



Evaluation of Correlation of Preoperative Vitamin D Levels with Respiratory Complications in Patients undergoing General Anaesthesia

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ABSTRACT

Introduction: Respiratory problems are a significant cause of mortality and morbidity during the peri-operative period and they warrant significant attention. Serum Vitamin D levels and pulmonary function and inflammatory responses are known to be correlated. In respiratory disorders including bronchial asthma, COPD, and pneumonia, this association is quite obvious. Studies on the inflammatory pathway, airway constriction, and remodelling processes of smooth muscle cells in the airways revealed that vitamin D may modulate these processes.

Aims/ objective: to determine whether pre-operative vitamin D levels were associated with respiratory issues during induction, extubation, and early post-operative period in patients undergoing elective abdominal surgery under general anaesthesia.

Materials and Method: General anaesthesia was maintained through Sevoflurane 2 percent, remifentanyl 0.25 mg per kg per min infusion, 2 litters oxygen + two litters dry air with 0.8 ml per kg tidal volume at a rate of 12/min, and maintenance of end-tidal CO₂ level between 30 to 35 mmHg. At the last moment of surgical procedures, neostigmine at dose of 0.05 mg per kg and atropine at dose of 0.02 mg per kg were administered and then subjects were extubated. Incidence of cough, bronchospasm or desaturation of blood oxygen levels (SpO₂ < 90%) were recorded during intubation, extubation and during recovery from anaesthesia

Results: Overall, there was greater incidence of respiratory complication in patients with vitamin D deficiency. Incidence of desaturation (SpO₂<90%) in recovery phase (50.00%) in patients with vitamin D deficiency was significantly greater than the incidence (23.53%) in patients with serum vitamin D greater than 20 ng/ml (p<0.05). Incidence of bronchospasm and cough was also greater in patients with low serum vitamin D levels. Serum vitamin D levels was significantly lower in patients with respiratory complication with greatest correlation with desaturation (SpO₂<90%).

Conclusion: There was a significant positive correlation between serum vitamin D levels and incidence of intra-operative and post-operative respiratory complications. We suggest that correcting serum vitamin D levels in the pre-operative period will be helpful in terms of reducing respiratory issues for elective surgery, particularly for patients in the older age group.

Keywords: Vitamin D, General Anaesthesia, Elective Abdominal Surgery, Respiratory Complications.

INTRODUCTION

Respiratory problems are a significant cause of mortality and morbidity during the peri-operative period and they warrant significant attention. A variety of serious unexpected ventilation issues in the postoperative care unit (POCU), such as low blood oxygen levels (haemoglobin oxygen saturation less than 90%), hypoventilation (respiratory rate below 8 breaths per min or arterial CO₂ (carbon dioxide) tension greater than 50 mmHg), or upper airway obstruction (laryngospasm and stridor) necessitate physical intervention such as application of oral or nasal airway, mechanical ventilation, tracheal intubation or use drugs such as opioid antagonist and drugs for reversal of action of skeletal muscle relaxant.¹

The frequency of serious respiratory episodes in the POCU varies greatly, with many observational and prospective research estimating a range of 0.8% to 6.9%.¹⁻⁴ Post-operative pulmonary complications include a variety of causes, including surgical, anaesthetic, and demographic factors. 2-4 Surgical risk factors consist of the

kind of surgical procedures, length of the procedure, and urgent need for surgery.^{2, 4} The administration of drugs such as opioids, neuromuscular blocking agents, and general anaesthetic are examples of anaesthetic triggers.² COPD (chronic obstructive pulmonary disease), obesity, type 2 diabetes, and non-modifiable risk factors like old age and male gender are examples of patient risk variables.²⁻⁴

A fat-soluble steroid pro-hormone, vitamin D is primarily produced in the dermis from dehydro-cholesterol by a photochemical process. Around the world, vitamin D deficiency is a widespread health issue.^{5, 6} Serum Vitamin D levels and pulmonary function and inflammatory responses are known to be correlated. In respiratory disorders including bronchial asthma, COPD, and pneumonia, this association is quite obvious.^{7, 8} Studies on the inflammatory pathway, airway constriction, and remodelling processes of smooth muscle cells in the airways revealed that vitamin D may modulate these processes.⁹



