had been presented as mean \pm SD. At the same time, numbers and percentages were used for categorical variables and then compared using Chi-Square Test and/or Fisher Exact Test as appropriate. Moreover, Multivariate and Univariate Binary Logistic Regression Analysis too had been used to study the relationship between the status of 25-(OH)-D and the Dependent Variable of nCOVID-19 disease severity.

RESULTS

An electronically generated information of 134 COVID-19 confirmed PCR cases was utilized in the current study, 71 males and 63 females (53% vs. 47%), respectively. Participants' mean age was 41.6 ± 13.9 years. In terms of disease severity, 91 (67.9%) were asymptomatic and accordingly treated as out-patients (group 1), whereas 43(32.1%) were severely ill and had been hospitalized in ICUs (group 2). Among cases who had been admitted to ICUs, their mean age and gender ratio was skewed towards males. Regarding nationalities, most of them (55.2%) were non-Saudi, respectively. Among the two groups, a significant difference was noticed concerning the mean level of 25(OH)-D, which was 38.66 ± 12.9 in the group (1), whereas in the group (2) was 32.09 ± 9.57 . Moreover, a statistically significant difference was observed too in terms of gender and mean age concerning COVID-19 status (P-value < 0.05) (Table1).

Moreover, Table 2 displays the adjusted odds ratios for males and females based on

multivariate analysis with 95% confidence intervals for each, which shows a significant difference between 25(OH) vitamin D levels and nCOVID-19 severity (CI= 0.77(0.65-1.14) and P-value = 0.001). Additionally, the results revealed that there was a higher prevalence of 25- (OH)- D deficiency among females than in males (32% vs. 16%), although statistically, this difference was not significant with P-value = 0.061 (Table3).

When assessing the status of 25-(OH)-D, the results show that deficient, insufficient, and adequate levels according to gender (females vs. males) were (32% vs. 16%), (42% vs. 22%), and (25% vs. 62%) as illustrated in Figure (1) respectively. Although, this difference was statistically not significant (the *P*-value was >0.05).

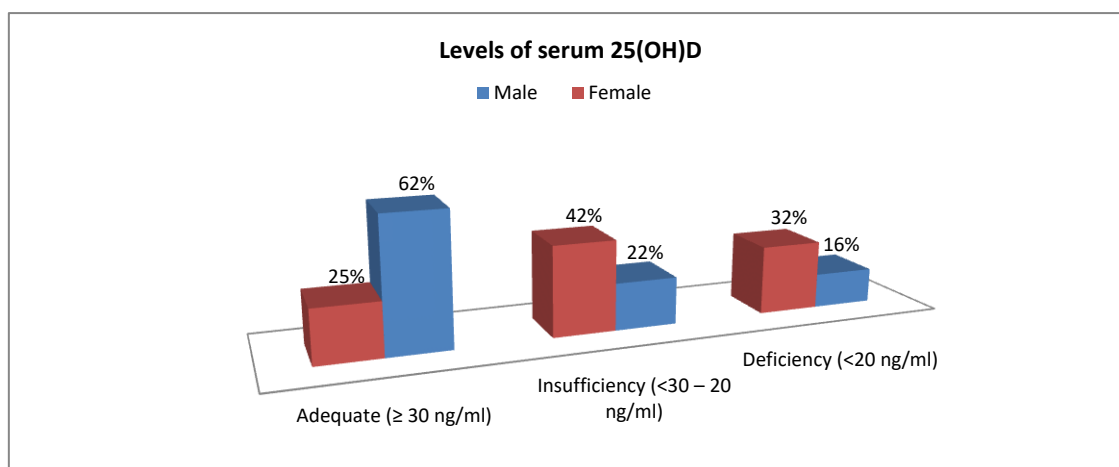
Among the studied sample, 25(OH) vitamin D deficiency was inversely correlated to age. Unexpectedly, vitamin D deficiency was higher among the youngest age groups (under 19 years old) than among those between 20 and 39 years old (Figure2).

The distribution of serum 25-(OH)-D among the entire data (2 groups), the results show that the prevalence of 25-(OH)-D deficiency, insufficiency, and adequate were 23.1%, 32.1%, and 44.8%. Although, the difference was statistically insignificant (with a *P*-value > 0.05). Furthermore, a significant difference was noticed between the mean \pm SD of serum 25-(OH)-D levels among groups which were (38.66 \pm 12.9 vs. 32.09 \pm 9.57) respectively (Table4).

