Influence of vitamin D levels on outcomes and nosocomial COVID-19 infection in patients undergoing total knee arthroplasty - a cohort study

Keyur B. Desai a, Kishore Karumuri a,*, Shruti A. Mondkar b, Chiranjeevi Thayi a, Ratnakar Vecham a, Adarsh Annapareddy a, A.V. Gurava Reddy a

a Department of Orthopaedics, Sunshine Hospitals, Paradise Circle, Secunderabad, Telangana, India
b Growth and Paediatric Endocrinology Unit, Hirabai Cowasji Jehangir Medical Research Institute, Jehangir Hospital, Pune, Maharashtra, India

ARTICLE INFO

Keywords:
Vitamin D3
Nosocomial COVID-19
Functional outcomes
Total knee arthroplasty
COVID-19

ABSTRACT

Purpose: This study aimed to audit the effects of vitamin D3 on the early functional outcomes, the incidence of nosocomial COVID-19 infection and complications in patients undergoing elective Total Knee Arthroplasty (TKA).

Methods: This was a retrospective study involving patients undergoing primary unilateral TKA between January 2020 to May 2021 operated by a single surgeon using a single implant. Participants were divided into two cohorts, Deficient-vitamin D3 level <20 ng/ml and Sufficient-vitamin D3 level ≥20 ng/ml. Assessment for Knee Society Score and Oxford Knee Score (OKS) was done preoperatively and one year after TKA. Nosocomial COVID-19 infection rate, 30-day re-admissions and complications were noted during the study.

Results: 235 patients were divided into 2 cohorts matched by age, gender and ASA grades. 74 patients belonged to the deficient group and 161 belonged to the sufficient group. The mean preoperative scores in the sufficient group were higher than the deficient group (OKS = 15.74 vs 12.95; KSS = 88.91vs 85.62). Similarly, the one-year postoperative scores in the sufficient group were significantly higher (OKS = 36.54 vs 35.16; KSS = 164.01 vs 161.22). A linear correlation was present between preoperative score (r = 0.273) & post-operative scores (r = 0.141) with serum vitamin D3 levels. Vitamin D3 deficient individuals had higher nosocomial COVID-19 infection rate (10.81% vs 4.96%,p = 0.16). The incidence of complications like DVT, embolism, stroke, infection and fracture were not statistically different in the two groups.

Conclusion: Vitamin D positively influences the outcomes of TKA and protects against nosocomial COVID-19 infection in patients undergoing elective TKA.

1. Introduction

The SARS-CoV-2 coronavirus (COVID-19) was declared an international public health emergency on the January 30, 2020.1 A nationwide lockdown was announced by the government of India on March 24, 2020, to curb the spread of this novel virus.2 Elective surgeries nationwide, including arthroplasty, bore a major brunt of lockdown as a majority of the healthcare resources were directed towards the management of COVID-19.3

Patients suffering intolerable knee pain during the COVID-19 pandemic expressed their dissent worldwide due to the restricted access to Total Knee Arthroplasty (TKA), an elective surgical procedure.4 It was a challenge for the orthopaedic community worldwide to balance the benefit of the surgery with a higher risk of acquiring the infection.

Vitamin D, a seco-steroid produced in the skin, plays an important role in calcium and phosphate homeostasis.5 Newer evidence has shown a light on the role of vitamin D in immune and cell signaling pathways.6 Deficiency of vitamin D has been associated with adverse postoperative outcomes, longer hospital stays and prosthetic joint infections (PJI) in patients undergoing total joint arthroplasty.7–9 Various studies report a high incidence of vitamin D deficiency in patients undergoing TKA, ranging from 36.4 to 76.2%.10,11 This deficiency
may be attributed to restricted mobility and outdoor activity associated with advanced osteoarthritis. Restricted outdoor activity and work-from-home culture owing to COVID-19 lockdown have been reported to add to the burden of vitamin D deficiency in a country like India where it is already rampant.

