Original Article

Correlation between Serum Vitamin D Levels, COVID-19 Severity, and Inflammation in Diabetic Patients: A Retrospective Study

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Abstract

The recent COVID-19 pandemic has created significant health challenges, necessitating the enhancement of our immune systems. Through the modulation of immune response, Vitamin D vitally reduces the risk of infection and minimizes mortality rates. This retrospective study aimed to assess the relationship between the severity of COVID-19 infection in diabetes individuals and their blood vitamin D levels. A total of 2070 COVID-19 patients were split into two groups for this case-control retrospective study: non-diabetic (n=1723) and diabetic (n= 347). Electronic medical records from March to August 2020 obtained from the King Faisal Specialist Hospital and Research Center and Al-Noor Specialist Hospital, Saudi Arabia, were used as the base of the extraction of Demographic and clinical laboratory data. COVID-19 infection was confirmed in all patients through RT-PCR. Serum vitamin D level was measured by automated ELISA. A significant difference ($p<0.05$) in blood vitamin D levels between COVID-19 individuals with diabetes and those without was noted from the results of the study. We observed a marginal but significant negative correspondence between vitamin D levels and oxygen saturation as a measure of COVID-19 severity ($p=0.016$). Vitamin D levels were also found to be positively correlated with inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate ($p=0.038$ and $p<0.001$,) while showing a negative correlation with D-dimer ($p=0.017$). The results of our investigation suggest that vitamin D supplementation may be helpful in the management and prevention of COVID-19 infection, as well as in reducing the severity of risk and inflammation among diabetic patients.

Keywords: Diabetes, COVID-19, Vitamin D, Inflammation

Introduction

The outbreak of a novel respiratory pneumonia pandemic in 2019 caused by SARS-CoV-2 (severe respiratory acute syndrome-2) has become a global health issue, nominated as COVID-19 disease [1]. The consequence of SARS-CoV-2 infection varies from asymptomatic to ARSD (acute respiratory distress syndrome) and ultimately leads to the patient's death [2]. SARS-CoV-2 poses the threat of death to its patients of advanced age, hyper-immune response, and those with comorbid conditions such as diseases associated with blood vessels and heart, obesity, malignancy, chronic kidney and lung diseases, and especially diabetes that contribute to hospitalization and mortality up to 22% [3-6]. Diabetic patients are highly susceptible to microbial infection owing to a weak immune system, a low clearance rate for viruses, and impaired metabolic activity [7].

Vitamin D decreases microbial disease and mortality in patients by modulating the immune system [8]. Vitamin D increases the expression of genes associated with antioxidants, and more importantly, it upregulates the expression of ACE (angiotensin-converting enzyme)-2 receptors, which are required for pathogenesis induced by SARS-CoV-2 [9, 10]. The elevated population burden of SARS-CoV-2 infection has been reported in regions with a high frequency of low vitamin D levels [11]. Several observational pieces of evidence demonstrated the

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association between vitamin D insufficiency and human diseases, especially diabetes and respiratory diseases [12-14]. Evidence from hospitalized COVID-19 patients showed a lower level of vitamin D in COVID-19 patients compared to the general population [15, 16]. Recent studies on hospitalized COVID-19 patients also demonstrated a link between elevated COVID-19 infection severity, low serum vitamin D levels, and unfavorable clinical outcomes [17, 18]. Several recent observational reports showed the correlation between high vitamin D levels in serum and less severe symptoms and hypothesized vitamin D's effectiveness in managing COVID-19 [19-22]. Existing clinical reports indicated a possible correlation between COVID-19 and vitamin D, with uncertainty about its usefulness in managing and preventing SARS-CoV-2 infection [23, 24]. There was a dearth of information available on the subject of the correlation between the severity of COVID-19 in diabetics and blood vitamin D levels. Consequently, this retrospective study aimed to assess the link between COVID-19 in patients with diabetes and blood vitamin D levels, as well as the gravity of COVID-19 disease in diabetics.

