

**Manuscript type:** Original Article

DOI: 10.5152/TurkThoracJ.2019.18139

**Title: Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis**

**Short Title:** Vitamin D deficiency in bronchiectasis

**Authors:** Elif Yelda Niksarlıođlu<sup>1</sup>, Lutfiye Kılıç<sup>1</sup>, Deniz Bilici<sup>2</sup>, Burcu Yiđitbař<sup>1</sup>, M.Atilla Uysal<sup>1</sup>, Gungor Camsarı<sup>1</sup>

**Institutions:** <sup>1</sup>Health Science University, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Department of Chest Diseases, Istanbul, Turkey

<sup>2</sup>Giresun Dr. Ali Menekře Chest Diseases Hospital, Department of Chest Diseases, Giresun, Turkey

**Address for correspondence:** Elif Yelda Ođgun Niksarlıođlu, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Department of Chest Diseases, Kazlıcesme Street, no:1, 34500, Zeytinburnu, Istanbul, Turkey

**E-mail:** eyelda2003@yahoo.com

**Received:** 31.08.2018

**Accepted:** 05.03.2019

**Cite this article as:** Niksarlıođlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18139

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıođlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100

©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

## Abstract

**Objective:** Vitamin D may play important role in immunity and vitamin D deficiency has been related to increased respiratory infections. The aim of this study to detect prevalence of vitamin D deficiency and to investigate relationship between radiologic and clinical effects on adult bronchiectasis(BR) patients.

**Material and Methods:** A 130 patients with BR and 73 healthy people as a control group were enrolled to the study. Radiological severity was assessed using Modified Reiff Score.

**Results:** The mean age of patients was  $41.9 \pm 9.1$  (Range 18-85). The mean 25(OH)D level of BR patients was  $14.7 \pm 9.6$  ng/ml and  $19.8 \pm 6.9$  ng/ml in control group ( $p=0.001$ ). We found that 95(73.1%) of adult BR patients would be categorized as vitamin D deficient. Patients with vitamin D deficiency group were significantly higher mMRC scores than those in the group without vitamin D deficiency ( $p=0.036$ ) The mean modified reiff score was higher in vitamin D deficient group than normal serum level 25(OH)D BR group ( $6.9 \pm 3.8$  vs  $4.9 \pm 2.7$ ,  $p=0.001$ ). Forced vital capacity% predicted value was lower in the vitamin D deficient group too ( $p=0.02$ ). This model showed that reiff score (OR 1.285(1.039-1.590),  $p=0.021$ ) was independently related to vitamin D deficiency

**Conclusion:** We found that vitamin D deficiency is commonly seen in adult BR patients in a stable period. Likewise, It might be related to severe radiological findings on chest CT and worse lung functions.

**Keywords:** Bronchiectasis, Bronchiectasis severity index, Radiology, Reiff's score, vitamin D deficiency

## Introduction

Vitamin D is a fat-soluble steroid synthesized in the skin from 7-dehydrocholesterol (as a hormone) or ingested with food (as a vitamin). Vitamin D plays a primary role throughout the body, especially in the musculoskeletal system. It also plays an important role in directly

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100

©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

regulating the immune system, and inducing the secretion of antimicrobial proteins against pathogens, including *Pseudomonas aeruginosa* (1,2).

Recent studies have shown that vitamin D deficiency in patients with chronic respiratory diseases, such as chronic obstructive lung disease (COPD), asthma, and cystic fibrosis, is highly prevalent, and associated with recurrent infection, disease severity and declining lung function (3,4,5). Non-cystic fibrosis bronchiectasis (BR) is a chronic respiratory disease characterized by destruction and dilatation of medium-sized airways, cough, abnormal sputum production, and recurrent infections. BR patients have a vicious cycle of chronic bronchial infections, inflammation, impaired mucociliary clearance, and structural lung damage, especially in the lower airways (6). Some studies have shown that vitamin D has an anti-inflammatory effect that reduces cytokines and chemokines that promote tissue destruction (7,8). Low 25-hydroxy vitamin D levels were detected in adult non-cystic fibrosis BR patients (4). However, in a recent study, reported that 25-hydroxyvitamin D levels was higher in the BR group than the adult population (9).