The prevalence of low serum vitamin D levels in the wider population is rising daily, and there is mounting proof that vitamin D plays a crucial role in pulmonary health.^{10,11} Low serum vitamin D levels raises the risk of death from RTI (respiratory tract infections) and pulmonary diseases.¹² Patients' cardio-pulmonary functioning are adversely affected by surgical procedures and anaesthetic administration. General anaesthetic technique is more likely to cause respiratory difficulties than other anaesthetic techniques, which can lead to substantial morbidity and mortality rates.¹³

Particularly for patients with additional pulmonary disorders or those who may develop these additional disorders in the future, a thorough assessment prior to surgery is crucial. Despite the fact that there are several clinical research on Vitamin D deficiency that involve general health issues such as disorders of musculo-skeletal and respiratory systems, there don't seem to be sufficient studies on these subjects in patients undergoing surgery. Most of these few research deal with issues including discomfort following surgery, cardiovascular morbidity, and infections.^{6,14}

In this study, we sought to determine whether pre-operative vitamin D levels were associated with respiratory issues during induction, extubation, and early post-operative period in patients undergoing elective abdominal surgery under general anaesthesia.

MATERIALS AND METHODS

This was an observational & prospective study done in patients undergoing elective abdominal surgery in tertiary care centre of eastern India from July 2022 to June 2023 after getting permission from institutional ethics committee as per principles of Good Clinical Practice and Declaration of Helsinki. Patients were screened for inclusion and exclusion criteria and then enrolled in the study after providing participant information sheet and taking written informed consent from them.

Inclusion Criteria: Patients of either sex aged between 18 to 60 years in the ASA (American Society of Anaesthesiologist) 1-2 class planned for elective abdominal surgery under general anaesthesia were included in our study.

Exclusion Criteria: Patients with chronic obstructive pulmonary disease (COPD) or other respiratory complications, diabetes mellitus or other endocrine disorders, obesity, or patients with history of smoking or using Vitamin D tablets were excluded from our study.

Consecutive sampling method was used and every patient fulfilling our eligibility criteria from July 2022 to June 2023 and giving written informed consent were enrolled in our study.

Serum Vitamin D levels were assessed with the CLIA method and levels lower than 20 ng/mL were accepted as vitamin D deficiency and were defined as case. Fasting sample were obtained from all patients in the early

morning on the day of surgery. Patients having serum vitamin D level greater than or equal to 20 ng/ml were defined as control.

Heart rate measurement, non-invasive blood pressure measurement, pulse oximetry, monitoring of end-tidal CO₂ level, and assessment of neuromuscular block were all started when the study participants entered the operation theatre. After inserting a 20-gauge IV cannula into the dorsum of the hand of the subjects, IV fluid administration was started. After rocuronium (0.6 mg per kg), fentanyl (0.5 g per kg), and propofol (2-4 mg per kg) were administered for induction, the subjects were intubated when TOF equal to 0 was reached as per standard general anaesthesia protocol.

General anaesthesia was maintained through Sevoflurane 2 percent, remifentanyl 0.25 mg per kg per min infusion, 2 liters oxygen + two liters dry air with 0.8 ml per kg tidal volume at a rate of 12/min, and maintenance of end-tidal CO₂ level between 30 to 35 mmHg. At the last moment of surgical procedures, and after obtaining 2 responses from TOF stimulation, neostigmine at dose of 0.05 mg per kg and atropine at dose of 0.02 mg per kg were administered and then subjects were extubated.

Only the recovery phase and early post-operative period were used to characterize post-operative outcomes measures (respiratory complications) in the present research. Incidence of cough, bronchospasm or desaturation of blood oxygen levels were recorded during intubation, extubation and during recovery from anaesthesia. Desaturation is characterized as oxygen saturation below 90% from the initial SpO₂ of above 90% and below 95% in the post-operative care unit with room air. Bronchospasm is described as Rhonci audible in the major bronchi on expiration.¹⁵ Acute respiratory failure, which was characterized as acute severe dyspnoea, a respiratory rate more than 25 breaths per minute, and active contraction of accessory muscles, was a postoperative requirement for mechanical ventilator assistance.¹⁶

Statistical Analysis

Peri-operative data regarding baseline characteristics and outcome measures were presented in the tabular form using Microsoft Excel 365 and then transferred to SPSS version 24 for further statistical tests. Continuous data such as age, body mass index, vitamin D level, and duration of surgery were expressed as mean \pm standard deviation (SD) and unpaired t-test was used to determine statistical significance of difference between case and control. Categorical data such as gender, ASA status, and frequency of respiratory complication were expressed as frequency and percentage and fisher's exact test was used to determine statistical significance of difference between cases and controls. A p-value of less than 0.05 was used as a measure of statistical significance of difference between cases and controls.