Table(1): The demographic characteristics of studied data (n =134)

| Variable | Characteristics | Group(1) (n=91) (Asymptomatic) | Group(2) (n=43) (Critically ill) | P-value |
|------------------|---------------------|-----------------------------------|-------------------------------------|---------|
| Gender | Male | 53 | 18 | 0.021* |
| | Female | 38 | 25 | |
| Age in years | Mean \pm SD | 39.52 \pm 9.32 | 57.18 \pm 11.61 | 0.001** |
| Weight in kgs | Mean \pm SD | 74.31 \pm 10.29 | 80.11 \pm 9.85 | 0.081 |
| Nationality | Saudi vs. non-Saudi | 41:50 | 19:24 | 0.06 |
| Level of 25(OH)D | Mean \pm SD | 38.66 \pm 12.9 | 32.09 \pm 9.57 | 0.001* |

*Unpaired T-Test, **Chi-Square-Test[*]
(P-value<0.05)] Considered a Statistically significant difference



Figure(1): Levels of Serum 25-(OH)-D among studied cases' information(n=134)

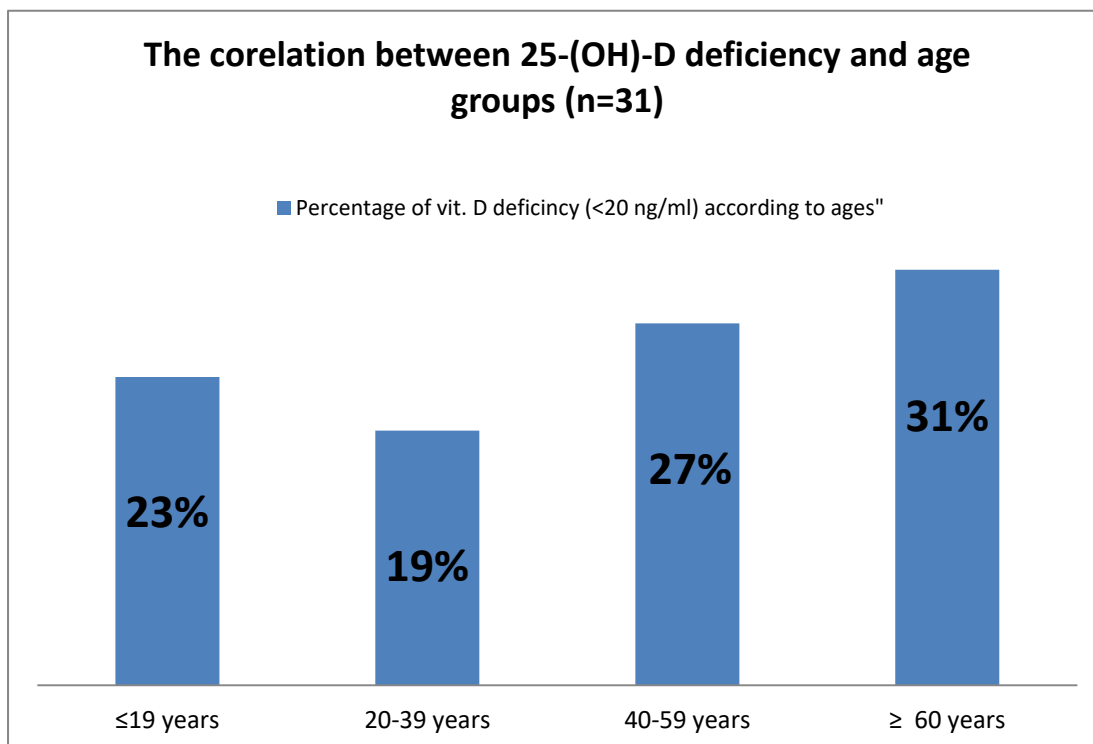


Figure2: Correlation between Vit D deficiency and age groups (n=31)

Table(2): Correlation between certain demographic characteristics and levels of 25-(OH)-D

| Status of Vitamin D | Univariate | | Multivariate ² | |
|------------------------------|------------------|-----------------|---------------------------|-----------------|
| | OR (95% CI) | <i>p</i> -value | OR (95% CI) | <i>p</i> -value |
| Adequate (≥ 30ng/ml) | 0.91 (0.93–0.87) | 0.011* | 1.01 (0.82–1.31) | 0.101 |
| Insufficiency (<30 –20ng/ml) | 1.56 (1.05–1.76) | 0.113 | 0.89 (0.61–1.21) | 0.611 |
| Deficiency (<20 ng/ml) | 1.22 (0.88–1.62) | 0.021* | 0.77 (0.65–1.14) | 0.001* |

²= Multivariable logistic regression which adjusted for nationality, weight, and age

* The difference is significant (P-value <0.05)