Owing to the controversial literature regarding the role of vitamin D3 on the results of TKA and its effect on complications, this study aimed to audit the functional results and complications of total knee arthroplasty in two cohorts of patients, those deficient and sufficient in serum vitamin D3 levels, operated by a single surgeon, in a high-volume arthroplasty centre, during the era of the novel COVID-19 pandemic. We also aimed to study the incidence of 30-day re-admissions and peri-operative nosocomial COVID infection in this group of patients.

2. Materials and methods

A retrospective observational study was undertaken at our tertiary care orthopaedic hospital, comparing the results and complication rates in two cohorts of patients operated for unilateral primary TKA between January 2020 to May 2021. The study was commenced after obtaining necessary ethical approvals from the Institutional Review Board (SIEC/2021/460).

Between January 2020 and May 2021, serum vitamin D3 levels were measured from the routine blood samples of all the patients awaiting TKA during their pre-admission visit. Measurements of serum Vitamin D3 levels were taken from the blood samples of all the patients, irrespective of their prior vitamin D supplementation status. A fully automated Maglumi 1000 analyzer (SNIBE Co, Ltd, China) was used for its measurement using the chemiluminescence immunoassay technique.

The data including serum vitamin D3 levels, serum albumin levels, baseline patient demographic data, comorbidity status, Body Mass Index (BMI), physical status classification grade (American Society of Anaesthesiologist- ASA grade), preoperative scores- Oxford Knee Score (OKS) and Knee Society Scores (KSS), and Length of Hospital Stay (LOS) were prospectively recorded for all the patients in the hospital database.

From this repository, data of 318 patients undergoing unilateral conventional primary TKA, operated on by a single surgeon in a single tertiary care arthroplasty centre, were retrieved. Of these, 33 patients who underwent surgery on the opposite side during the study duration were excluded. Patients with stroke, dementia and parkinsonism were also excluded to avoid significant outcome outliers. Patients who were diagnosed COVID-19 positive by Real-Time Polymerase Chain Reaction (RT-PCR) during the time of admission were deferred from the surgery and excluded from the study.

All the patients were operated on by the surgeon through a standard medial parapatellar approach using cemented PFC Sigma Posterior Stabilized implant (Depey Inc., Warsaw, IN). All the COVID-19 preventive precautions were taken including the ‘Green safe pathways’ as per the guidelines of the British Orthopaedic Association (BOA) which were suitably modified for the existing infrastructure to provide safe corridors for care during hospital admission. All hospital personnel were trained concerning the donning/doffing procedures with a separate area earmarked near the operating room. The operation theatres were thoroughly sanitized before and after the surgical procedure. Despite all the preventive measures, the risk of nosocomial and peri-operative COVID-19 infection was explained to all the patients before the surgery.

All the patients were mobilized with identical protocols and discharged on day two or three in absence of any complications. Patients having fever or COVID-19 suspected symptoms were presumptively isolated and subjected to an RT-PCR, which if positive were shifted to an isolation ward or home care as suitable.

2.1. Study cohorts

As suggested by the clinical practice guidelines of the Endocrine Society, our patients were divided into two groups according to their vitamin D3 (25-Hydroxy) levels. Those having vitamin D3 levels ≥20 ng/ml (50 nmol/l) were deemed to be sufficient and those with concentration <20 ng/ml were deemed to be deficient. 50 patients were lost to follow-up leaving us with two cohorts of 161 and 74 patients respectively, comparable for age, gender, comorbidities and ASA grade.

2.2. Primary outcome variables

These patients were followed up at one year postoperatively when functional outcome score (KSS) and Patient-reported outcome measures (OKS) were measured by the same research fellow who measured the preoperative scores.

2.3. Secondary outcome variables

The incidence of nosocomial COVID-19 infection in all the patients was noted. Similar to the contemporary literature, nosocomial COVID-19 infection was defined as meeting the following criteria: a) Patient being tested negative on screening with an RT-PCR test during the time of admission, b) Patient developing symptomatic COVID-19 infection during the period of hospitalization or the first 14 days following discharge.

The rate of readmission due to surgical causes or other non-covid medical causes within the first 30-days was also noted in both the groups.