RESULTS

30 patients (Case) with vitamin D deficiency (serum vitamin D <20 ng/ml) and 34 patients with serum vitamin

D > 20 ng/ml (Control) were enrolled in the study. Baseline demographic and clinical characteristics of cases and control is given in table 1.

Table 1: Baseline Demographic and Clinical Characteristics of Cases and Controls

Variables	Case n = 30	Control n = 34	P-Value
Age in years (mean ± SD)	38.27 ± 10.46	41.72 ± 11.13	0.21*
BMI in kg/m ² (mean ± SD)	25.43 ± 3.64	25.24 ± 3.38	0.83*
Duration of Surgery in minutes (mean ± SD)	97.81 ± 10.38	91.19 ± 10.27	0.01*
Serum Vitamin D Level in ng/ml (mean ± SD)	13.11 ± 2.58	31.04 ± 4.15	<0.0001*
Gender, n (%)			
Male	16 (53.33)	19 (55.88)	>0.99
Female	14 (46.67)	15 (44.12)	
ASA physical status, n (%)			
1	17 (56.67)	24 (70.59)	0.30
2	13 (43.33)	10 (29.41)	
*Unpaired t-test **Fisher's Exact Test			

Both cases and control were comparable with respect to age, body mass index (BMI), gender and ASA physical status with no statistically significant difference. However, duration of surgery was significantly greater in patients with low vitamin D levels.

Table 2: Comparison of Respiratory Complications in Cases and Controls

Period	Complication	Case n = 30	Control n = 34	P-Value (Fisher's Exact Test)
Induction, n (%)	Bronchospasm, n (%)	6 (20.00)	3 (8.82)	0.28
Extubation, n (%)	Cough, n (%)	7 (23.33)	4 (11.76)	0.32
	Bronchospasm, n (%)	3 (10.00)	1 (2.94)	0.33
	Desaturation, n (%)	13 (43.33)	6 (17.65)	0.03
Recovery, n (%)	Desaturation, n (%)	15 (50.00)	8 (23.53)	0.04

Overall, there was greater incidence of respiratory complication in patients with vitamin D deficiency. Incidence of desaturation (SpO₂<90%) in recovery phase (50.00%) in patients with vitamin D deficiency was significantly greater than the incidence (23.53%) in patients with serum vitamin D greater than 20 ng/ml (p<0.05). Incidence of bronchospasm and cough was also greater but the difference was not statistically significant.

Table 3: Comparison of Serum Vitamin D Level between Group of Patients with Complication and Group of Patients without Complication

Period	Complication	Serum Vitamin D Level in ng/ml (mean ± SD)		P-Value (Unpaired t-test)
		With Complication	Without Complication	
Induction	Bronchospasm	19.51 ± 7.03	25.06 ± 8.67	0.007
Extubation	Cough	19.95 ± 6.89	24.48 ± 8.53	0.02
	Bronchospasm	20.24 ± 7.51	25.19 ± 8.76	0.02
	Desaturation	18.76 ± 7.72	24.81 ± 9.03	0.006
Recovery	Desaturation	16.89 ± 7.80	25.86 ± 9.17	<0.0001

Serum vitamin D levels was significantly lower in patients with respiratory complication with greatest correlation with desaturation (SpO₂<90%).