Materials and Methods

This case-control retrospective study involving 2070 COVID-19 patients was carried out at the King Faisal Specialist Hospital and Research Center (KFSHRC) in Jeddah and Al-Noor Specialist Hospital in Makkah, Saudi Arabia, from March 2020 to August 2020 after obtaining ethical clearance from institutional review board (HAPO-02-K-012-2020-06-393) and the biomedical ethics committee at the faculty of medicine, Umm Al-Qura University. Eligible COVID-19 patients were randomly selected from the electronic medical records database. All confirmed cases of COVID-19 patients were matched in gender distribution and split into two: diabetes (n=347) and non-diabetes (n=1723). Inclusion criteria were as follows: (i) diabetic and non-diabetic patients with confirmed SARS-CoV-2 infection through RT-PCR, (ii) patients aged ≥18 years, and (iii) reported measurement of vitamin D level. The study eliminated patients who did not match the inclusion criteria. Demographic (age and gender) and clinical laboratory data (vitamin D level, fasting blood glucose (FBG), random blood glucose (RBG), hemoglobin A1c (HbA1c), systolic blood pressure (SBP), diastolic blood pressure (DBP), inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and D-dimer, oxygen saturation, oxygen requirement and days at hospitals) were retrospectively extracted from the electronic medical records available at the hospital. Serum vitamin D level in patients was measured by automated ELISA.

Statistical Analysis

IBM, Armonk, New York, USA, SPSS software, version 23.0, was used for all statistical analysis. Standard descriptive summaries were used to describe the data in the form of interquartile ranges and medians for continuous variables whereas percentages and numbers were used for categorical variables. Data normality was assessed using the Shapiro-Wilk test, and results $p<0.05$ were considered substantial statistically. To assess qualitative factors between the COVID-19 groups with and without diabetes, the Mann-Whitney U test was utilized, whereas for the categorical variable (gender) among study groups the Chi-squared test was employed. The correlations between vitamin D levels, other non-parametric variables (inflammatory markers like CRP, ESR, and D-dimer), and the severity of COVID-19 features (oxygen saturation, oxygen requirement, and days of stay at the hospitals) were assessed by using the Spearman's rank correlation test, ($p<0.05$) was considered statistically significant.

Results and Discussion

The diabetic COVID-19 group consisted of 347 patients (53% male and 47% female), whereas their counterparts consisted of 1723 patients (55% male and 45% female), **(Table 1)**. The two groups exhibited non-significant differences in gender distribution, DBP, and oxygen saturation. However, they exhibited significant age differences ($p<0.001$), FBG, RBG, HbA1c, SBP and oxygen requirement. The diabetic COVID-19 group had a decreased blood vitamin D level (36 ± 28) contrasted to their counterparts (42 ± 32, median ± interquartile range). A significant difference was observed in serum vitamin D levels in COVID-19 patients who had diabetes and those without it ($p<0.05$), **(Figure 1)**. **Table 2** exhibits the correlation between inflammatory indicators and blood vitamin D levels and the severity of COVID-19 infection in patients with diabetes. A non-significant correlation was observed between serum vitamin D level oxygen requirement and length of stay at the hospital ($p>0.05$). However, the serum vitamin D level and oxygen saturation showed a significant negative connection ($r=-0.16$, $p=0.016$). CRP and ESR (inflammatory markers) exhibited significant positive correlations with serum vitamin D levels ($r=014$, $p=0.038$ and $r=0.43$, $p<0.001$, respectively). The significantly negative relationship between D-dimer and vitamin D level was shown to be weak. ($r=-0.13$, $p=0.017$).