Major complications like prosthetic joint infection, instability and fractures, pulmonary embolism, cardiovascular event, etc., and minor complications like superficial wound gaping, urinary tract infection and deep vein thrombosis were monitored during the follow-up period.

2.4. Statistical analysis

Descriptive statistics including mean, standard deviation and proportions were used for the baseline patient data like age, gender etc. Functional scores were treated as continuous variables. The normality assumption of KSS and OKS were fulfilled with the Kolmogorov-Smirnov test, allowing parametric tests to be performed. An independent t-test was used to test the difference between the means of the two groups. Linear co-relation between pre and post-operative scores, vitamin D3 level, age and BMI was analyzed using the Pearson correlation coefficient (r). Multivariate linear regression was used to test the relationship between postoperative scores and vitamin D3 level, adjusted for age and ASA grade. SPSS version 25 (SPSS Inc., Chicago, IL, USA) was used for performing the statistical analysis.

3. Results

3.1. Baseline patient demographics and preoperative status

235 patients operated for primary conventional unilateral TKA were divided into two groups, deficient (<20 ng/ml) and sufficient (>20 ng/ml) with 74 and 161 patients respectively. The mean age of the patients enrolled in this study was 63.99 years (SD = 9.42). Both the groups were comparable in their age, comorbidities, ASA grade and BMI (Table 1).

Mean serum vitamin D3 levels in the deficient group was 14.91 ng/ml (SD = 3.83), and that in the sufficient group was 33.35 ng/ml (SD = 13.07), p < 0.0001. Bivariate analysis revealed no correlation between the vitamin D3 levels and age, BMI and serum albumin levels (2-tailed) (Table 2).

The preoperative scores in both the groups were statistically different despite their similarity in age, comorbidities, ASA grade and BMI. The mean of preoperative KSS scores in the sufficient group was significantly higher than the deficient group (15.74 (SD = 2.453) vs 12.95(SD = 2.086); p < 0.0001). Similarly, the mean preoperative KSS scores were significantly higher in the sufficient group when compared...
Table 1
Comparison of baseline demographic parameters between 2 cohorts.

|       | VIT D3 DEFICIENT (n = 74) | VIT D3 SUFFICIENT (n = 161) | P Value | TOTAL (n = 235) |
|-------|--------------------------|----------------------------|---------|----------------|
| Mean Age | 61.32 (±9.74)          | 63.99 (±9.42)             | 0.051   | 63.15 (±9.58)  |
| Mean BMI | 28.166 (±5.131)        | 27.495 (±3.943)           | 0.321   | 27.706 (±4.352) |
| Mean VIT D3 level | 14.93 (±3.83)      | 33.35 (±13.07)            | p < 0.0001* | 14.93 (±13.971) |

| Number (%) | Number (%) | P value (chi-square) | Number (%) |
|-----------|------------|----------------------|------------|
| Sex (F:M) | ASA grade |                      |            |
| 1         | 2          | 3                    |            |
| 41/33     | 14 (18.91) | 14 (18.91)           | 0.6677     |
| 90/71     | 53 (71.62) | 126 (78.26)          | 0.2682     |
| 0.049     | 7 (9.45)   | 6 (3.72)              | 0.0748     |
| 131/104   | 50 (67.56) | 109 (67.70)          | 0.9837     |
| HTN       | DM         | Hypothyroidism        | Respiratory illness (Anthem/A COPD) |
| 27 (34.68) | 2 (2.70)  | 12 (16.21)           | 4 (5.40)   | 50 (67.56)  |
| 55 (34.16) | 6 (3.72)  | 30 (18.63)           | 10 (6.21)  | 109 (67.70) |
| 0.7289    | 0.6883    | 0.6539               | 0.8089     |
| 82 (34.89)| 8 (3.40)  | 42 (17.87)           | 14 (5.95)  |
| HTN       | DM         | Hypothyroidism        | Respiratory illness (Anthem/A COPD) |
| 5 (6.75)  | 2 (2.70)  | 12 (16.21)           | 4 (5.40)   | 50 (67.56)  |
| 16 (9.93) | 6 (3.72)  | 30 (18.63)           | 10 (6.21)  | 109 (67.70) |
| 0.4282    | 0.6883    | 0.6539               | 0.8089     |
| 21 (8.93) | 8 (3.40)  | 42 (17.87)           | 14 (5.95)  |
| Chronic Kidney Disease | 3 (4.05) | 4 (2.48) | 0.5118 | 7 (2.97) |