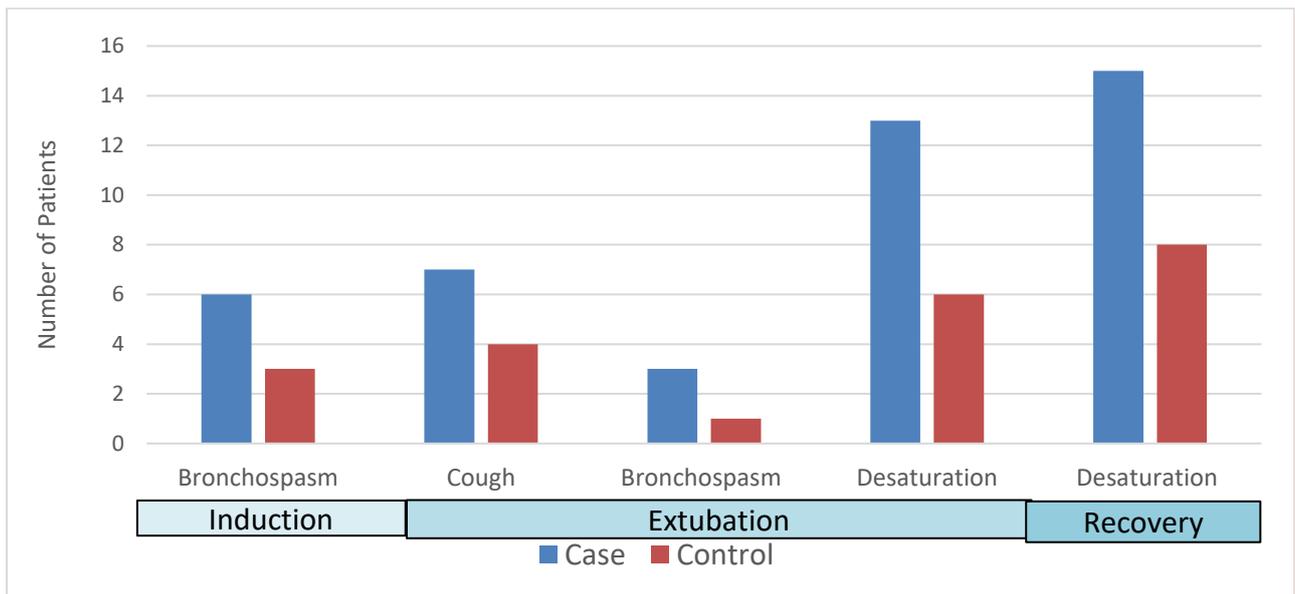


Figure 1: Frequency of Respiratory Complications in Cases and Controls

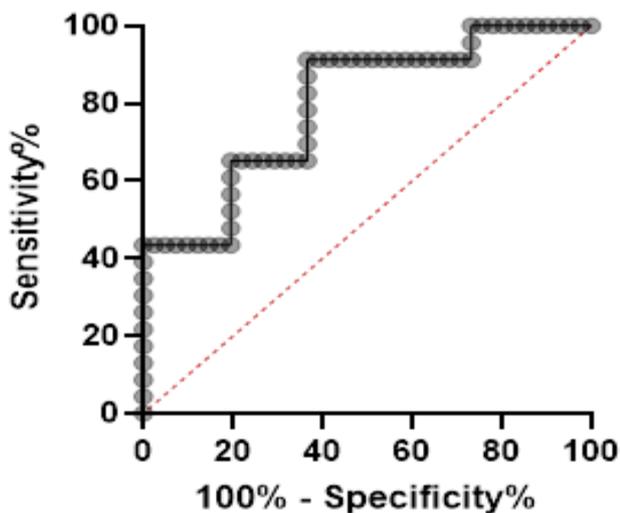


Figure 2: Receiver Operating Characteristic (ROC) curve for Vitamin D Level Association with Oxygen Desaturation in Recovery Phase (AUC = 0.7985)

DISCUSSION

The primary cause for the rise in morbidity and death associated with general anesthesia is respiratory complications.¹³ Decrease in SpO₂ levels, laryngospasm, bronchospasm, coughing, and excessive secretions are the most frequently seen adverse consequences.^{17,18} The most frequent complication among the patients with vitamin D deficiency in our research was decrease in SpO₂ level (desaturation). The need for thorough pre-operative screening and planning is clear given the substantial association between desaturation and related peri-operative respiratory problems with comorbidities.¹⁹ The mortality and morbidity associated with these problems can be decreased by doing a thorough pre-operative examination.²⁰

Numerous studies have demonstrated a significant relationship between adult pulmonary function and serum

vitamin D levels. Insufficient vitamin D levels lower pulmonary function and lead to the degeneration of pulmonary tissue. Admission to post-anaesthetic critical care and greater death rates are linked to anaesthesia-related pulmonary complications including respiratory failure, bronchospasm, and re-intubation.¹⁹ Acute respiratory failure has been linked to vitamin D deficiency in pre-hospitalization phase.¹⁴

Patients with low serum vitamin D levels are frequently seen by anaesthesiologist and re-animation specialists in the Intensive Care Unit (ICU), during aggressive therapy, and during the pre-operative period. Although there aren't sufficient research studies on this subject including patients undergoing surgery, vitamin D deficiency is reportedly linked to adverse health outcomes in the general population. An assessment of the relationship between serum vitamin D levels and post-operative death rates in 3509 patients planned for non-cardiac surgery revealed that serum levels below 13 ng/ml of vitamin D were associated with higher death rates and morbidity.⁶