Vitamin D is a steroid hormone primarily involved in the maintenance of bone health [25]. Many studies also showed that it regulates various extra-skeletal functions such as immune modulation, and antiviral and anti-inflammatory effects [26, 27]. Several lines of evidence also showed that low vitamin D levels are responsible for multiple kinds of respiratory diseases and acute lung injuries [28, 29]. Despite this, insufficiency of vitamin D is also implicated in autoimmune and immunological disorders [30, 31]. Komisarenko *et al*. [32] demonstrated a correlation between a vitamin D deficit and a higher risk of immune-related diseases and conditions, including type 1 diabetes, respiratory infections, and COVID-19. A low dose of vitamin D has also been reported in diabetic patients infected with COVID-19 suggesting that both diseases share common pathogenic mechanisms [33-35]. It is still debatable if there is a link

between the severity of SARS-CoV-2 infection with blood vitamin D levels in diabetic individuals.

Our study findings observed a notable variation in the age distribution between the groups with and without diabetes who were infected with COVID-19. There has been a noticeable shift in the age distribution of people with diabetes compared to those without the disease [34]. In the current reports, we observed a non-significant difference in gender distribution in diabetes and non-diabetes groups with COVID-19 disease. A recent observational study found a non-significant difference between diabetic and non-diabetic patients with COVID-19 disease [36]. Hypertension is a well-documented risk factor for mortality and infection severity linked with COVID-19 [37, 38]. A significant difference in systolic blood pressure was noted while a non-significant difference in diastolic blood pressure in diabetic and non-diabetic patients infected with COVID-19 in a recent study. This was echoed by other observations, a hospital-based retrospective study observed a significant difference in diabetic and non-diabetic with COVID-19 disease [25]. An epidemiological report found a significant difference in systolic blood pressure between diabetic and non-diabetic patients infected with COVID-19 [39].

A significant difference was noticed in random and fasting blood glucose of COVID-19 patients suffering from diabetes and those without it in the current study which was echoed in other research [34] and another hospital-based observational study [40]. Our study found a significant difference in oxygen saturation while a non-significant difference was observed in oxygen requirement between diabetic and non-diabetic COVID-19 patients. Similar findings were also reported by many studies [41, 42]. A recent study based on two case reports also observed similar findings between diabetic and non-diabetic COVID-19 patients [43]. Glycated hemoglobin (Hb1Ac) is a marker of glucose control and a risk factor for problems in people with diabetes. Significant differences in Hb1Ac between non-diabetic and diabetic individuals were observed in many lines of the research. COVID-19 individuals [44, 45]. Diabetes is a relatively more prevalent risk factor for mortality and infection severity linked to COVID-19 disease [7]. The current study also reported similar findings regarding Hb1Ac.

Numerous observational studies have documented the connection between COVID-19 individuals with diabetes and low vitamin D levels [34, 35]. A systematic review revealed the association between low serum levels of vitamin D in patients with COVID-19 and diabetes [33]. Compared to their counterparts, Vitamin D deficiency was shown to be more common in diabetic COVID-19 patients, according to the current investigation. This disparity could be connected to an increased risk of infection, illness severity, and, ultimately, higher morbidity and mortality rates in vitamin D-deficient patients. The results of our investigation showed a little but significant inverse correlation between vitamin D levels and oxygen saturation. This indicated that those with vitamin D deficiency may have a more severe case of the illness. However, there were no discernible correlations between the need for oxygen and vitamin D levels. Growing data indicated a possible link between low vitamin D levels and severe COVID-19 infection [33-35]. Another observational study conducted in the United States revealed a strong inverse correlation between the prevalence of SARS-CoV-2 infection and vitamin D deficiency [46]. Ali *et al*. [47] also found no association between the severity of COVID-19 infection and death, but they did detect a negative link between low blood levels of vitamin D and the infection's severity.

The current study also observed a significant positive correlation between low serum levels of vitamin D and inflammatory markers, particularly CRP and ESR, and a significant inverse correlation with D-dimer suggesting high levels of inflammation in COVID-19 patients with vitamin D deficiency. Several researchers observed the positive correlation of CRP, ESR, and D-dimer with low vitamin D levels [48-50]. Khan *et al*. [48] reported the strong correlation of inflammatory markers and D-dimer with low vitamin D levels in diabetic COVID-19 patients.