VIT D3: 25-Hydroxy Vitamin D3.
BMI: Body Mass index.
F:M: Female:Male.
ASA: American Society of Anaesthesiologist.
HTN: Hypertension.
DM: Diabetes Mellitus.
COPD: Chronic Obstructive Pulmonary Disease.

Table 2
Comparison of baseline demographic parameters between 2 cohorts.

| AGE | BMI | Sr. ALBUMIN |
|-----|-----|-------------|
| PRE-OP VITD3 Pearson correlation coefficient | 0.119 | -0.049 | -0.017 |
| P value | 0.07 | 0.456 | 0.799 |

**Correlation is significant at the 0.01 level (2-tailed), n = 235.

Table 3
Preoperative and Post-operative scores in vitamin D3 deficient and sufficient groups.

|       | OKS               | KSS               | P value (Independent t-test) |
|-------|-------------------|-------------------|------------------------------|
|       | Pre-op Mean (SD)  | Post-op Mean (SD) | Pre-op Mean (SD)  | Post-op Mean (SD) |               |
| Vitamin D3 Deficient (n = 74) | 12.95 (2.086) | 35.16 (4.065) | 85.62 (5.886) | 161.22 (11.891) | P < 0.00001 |
| Vitamin D3 Sufficient (n = 161)| 15.74 (2.453) | 36.54 (1.581) | 88.91 (5.646) | 164.01 (8.717) | P < 0.00001 |

OKS: Oxford Knee Score.
KSS: Knee Society Score.
SD: Standard deviation.

with the deficient (88.91 (SD = 5.64) vs 85.62 (SD = 5.886); p = 0.0001).

3.2. Postoperative functional assessment and analysis

There was an improvement in the mean postoperative scores after TKA in both groups. The deficient group showed an OKS improvement from 12.95(SD = 2.08) to 35.16 (SD = 4.06) whereas the sufficient group showed an improvement from 15.74(SD = 2.45) to 36.54(SD = 1.58). TKA improved the KSS scores significantly in both groups (Table 3).

Independent t-test revealed statistically higher postoperative OKS (36.54 (SD = 1.58) vs 35.16(SD = 4.06); p < 0.0002) and KSS scores (164.01(SD = 8.71) vs 161.22 (SD = 11.89); p = 0.044) in the vitamin D3 sufficient group when compared to the deficient group.

There was a positive linear correlation between the pre-operative and post-operative scores with vitamin D3 status. Pearson’s coefficients for preoperative and postoperative OKS were r = 0.273 (p = 0.0001) and r = 0.141 (p = 0.031) respectively. Similarly, the coefficients for preoperative and postoperative KSS were r = 0.185 (p = 0.04) and r = 0.307 (p = 0.0001) respectively (Table 4).

Multivariate linear regression revealed a correlation coefficient of post-operative scores (KSS: r = 0.365, p = 0.0001; OKS: r = 0.191, p = 0.01) with vitamin D3 level adjusted for age and ASA grade (Table 5).

3.3. COVID-19 and other complications

8 patients (10.81%) in the deficient group and 8 patients (4.96%) from the sufficient group suffered from symptomatic nosocomial COVID-19 infection. Three of the eight from the deficient group required readmission for the same. None of the patients required ICU stay. The median duration from discharge to the onset of symptoms was 5.6 days, fitting into the definition of nosocomial infection where symptoms related to COVID-19 infection started during or within 14 days of discharge. Though the difference in COVID-19 incidence among the two groups was statistically insignificant (p = 0.16), it was clinically significant.