Again, studies on bariatric surgery by Quraishi et al. revealed an association between lower serum vitamin D levels and infections following surgery.¹⁴ Data from the National Health and Nutrition Examination Survey (2001–2006) indicate a substantial correlation between lower serum vitamin D levels and respiratory complications.^{10,21} Early respiratory problems associated with general anaesthesia and serum vitamin D levels in our patients were found to be significantly correlated in our research. There was a strong correlation between the pre-operative serum vitamin D levels in our patients and various complications, including bronchospasm during the induction of anaesthesia, cough, bronchospasm, and low SpO₂ level (desaturation) during the extubation phase, as well as initial post-operative recovery time.

According to our research, patients who experienced desaturation (SpO₂ < 90%) throughout their recovery from

anaesthesia had the lowest serum vitamin D levels among all patients who had any respiratory complications. Again, in comparison to cases without difficulties, serum vitamin D levels in our patients with peri-operative bronchospasm and desaturation (SpO₂) levels in the recovery phase were significantly reduced. Reintubation which is most serious post-operative respiratory complication has been shown to ten-fold elevate the probability of mortality.¹⁹

It has been established that vitamin D deficiency levels are associated with adverse clinical consequences and that these low serum vitamin D levels in patients lead to dysfunction of nervous system, compromised exchange of gases, and weakness in the muscles, all of which have an impact on the need for a mechanical ventilation. In our research, however, needs for re-intubation and mechanical ventilation support weren't noticed.^{12, 22} Additionally, nearly fifty percent of all patients admitted to hospitals suffer from vitamin D deficiency, which has been shown to be linked to muscular weakness, most frequently in the proximal muscle groups.^{6, 23}

It has long been believed that a vitamin D deficit weakens the intercostal and diaphragm muscles, making it harder to remove secretions from the lungs.²² The most prominent causes of the frequently observed respiratory complications are disturbance of the structural integrity of the chest wall and lowering of lung volumes.²⁰

Studies have found a strong correlation between baseline pulmonary function (FEV₁ and forced vital capacity) and serum vitamin D levels.²⁴ According to an experimental investigation by Zosky et al., discrepancies in lung sizes are predominantly brought on by vitamin D insufficiency. The researchers noted that lack of vitamin D in the general population was a key factor impacting pulmonary health and that this deficit impaired lung functioning.^{25, 26}

In the present study, we demonstrated a link between inadequate levels of vitamin D and anaesthesia-related peri-operative respiratory complications. Although not doing pre-operative lung function tests for assessing patients' pulmonary capacities and volumes is the study's most major shortcoming, Lung function test is not typically used as a pre-operative evaluation technique generally. It is well known that over fifty percent of all hospital patients suffer from a low serum vitamin D level in general. Therefore, during the peri-operative time, it is appropriate to evaluate and investigate patients in this manner.

CONCLUSIONS

There was a significant positive correlation between serum vitamin D levels and incidence of intra-operative and post-operative respiratory complications. It takes a lengthy course of treatment to detect serum vitamin D levels in all hospitalized patients prior to surgery and restore levels to normal. It is obvious that urgent surgical situations cannot wait for the pre-operative period during which vitamin D levels should be at the proper levels. However, we suggest that correcting serum vitamin D levels in the pre-operative period will be helpful in terms of reducing respiratory issues

for elective surgery, particularly for patients in the older age group.