Table(3): Serum 25-(OH)D levels based on gender among sample (n=134)

| Status of Vitamin D | Total sample (n=134) | Male (n=71) | Female (n=63) | P-value |
|------------------------------|----------------------|-------------|---------------|---------|
| | n (%) | n (%) | n (%) | |
| Adequate (≥ 30ng/ml) | 60 (44.8%) | 44 (62%) | 16 (25%) | 0.111 |
| Insufficiency (<30 –20ng/ml) | 43 (32.1%) | 16 (22%) | 27 (42%) | |
| Deficiency (<20 ng/ml) | 31(23.1%) | 11 (16%) | 20 (32%) | |

Table (4): The distribution (mean \pm SD) 25-(OH)-D serum levels among the cases' information (n=134)

| Vitamin D status | Total sample (n=134) | Group 1 (n=91) | Group 2 (n=43) | OR(95%CI) | P-value |
|------------------------------|----------------------|----------------|----------------|-----------------|---------|
| Adequate (≥ 30 ng/ml) | | | | | |
| N(%) | 60 (44.8%) | 47(51.7%) | 13 (30.2%) | 0.41(0.21-0.63) | 0.001* |
| Mean \pm SD | 37.8 \pm 6.5 | 41.4 \pm 5.1 | 33.1 \pm 7.9 | | |
| Insufficiency (<30–20 ng/ml) | | | | | |
| N(%) | 43 (32.1%) | 35(38.5%) | 8(18.6%) | 0.73(0.28-0.94) | 0.051 |
| Mean \pm SD | 25.1 \pm 2.6 | 26.7 \pm 2.8 | 21.9 \pm 3.1 | | |
| Deficiency (<20 ng/ml) | | | | | |
| N(%) | 31(23.1%) | 9(9.9%) | 22(51.2%) | 6.01(2.31-9.11) | 0.012* |
| Mean \pm SD | 15.1 \pm 1.1 | 16.2 \pm 2.3 | 13.8 \pm 4.1 | | |

Multivariable logistic regression.

* The difference is significant (P-value <0.05)

DISCUSSION

This survey aimed to study the relationship between nCOVID-19 severity and serum levels 25-(OH)-D among humans. Numerous studies concluded that the deficiency in 25-(OH)-D has been noticed to have a major role in susceptibility to various chronic and infectious diseases, including nCOVID-19^{25,26,27,28,29}.

In the current study, it was noticed that the mean level of 25-(OH)-D among seriously ill patients (ICUs cases) was lower significantly than that reported among unadmitted mild cases (13.8 \pm 4.1 vs. 16.2 \pm 2.3), which indicates a potential correlation between the severity of nCOVID-19 and serum 25-(OH)-D levels which hypothesized that level of serum 25-(OH)-D is proportionally inverse with the severity of nCOVID-19. These concluded results were in line with some previous studies carried out by Pinzon et al., Biesalski, Laird et al., Mendy et al., and Ricci et al., who argued that levels of serum 25-(OH)-D were noticed to be

decreased among severely critically patients^{30,31,32,33,34}.

Moreover, it had been observed that deficiency in 25-(OH)-D was correlated strongly with age which enhances the vulnerability to acquiring nCOVID-19. In the same line, Ilie et al., Jain et al., and Singh et al. also hypothesized that older adults have low vitamin-D levels, making them vulnerable to acquiring infections including nCOVID-19^{35,36,37}.

On the other hand, these findings regarding age were in disagreement with a study conducted by Plotnikoff and Quigley, who reported that in the United States of America (USA), young generations seem to have serious 25-(OH)-D deficiency rather than elderly people^{38,39}.

In terms of the gender issue, the current survey shows a difference between the mean level of 25-(OH)D among males versus females in favor of the male gender, although the difference was not significant, which is supported by Rizaldy et al. who

documented that females show lower levels in 25-(OH)-D than males⁴⁰.

CONCLUSION AND RECOMMENDATIONS

Current survey, 25-(OH)-D deficiency was prevalent among the studied sample, 23.1%. Therefore, it has been concluded that 25(OH)D is one of the important determinants of the severity of illness; besides, it has a crucial role in preventing COVID-19 complications among patients.

Moreover, it has been noticed that deficiency in vitamin D raises the likelihood of acquiring nCOVID-19-related adverse consequences. Therefore, 25-(OH)-D supplementation is highly recommended for people, especially elderly ones at greater risk of acquiring COVID-19.

Limitations

Numbers of limitations exist in this study. A noteworthy one was the relatively small sample size; besides, we didn't consider the traditional dresses for females. Accordingly, our results may not be generalized due to the limited sample size.

Ethical approval and consent for publication

Ethical approval was obtained from Najran University-deanship of scientific research. (number REC2\2021). Moreover, confidentiality and participants' privacy were strictly followed throughout the study.

Conflict of interest

All authors declare no potential conflict of interest in preparing this article.

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Data availability

According to participants' preference, data was kept confidentially with authors

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