Complication rates among both the groups were analyzed (Table 6), however, the power of the study was inadequate to prove its statistical relevance. Analysing the 30-day re-admission rates between the two groups, the deficient group had three COVID-19 related re-admission requiring supplemental oxygen and steroids and one patient was admitted for disorientation due to hyponatremia. Among the sufficient group, two patient were admitted for Non-COVID medical reasons (acute diarrhoea and hyponatremia).

Among the other complications, there were no significant differences in the rate of Deep vein thrombosis (p = 1), Pulmonary thromboembolism (p = 0.3149), perioperative fracture (p = 0.5316), deep infection (p = 0.5316), Cerebrovascular event (p = 0.3149), Urinary tract infection (p = 1).
services were gradually re-introduced with precautionary ‘green recovery pathways’ in place.

Literature supports higher perioperative mortality, post-operative complications and intensive care unit (ICU) admissions in confirmed perioperative COVID-19 infections.

Mortality as high as 30.5% was seen in patients undergoing emergency surgery for hip fractures with concomitant COVID-19 infection.21 Higher mortality could have been attributed to a higher pro-inflammatory body status arising out of a synergistic effect of trauma, surgery and concomitant COVID-19 infection.22 Similar complications have been described for cases in general surgery, gastro-esophageal, hepatobiliary, and colorectal surgery with concomitant COVID-19 infection.23

Literature supports relatively benign postoperative course in patients undergoing elective orthopaedic surgeries with preventive protocols. In a study by Zorzì et al., none of 614 patients undergoing elective orthopaedic surgeries with preventive protocols. In our study, there was a clinically significant (statistically insignificant) association between COVID-19 nosocomial infection and preoperative vitamin D3 status where 8 out of 74 patients from the deficient group and 8 out of 161 patients in the sufficient group were diagnosed with COVID-19 infection during the first 30 days of surgery, out of which only 1 patient required ICU care.

The rate of nosocomial COVID-19 infection ranged from 4.9% to 20%, depending upon the time of the study, utilization of preventive precautions and immunization status of the study population.25,26 Lakhan et al. found a nosocomial infection rate of 6.8% for COVID-19, which was subsequently reduced after introducing preventive protocols.27 In our study, 16 out of 235 (6.8%) patients were diagnosed with COVID-19 infection during the first 30 days of surgery, out of which only 3 required hospital admission and none required ICU care.

In our study, there was a clinically significant (statistically insignificant) association between COVID-19 nosocomial infection and preoperative vitamin D3 status where 8 out of 74 patients from the deficient group and 8 out of 161 patients in the sufficient group were diagnosed with COVID-19 infection during the first 30 days of surgery, out of which only 1 patient required ICU care.
positive within the first 30 days. A retrospective swiss study showed significantly low levels of vitamin D3 in COVID-19 positive patients. A 1.77 times greater relative risk of testing positive for COVID-19 was found in Vitamin D3 deficient patients when compared with the sufficient group in a retrospective cohort study of 489 patients. Weir et al. and Demir et al. associated vitamin D deficiency with higher severity of COVID-19 owing to its role in T regulatory lymphocyte function. Lower levels of D-dimer and thus a lesser risk of intravascular coagulopathy were seen in the vitamin D sufficient group in a study by Demir et al. There are contradictory pieces of evidence for and against the correlation of preoperative functional status and vitamin D3 levels. The majority of the studies did not associate the preoperative function with the vitamin D3 levels. This was in contrast to our study, where the patients with lower vitamin D3 status had a poorer preoperative function. It may be vice-versa, where patients with poor function and mobility have lower vitamin D3 levels due to restricted outdoor mobility and sun exposure. This view was supported by Maniar et al. who reported worse preoperative WOMAC scores in vitamin D3 deficient patients.

There has been no unison among the studies co-relating post-operative clinical results with vitamin D3 status. Some studies showed comparable, whereas others showed significantly worse outcomes associated with lower vitamin D levels. The possible reason for the positive correlation between postoperative function and vitamin D3 levels was its possible effect on the function of the muscular system and prosthesis integration.