To our knowledge, there are limited studies investigating the prevalence of vitamin D deficiency in adult bronchiectasis patients. This study aimed to assess the prevalence of vitamin D deficiency and to investigate its association with radiological and clinical effects in adult BR patients.

## **Material and Method**

This case-control study was carried out on patients who had been diagnosed with bronchiectasis by high-resolution computed tomography (HRCT) of the chest between 15 December 2016 and 15 December 2017. All BR patients were clinically stable for at least four weeks before enrollment in the study. Demographic parameters, clinical data (respiratory symptoms, duration of illness), pulmonary function tests, HRCT findings, complete blood count, and sputum culture results were all recorded. Sputum samples were considered acceptable if they contain less than ten squamous cells and more than 25 leukocytes per low-power microscopic field (10). The study was approved by the Local Ethics Committee of xxxxx Hospital (Approval no: 2016/66). Each participant signed an informed consent form.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. *Turk Thorac J* 2019; DOI: 10.5152/TurkThoracJ.2019.18100

©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

Case group: A total of 130 adult BR patients between 18 and 85 years, who were previously diagnosed with BR, were included in the study. Exclusion criteria were age <18 years, cystic fibrosis (previously diagnosed CF patients according to guideline), interstitial lung disease, allergic bronchopulmonary aspergillosis, active tuberculosis, supplementation of vitamin D prior to, or during the study, non-stable bronchiectasis, and the use of antibiotics at least four weeks prior to the study (11).

Control group: Seventy-three age, gender, and body mass index-matched healthy people with no history of the disease, and no supplementary use of vitamin D before, or during the study, were recruited from the community.

The radiological severity of BR was assessed using the modified Reiff score, which evaluates the number of lobes involved (the lingula was considered as a separate lobe, tubular BR = 1, varicose BR = 2 and cystic BR = 3 points). The minimum score is 1, and the maximum score is 18 (12). The Bronchiectasis Severity Index (BSI) was applied to determine disease severity. The nine BSI parameters include age, body mass index (BMI), forced expiratory volume in 1-second (FEV<sub>1</sub>) % predicted, hospitalization with a severe exacerbation in the past 2 years, number of exacerbations in previous year, the Modified Medical Research Council (mMRC) dyspnea scale, *Pseudomonas* colonization, colonization with other organisms and radiological severity ( $\geq 3$  lobes involved or cystic bronchiectasis). These scores classify patients into mild (0-4 points), moderate (5-8 points) and severe (9+ points) groups and identify patients at risk of future mortality, hospitalization, and exacerbation (13). The bronchiectasis etiology and comorbidity index (BACI) was used to assess any comorbidity that carried an independent prognostic value relating to exacerbation and *Pseudomonas aeruginosa* infection (14).

The major circulating form of vitamin D is 25-hydroxy vitamin D (25[OH] D) and is the best indicator of overall vitamin D status. The blood sample for 25(OH)D were taken between 8:00 to 10:00 a.m. Vitamin D was measured by liquid chromatography tandem mass spectroscopy, accepted as the gold standard for 25(OH)D status. Assessment of vitamin D levels, as suggested by the Turkish Endocrinology and Metabolism association, was as

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100

©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

follows: < 20 ng/mL (50 nmol/L) = deficiency, 20-30 ng/mL (50-70 nmol/L) = insufficient, and  $\geq$  30ng/mL = sufficient (15,16).

Statistical analyses were carried out using the SPSS package version 20 (IBM, Armonk, NY, USA). Descriptive statistics of mean and standard deviation were used for continuous variables. Median and Interquartile Range (IQR) for continuous non-parametric data, and frequencies and percentages for categorical data were presented. Comparisons between two groups were performed using the unpaired t-test, Mann-Whitney U test or Chi-squared test, depending on data distribution. For the multivariate analysis, the possible factors identified with univariate analyses were further entered into a logistic regression analysis to determine the independent predictors of vitamin D deficiency. The Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. Statistical significance was considered as  $p < 0.05$ .