The limited sample size, and missing data regarding vitamin D supplementation, vaccination, mortality, and morbidity rates are the main drawbacks of this retrospective study. Therefore, randomized clinical trials and extensive cohort studies with comprehensive, detailed information are still required to confirm such findings and, importantly, to characterize the inter and intra relationships between vitamin D concentrations and supplementations with other factors related to demographics and clinical features, in addition to COVID-19 symptoms, severity, immunization, rates of morbidity and death.

Table 1. Demographic and clinical characteristics of the diabetic and non-diabetic COVID-19 patients

Variable*	Non-diabetic (n= 1,723)	Diabetic (n= 347)	P-value^
Age (years)	57(42-68)	63(54-71)	**<0.001**
Gender (M%, F%)	(55%, 45%)	(53%, 47%)	0.402
SBP (mmHg)	125(113-138)	131(119-144)	**0.002**
DBP (mmHg)	74(67-82)	72(65-82)	0.105
Body weight (kg)	70(65-80)	74(65-85)	**0.01**
BMI (kg/m2)	26(24-29)	27(24-32)	**0.008**
FBG (mmol/L)	102(91-128)	161(117-229)	**<0.001**
RBG (mmol/L)	115(97-164)	173(130-254)	**<0.001**
HbA1C (%)	6.6(5.7-8.8)	9.0(7.3-10.6)	**<0.001**
CRP (mg/dL)	19(5-88)	36(6-101)	0.104
ESR (mm/hr)	92(48-272)	98(49-290)	0.391
D-dimer (mg/L)	0.80(0.4-2)	0.89(0.5-1.8)	0.626
Oxygen saturation (%)	97(95-98)	96(95-98)	**0.018**

Oxygen requirement (L)	2(1.5-3)	2(2-3)	0.845
Days at hospitals	6(3-14)	7(3-13)	0.111

*DBP: diastolic blood pressure, SBP: systolic blood pressure, FBG: fasting blood glucose, BMI: body mass index, RBG: random blood glucose, HbA1c: Glycated hemoglobin, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate. Data are expressed as median and interquartile range.
^ P-values were calculated using the Chi-square test for categorical variables (gender) and the Mann-Whitney U test for non-parametric ones p-value <0.05 was considered statistically significant.

Table 2. Demographic and clinical characteristics of the diabetic and non-diabetic COVID-19 patients

Variable*	Correlation Coefficient^	P-value^
CRP (mg/dL)	0.144	0.038
ESR (mm/hr)	0.43	<0.001
D-dimer (mg/L)	- 0.130	0.017
Oxygen saturation (%)	- 0.16	0.016
Oxygen requirement (L)	0.01	0.923
Days of hospitalization (days)	- 0.07	0.432

* CRP: C-reactive protein, ESR: erythrocyte sedimentation rate.
^ The Spearman's rank correlation test was used. P-value <0.05 was considered statistically significant and represented in bold.

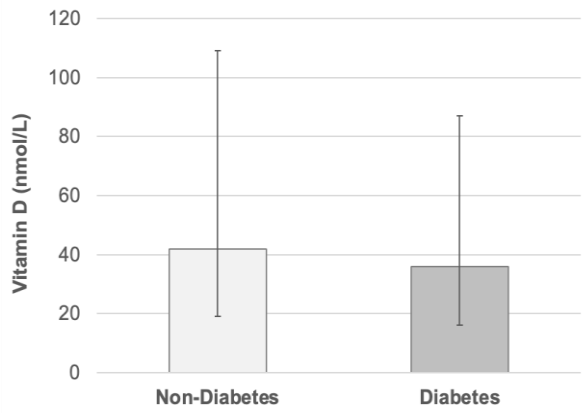

Figure 1. Status of vitamin D in diabetic and non-diabetic COVID-19 patients.
Data are expressed as median and interquartile range. The significant difference in vitamin D levels (nmol/L) between COVID-19 patients with and without diabetes was calculated using the Mann-Whitney U test, P-values <0.05.