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REFERENCES

- Rose DK, Cohen MM, Wigglesworth DF, DeBoer DP, Math M. Critical respiratory events in the postanesthesia care unit: Patient, surgical, and anesthetic factors. *Anesthesiology*. 1994;81:410–8.
- Pedersen T, Viby-Mogensen J, Ringsted C. Anaesthetic practice and postoperative pulmonary complications. *Acta Anaesthesiol Scand*. 1992;36:812–8.
- Hines R, Barash PG, Watrous G, O'Connor T. Complications occurring in the postanesthesia care unit: A survey. *Anesth Analg*. 1992;74:503–9.
- Mathew JP, Rosenbaum SH, O'Connor T, Barash PG. Emergency tracheal intubation in the postanesthesia care unit: Physician error or patient disease? *Anesth Analg*. 1990;71:691–7.
- Hutchinson K, Healy M, Crowley V, Louw M, Rochev Y. Verification of abbott 25-OH-Vitamin D assay on the architect system *Pract Lab Med*. 2017;7:27–35
- Turan A, Hesler BD, You J, Saager L, Grady M, Komatsu R, et al The association of serum Vitamin D concentration with serious complications after noncardiac surgery *Anesth Analg*. 2014;119:603–12.
- Bener A, Ehlayel MS, Bener HZ, Hamid Q. The impact of Vitamin D deficiency on asthma, allergic rhinitis and wheezing in children: An emerging public health problem *J Family Community Med*. 2014;21:154–61.
- Columbo M, Panettieri RA Jr., Rohr AS. Asthma in the elderly: A study of the role of Vitamin D *Allergy Asthma Clin Immunol*. 2014;10:48-53.
- Banerjee A, Panettieri R Jr.. Vitamin D modulates airway smooth muscle function in COPD *Curr Opin Pharmacol*. 2012;12:266–74.
- Quraishi SA, Camargo CA Jr.. Vitamin D in acute stress and critical illness *Curr Opin Clin Nutr Metab Care*. 2012;15:625–34.
- Mulligan JK, Nagel W, O'Connell BP, Wentzel J, Atkinson C, Schlosser RJ, et al Cigarette smoke exposure is associated with Vitamin D3 deficiencies in patients with chronic rhinosinusitis *J Allergy Clin Immunol*. 2014;134:342–9.
- Ginde AA, Mansbach JM, Camargo CA Jr.. Vitamin D, respiratory infections, and asthma *Curr Allergy Asthma Rep*. 2009;9:81–7.



13. Warner DO. Preventing postoperative pulmonary complications: The role of the anesthesiologist *Anesthesiology*. 2000;92:1467–72.
14. Quraishi SA, Bittner EA, Blum L, Hutter MM, Camargo CA Jr.. Association between preoperative 25-hydroxyvitamin D level and hospital-acquired infections following roux-en-Y gastric bypass surgery *JAMA Surg*. 2014;149:112–8.
15. Gebremedhn EG, Mesele D, Aemero D, Alemu E. The incidence of oxygen desaturation during rapid sequence induction and intubation *World J Emerg Med*. 2014;5:279–85.
16. Conti G, Cavaliere F, Costa R, Craba A, Catarci S, Festa V, et al Noninvasive positive-pressure ventilation with different interfaces in patients with respiratory failure after abdominal surgery: A matched-control study *Respir Care*. 2007;52:1463–71.
17. Zambouri A. Preoperative evaluation and preparation for anesthesia and surgery *Hippokratia*. 2007;11:13–21.
18. Dewachter P, Mouton-Faivre C, Emala CW, Beloucif S. Case scenario: Bronchospasm during anesthetic induction *Anesthesiology*. 2011;114:1200–10.
19. Ruscic KJ, Grabitz SD, Rudolph MI, Eikermann M. Prevention of respiratory complications of the surgical patient: Actionable plan for continued process improvement *Curr Opin Anaesthesiol*. 2017;30:399–408.
20. Doyle RL. Assessing and modifying the risk of postoperative pulmonary complications *Chest*. 1999;115:77S–81S.
21. Black PN, Scragg R. Relationship between serum 25-hydroxyvitamin d and pulmonary function in the third national health and nutrition examination survey *Chest*. 2005;128:3792–8.
22. Hendryx M, Luo J. A test of Vitamin D benefits on respiratory health mediated through inflammatory markers *Chron Respir Dis*. 2015;12:24–30.
23. Bozzetto S, Carraro S, Giordano G, Boner A, Baraldi E. Asthma, allergy and respiratory infections: The Vitamin D hypothesis *Allergy*. 2012;67:10–7.
24. Luger TJ, Kammerlander C, Luger MF, Kammerlander-Knauer U, Gosch M. Mode of anesthesia, mortality and outcome in geriatric patients *Z Gerontol Geriatr*. 2014;47:110–24.
25. Damera G, Fogle HW, Lim P, Goncharova EA, Zhao H, Banerjee A, et al Vitamin D inhibits growth of human airway smooth muscle cells through growth factor-induced phosphorylation of retinoblastoma protein and checkpoint kinase 1 *Br J Pharmacol*. 2009;158:1429–41.
26. Zosky GR, Berry LJ, Elliot JG, James AL, Gorman S, Hart PH, et al Vitamin D deficiency causes deficits in lung function and alters lung structure *Am J Respir Crit Care Med*. 2011;183:1336–43.

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