Our study is probably the second study that has reported poor postoperative outcomes associated with vitamin D deficiency through multivariate linear regression analysis corrected for age and ASA grade. In our study, vitamin D3 levels were retrieved from the database retrospectively at the end of the study. Neither the surgeon nor the researcher was aware of the vitamin D3 status of the patient during the study duration. All the patients received a fixed drug combination of Elemental calcium (225 mg) and vitamin D3 400IU per day irrespective of their vitamin D3 status for a period of 3 months. The limitation of our study was a small sample size, relatively short follow-up period, and unanticipation of the change in vitamin D status after surgery. Despite restriction in the usage of bolus vitamin D supplementation, several factors including a daily supplemental dosage of 400IU, improved mobility, and outdoor exposure could influence the vitamin D3 status over the period of one year. Besides, as the study included only patients undergoing unilateral TKA during the study duration, The Knee Society Score of the unoperated but affected contralateral knee, hip or spine could influence the results of the operated knee.

Though a majority of data in the study was collected prospectively, the retrospective analysis did not allow sample size calculation. However, post hoc analysis performed to test the difference between the post-operative KSS scores of the two groups with an alpha value of 0.05, revealed the power (1-b error) of 0.439.

Studying a cohort of patients operated by a single surgeon, using a single implant during the tough COVID-19 era was the strength of this study. A study by Maniar et al. has shown the benefit of preoperative bolus oral vitamin D3 supplementation over the functional outcomes of TKA patients. This strategy could be cost-effective in improving outcomes and reducing complications in pre-diagnosed vitamin D3 deficient patients planned for an elective TKA.

5. Conclusions

Vitamin D sufficiency results in better pre-operative function and postoperative functional outcomes after TKA, and also is associated with a lesser incidence of nosocomial COVID-19 infections. Hence active screening of serum vitamin D3 status prior to an elective TKA is recommended.
12 Coppeta L, Papa F, Magrini A. Are shiftwork and indoor work related to D3 vitamin deficiency? A systematic Review of current evidences. 8468742 J Environ Public Health. 2018. https://doi.org/10.1155/2018/8468742.

13 Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. J Bone Jt Surg Br. 1998;80(1):63–69. https://doi.org/10.1302/0301-620X.80b1.7859.

14 Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. Clin Orthop Relat Res. 1989;248:13–14.

15 Orthopaedic Association British. Re-starting Non-urgent Trauma and Orthopaedic Care: Full Guidance; 2020.1–13. May https://www.boa.ac.uk/uploads/assets/9380a53f-3c88-4782-96c2-6e691b89f615/BOA-Guidance-for-restart-full-doc-final2-v11.pdf.

16 Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911–1930. https://doi.org/10.1210/jc.2011-0385.

17 Lakhani K, Minguell J, Guerra-Farfán E, et al. Nosocomial infection with SARS-CoV-2 and main outcomes after surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.

18 Kolahchi Z, De Domenico M, Uddin LQ, et al. COVID-19 and its global economic impact. Adv Exp Med Biol. 2021;1318:825–837. https://doi.org/10.1007/978-3-030-65761-3_46.

19 Sarkar A, Chakraborti AK, Dutta S. Covid-19 infection in India: a comparative analysis of the second wave with the first wave. Pathogens. 2021;10(9). https://doi.org/10.3390/pathogens10091222.

20 Soni P. Effects of COVID-19 lockdown phases in India: an atmospheric perspective. Environ Der Sustain. 2021;23(8):12044–12055. https://doi.org/10.1002/ede.201156-4.

21 Kayani B, Onochie E, Patil V, et al. The effects of COVID-19 on perioperative morbidity and mortality in patients with hip fractures. Bone Joint Lett J. 2020;102-B (9):1136–1145. https://doi.org/10.1020/0001-620X.102B9.BJJ-2020-1127.R1.

22 Zhang AS, Berreta RS, Osorio C, Daniels AH. Nosocomial COVID-19 infection mortality following surgery for severe progressive cervical myelopathy: a case report. Spinal Cord Ser Cases. 2021;7(1):5–8. https://doi.org/10.1038/s41394-021-00465-8.