Conclusion

The susceptibility and severity of COVID-19 infection are significantly influenced by individuals' immune function and comorbidity conditions, particularly in patients with diabetes. Reduced vitamin D levels have been identified as a possible risk factor for higher COVID-19 disease susceptibility, severity, and increased risks of morbidity and death. When compared to people without diabetes, COVID-19 patients with diabetes often have lower vitamin D levels. Patients with diabetes who have lower vitamin D levels are linked to heightened inflammation and increased COVID-19 severity, particularly oxygen saturation. Thus, vitamin D supplementation may represent a potentially promise approach in preventing COVID-19 infection and reducing disease severity and poor outcomes in patients with high risk such as diabetes. Nevertheless, the establishment of large-scale prospective studies is imperative to comprehensively investigate the possibility of COVID-19 prevention and reduction of its morbidity, severity, and diabetic death rates through supplementing Vitamin D.

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References

1. Ghebreyesus TA. World health organization. WHO director-general's opening remarks at the media briefing on COVID-19-25 May 2020.
2. Yanga J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidity and its effects in patients infected with SARS-CoV-2: A systematic review and meta-analysis. Int J Infect Dis. 2020;94:91-5.
3. Corrao S, Pinelli K, Vacca M, Raspanti M, Argano C. Type 2 diabetes mellitus and COVID-19: A narrative review. Front Endocrinol. 2021;12:609470.
4. Batiha GE, Gari A, Elshony N, Shaheen HM, Abubakar MB, Adeyemi SB, et al. Hypertension and its management in COVID-19 patients: The assorted view. Int J Cardiol Cardiovasc Risk Prev. 2021;11:200121. doi:10.1016/j.ijcrp.2021.200121
5. Gibertoni D, Reno C, Rucci P, Fantini MP, Buscaroli A, Mosconi G, et al. COVID-19 incidence and mortality in non-dialysis chronic kidney disease patients. PLoS One. 2021;16(7):e0254525.
6. Gerayeli FV, Milne S, Cheung C, Li X, Yang CW, Tam A, et al. COPD and the risk of poor outcomes in COVID-19: A systematic review and meta-analysis. EClinicalMedicine. 2021;33:100789.
7. Berbudi A, Rahmadika N, Tjahjadi AI, Ruslami R. Type 2 diabetes and its impact on the immune system. Curr Diabetes Rev. 2020;16(5):442-9.
8. Hribar CA, Cobbold PH, Church FC. Potential role of vitamin D in the elderly to resist COVID-19 and to slow progression of Parkinson's disease. Brain Sci. 2020;10(5):284.
9. Singh S, Kaur R, Singh RK. Revisiting the role of vitamin D levels in the prevention of COVID-19 infection and mortality in European countries post infections peak. Aging Clin Exp Res. 2020;32(8):1609-12.
10. Teshome A, Adane A, Girma B, Mekonnen ZA. The impact of vitamin D level on COVID-19 infection: Systematic review and meta-analysis. Front Public Health. 2021;9:624559.
11. Heidari S, Mohammadi S, Fathi M, Cigary S, Alisamir M, Mirkarimi M, et al. Association of vitamin D status with COVID-19 disease severity in pediatric patients: A retrospective observational study. Health Sci Rep. 2022;5(3):e569.
12. Hansdottir S, Monick MM. Vitamin D effects on lung immunity and respiratory diseases. Vitam Horm. 2011;86:217-37.
13. Zhou YF, Luo BA, Qin LL. The association between vitamin D deficiency and community-acquired pneumonia: A meta-analysis of observational studies. Medicine (Baltimore). 2019;98(38):e17252.

14. Schwalfenberg GK. A review of the critical role of vitamin D in the functioning of the immune system and the clinical implications of vitamin D deficiency. Mol Nutr Food Res. 2011;55(1):96-108.
15. Merzon E, Tworowski D, Gorohovski A, Vinker S, Golan Cohen A, Green I, et al. Low plasma 25(OH) vitamin D level is associated with increased risk of COVID-19 infection: An Israeli population-based study. FEBS J. 2020;287(17):3693-702.
16. Kara M, Ekiz T, Ricci V, Kara Ö, Chang KV, Özçakar L. 'Scientific Strabismus' or two related pandemics: coronavirus disease and vitamin D deficiency. Br J Nutr. 2020;124(7):736-41.
17. Dror AA, Morozov N, Daoud A, Namir Y, Yakir O, Shachar Y, et al. Pre-infection 25-hydroxyvitamin D3 levels and association with severity of COVID-19 illness. PLoS One. 2022;17(2):e0263069.
18. De Smet D, De Smet K, Herroelen P, Gryspeerdt S, Martens GA. Serum 25(OH)D level on hospital admission associated with COVID-19 stage and mortality. Am J Clin Pathol. 2021;155(3):381-8.
19. Maghbooli Z, Sahraian MA, Ebrahimi M, Pazoki M, Kafan S, Tabriz HM, et al. Vitamin D sufficiency, a serum 25-hydroxyvitamin D at least 30 ng/mL reduced risk for adverse clinical outcomes in patients with COVID-19 infection. PloS one. 2020;15(9):e0239799.
20. Carpagnano GE, Di Lecce V, Quaranta VN, Zito A, Buonamico E, Capozza E, et al. Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory failure due to COVID-19. J Endocrinol Invest. 2021;44(4):765-71.
21. Pizzini A, Aichner M, Sahanic S, Böhm A, Egger A, Hoermann G, et al. Impact of vitamin D deficiency on COVID-19—a prospective analysis from the Covid Registry. Nutrients. 2020;12(9):2775.
22. Baktash V, Hosack T, Patel N, Shah S, Kandiah P, Van den Abbeele K, et al. Vitamin D status and outcomes for hospitalised older patients with COVID-19. Postgrad Med J. 2021;97(1149):442-7.
23. Abrishami A, Dalili N, Mohammadi Torbati P, Asgari R, Arab-Ahmadi M, Behnam B, et al. Possible association of vitamin D status with lung involvement and outcome in patients with COVID-19: A retrospective study. Eur J Nutr. 2021;60(4):2249-57.
24. Zidrou C, Vasiliadis AV, Tsatlidou M, Sentona M, Vogiatzis S, Beletsiotis A. The relationship between vitamin D status and the clinical severity of COVID-19 infection: A retrospective single-center analysis. Cureus. 2022;14(2):e22385.
25. Laird E, Ward M, McSorley E, Strain JJ, Wallace J. Vitamin D and bone health: Potential mechanisms. Nutrients. 2010;2(7):693-724.
26. L Bishop E, Ismailova A, Dimeloe S, Hewison M, White JH. Vitamin D and immune regulation: Antibacterial, antiviral, anti-inflammatory. JBMR Plus. 2020;5(1):e10405.
27. Ismailova A, White JH. Vitamin D, infections and immunity. Rev Endocr Metab Disord. 2022;23(2):265-77.
28. Hughes DA, Norton R. Vitamin D and respiratory health. Clin Exp Immunol. 2009;158(1):20-5.
29. Soliman AR, Abdelaziz TS, Fathy A. Impact of vitamin D therapy on the progress COVID-19: Six weeks follow-up study of vitamin D deficient elderly diabetes patients. Proc Singapore Healthcare. 2022;31:20101058211041405.
30. Illescas-Montes R, Melguizo-Rodríguez L, Ruiz C, Costela-Ruiz VJ. Vitamin D and autoimmune diseases. Life Sci. 2019;233:116744.
31. Aranow C. Vitamin D and the immune system. J Investig Med. 2011;59(6):881-6.
32. Komisarenko YI, Bobryk MI. Vitamin D deficiency and immune disorders in combined endocrine pathology. Front Endocrinol (Lausanne). 2018;9:600.