23 Inzunza M, Romero C, Irañazaval MJ, et al. Morbidity and mortality in patients with perioperative COVID-19 infection: prospective cohort in general, gastroesopagogic, hepatobiliary, and colorectal surgery. World J Surg. 2021;45(6):1652–1662. https://doi.org/10.1007/s00268-021-06068-6.

24 Zorzi C, Piován G, Scepes D, Natali S, Marocco S, Iacono V. Elective orthopaedic surgery during COVID-19: a safe way to get back on track. JBJS open access. 2020;5(4). https://doi.org/10.2106/JBJS.OA.20.00086.

25 Luong-Nguyen M, Hermand H, Abdalba S, et al. Nosocomial infection with SARS-CoV-2 within departments of digestive surgery. J Vis Surg. 2020;6:007. https://doi.org/10.1001/j.prionsurg.2020.04.016.

26 Vanhems P, Saadatian-Elahi M, Chuzeville M, et al. Rapid nosocomial spread of SARS-CoV-2 in a French geriatric unit. Infect Control Hosp Epidemiol. 2020;41(7):866–867. https://doi.org/10.1017/ice.2020.99.

27 Rathish B, Wilson A, Warrier A, et al. Analysis of an outbreak of nosocomial COVID-19 at a tertiary care centre in South India. J Roy Coll Phys Edinb. 2021;51(4):332–337. https://doi.org/10.4997/JRCPE.2021.404.

28 D’Avolio A, Avataneo V, Manca A, et al. 25-Hydroxyvitamin D concentrations are lower in patients with positive PCR for SARS-CoV-2. Nutrions. 2020;12(5). https://doi.org/10.3390/nu12051359.

29 Meltzer DO, Best TJ, Zhang H, Vokes T, Arora V, Solway J. Association of vitamin D status and other clinical characteristics with COVID-19 test results. JAMA Netw Open. 2020;3(9), e2019722. https://doi.org/10.1001/jamanetworkopen.2020.19722.

30 Demir M, Demir F, Aygun H. Vitamin D deficiency is associated with COVID-19 positivity and severity of the disease. J Med Virol. 2021;93(5):2992–2999. https://doi.org/10.1002/jmv.26832.

31 Maniar RN, Patil AM, Maniar AR, Gangaraju B, Singh J. Effect of preoperative vitamin D levels on functional performance after total knee arthroplasty. Clin Orthop Surg. 2016;8(2):153–156. https://doi.org/10.4055/ciosción.2016.8.2.153.

32 Lee A, Chan SKC, Samy W, Chiu CH, Gin T. Effect of hypovitaminosis D on postoperative pain outcomes and short-term health-related quality of life after knee arthroplasty: a cohort study. Medicine (Baltimore). 2015;94(42), e1812. https://doi.org/10.1097/MD.0000000000001812.

33 Maniar RN, Maniar AR, Jain D, Bhatnagar N, Gajjar A. Vitamin D trajectory after hip fracture surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.

34 Maniar RN, Maniar AR, Jain D, Bhatnagar N, Gajjar A. Vitamin D trajectory after hip fracture surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.

35 Maniar RN, Maniar AR, Jain D, Bhatnagar N, Gajjar A. Vitamin D trajectory after hip fracture surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.

36 Maniar RN, Maniar AR, Jain D, Bhatnagar N, Gajjar A. Vitamin D trajectory after hip fracture surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.

37 Maniar RN, Maniar AR, Jain D, Bhatnagar N, Gajjar A. Vitamin D trajectory after hip fracture surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.

38 Maniar RN, Maniar AR, Jain D, Bhatnagar N, Gajjar A. Vitamin D trajectory after hip fracture surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.

39 Maniar RN, Maniar AR, Jain D, Bhatnagar N, Gajjar A. Vitamin D trajectory after hip fracture surgery within an orthopaedic surgery department in a tertiary trauma centre in Spain. Int Orthop. 2020;44(12):2505–2513. https://doi.org/10.1007/s00264-020-04798-1.