33. Singh SK, Jain R, Singh S. Vitamin D deficiency in patients with diabetes and COVID- 19 infection. Diabetes Metab Syndr. 2020;14(5):1033-5.
34. AlHewishel MA, Bahgat M, Al Huwaiyshil A, Alsubie MA, Alhassan A. 25 (OH) D serum level in non-diabetic and type II diabetic patients: A Cross-Sectional Study. Cureus. 2020;12(6).
35. Alguwaihes AM, Al-Sofiani ME, Megdad M, Albader SS, Alsari MH, Alelayan A, et al. Diabetes and Covid-19 among hospitalized patients in Saudi Arabia: A single-centre retrospective study. Cardiovasc Diabetol. 2020;19(1):1-2.
36. Liu Z, Li J, Huang J, Guo L, Gao R, Luo K, et al. Association between diabetes and COVID-19: A retrospective observational study with a large sample of 1,880 cases in Leishenshan hospital, Wuhan. Front Endocrinol (Lausanne). 2020;11:478.
37. de Almeida-Pititto B, Dualib PM, Zajdenverg L, Dantas JR, De Souza FD, Rodacki M, et al. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: A meta-analysis. Diabetol Metab Syndr. 2020;12(1):1-2.
38. Peng M, He J, Xue Y, Yang X, Liu S, Gong Z. Role of hypertension on the severity of COVID-19: A review. J Cardiovasc Pharmacol. 2021;78(5):e648-55.
39. Moftakhar L, Moftakhar P, Piraee E, Ghaem H, Valipour A, Azarbakhsh H. Epidemiological characteristics and outcomes of COVID-19 in diabetic versus non-diabetic patients. Int J Diabetes Dev Ctries. 2021;41(3):383-8.
40. Elamari S, Motaib I, Zbiri S, Elaidaoui K, Chadli A, Elkettani C. Characteristics and outcomes of diabetic patients infected by the SARS-CoV-2. Pan Afr Med J. 2020;37:32.
41. Hu R, Gao H, Huang D, Jiang D, Chen F, Fu B, et al. Successful blood glucose management of a severe COVID-19 patient with diabetes: A case report. Medicine (Baltimore). 2020;99(26):e20844.
42. Li G, Deng Q, Feng J, Li F, Xiong N, He Q. Clinical Characteristics of COVID-19 patients with and without diabetes in Wuhan red cross hospital. J Diabetes Res. 2020;2020.
43. Dey RK, Hilmy AI, Imad HA, Yoosuf AA, Latheef AA. COVID-19 and emergencies in patients with diabetes: two case reports. J Med Case Rep. 2021;15(1):57.
44. Wang Z, Du Z, Zhu F. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. Diabetes Res Clin Pract. 2020;164:108214.
45. Alhakak A, Butt JH, Gerds TA, Fosbøl EL, Mogensen UM, Krøll J, et al. Glycated haemoglobin levels among 3295 hospitalized COVID-19 patients, with and without diabetes, and risk of severe infection, admission to an intensive care unit and all-cause mortality. Diabetes Obes Metab. 2022;24(3):499-510.
46. Kaufman HW, Niles JK, Kroll MH, Bi C, Holick MF. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. PloS one. 2020;15(9):e0239252.
47. Ali N. Role of vitamin D in preventing of COVID-19 infection, progression and severity. J Infect Public Health. 2020;13(10):1373-80.
48. Khan MUF, Ali BR, Mohammed HQ, Al-Shammari HMT, Jalil AT, Hindi NKK, et al. Retracted article: Serum level estimation of some biomarkers in diabetic and non-diabetic COVID-19 infected patients. Appl Nanosci. 2023;13(4):1-8.
49. Wu T, Zuo Z, Kang S, Jiang L, Luo X, Xia Z, et al. Multi-organ dysfunction in patients with COVID-19: A systematic review and meta-analysis. Aging Dis. 2020;11(4):874-94.
50. Yan Y, Yang Y, Wang F, Ren H, Zhang S, Shi X, et al. Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. BMJ Open Diabetes Res Care. 2020;8(1):e001343.