Although there were no adequate epidemiological studies related to vitamin D deficiency in adult BR patients, the sample size was calculated using prevalence rate of 0.93 for vitamin D deficiency in adult Turkish people with 95% confidence level and 5% confidence interval For this study, we calculated that sample size of 101 patients was required. (17).

## Results

One hundred and thirty patients with BR were enrolled in the study. Their mean age was  $41.9 \pm 9.1$  (range 18-85), and 66 (50.8%) were women. Baseline characteristics of both the patient and control group are shown in Table 1. Only 29.2% of BR patients had comorbidities: COPD [20(15.4%)], hypertension [17(13.1%)], gastro-esophageal reflux [10(7.7%)], asthma [6(4.6%)], diabetes [6(4.6%)], and coronary arterial disease [4(3.1%)]. The mean 25(OH)D level of the BR patient group was  $14.7 \pm 9.6$  ng/mL, and  $19.8 \pm 6.9$  ng/mL in the control group ( $p = 0.001$ ) (Figure 1). Using the Turkish Endocrinology and Metabolism Association definitions for serum 25(OH)D concentrations, 95 (73.1%) of the adult BR patients could be categorized as vitamin D deficient (< 20 ng/mL). Vitamin D deficiency was present in 40 (54.8%) of the control group participants. Vitamin D insufficiency was present in 27 (20.8%) of the adult BR patients, and 27 (37%) of the control group. There was a

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100

©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

statistically significant difference between the two groups ( $p= 0.016$ ). Although blood samples were taken between 15 December 2016 and 15 December 2017, there was no significant difference in serum 25(OH)D levels vs. season between BR and control groups ( $p=0.421$ )

A sputum sample was taken in 95 (73.1%) patients, 35 (26.9%) could not give sputum in a stable period. Some patients (48, 36.9%) had negative sputum culture results. The most frequently isolated microorganism was *Pseudomonas aeruginosa* (27, 20.8%) in a stable period of BR patients. The BR patient group was divided into two sub-groups according to vitamin D deficiency, i.e., 25(OH)D levels  $< 20$  ng/mL and  $\geq 20$  ng/mL. The baseline characteristics, clinical symptoms, and radiological and clinical severity of the patients are summarized in Table 2. No significant difference was found between the two sub-groups regarding age, gender, smoking history, BMI, comorbidity, respiratory symptoms, BSI, any microorganism or *Pseudomonas* colonization in the sputum ( $p> 0.05$ ). FEV<sub>1</sub>% predicted value was lower in those BR patients with vitamin D deficiency ( $p=0.051$ ) (Figure 2). But, this relationship was not statistically significant. Patients with vitamin D deficiency group were significantly higher mMRC scores than those in the group without vitamin D deficiency ( $p=0.036$ ) (Table 2). Also, the FVC% predicted value was lower in the vitamin D deficient group ( $p=0.02$ ) (Figure 3) and the mean modified Reiff score was higher in the vitamin D deficient group ( $6.9\pm 3.8$  vs.  $4.9\pm 2.7$ ,  $p=0.001$ ) (Table 2).

The first stepwise multivariate model for vitamin D was performed including the variables of the age, gender, BSI, FEV<sub>1</sub>% predicted, FVC% predicted. This model showed that none of these were independently related to vitamin D deficiency. When the Reiff score was added to the model, only Reiff score (OR 1.285 (1.039-1.590),  $p=0.021$ ) was a significant predictor of vitamin D deficiency (Table 3). However, pulmonary function tests results (FEV<sub>1</sub>% predicted and FVC% predicted values) did not indicate an increased risk for vitamin D deficiency.

## Discussion

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

To our knowledge, this is the only study to assess the role of vitamin D deficiency in Turkish adult BR patients. We found that the prevalence of vitamin D deficiency and insufficiency was high among adult BR patients during a stable period. Furthermore, vitamin D deficiency was associated with pulmonary function tests, especially FVC% predicted values. This study is also the first to investigate the influence of vitamin D deficiency on the radiological severity of BR. Our findings show that adult BR patients with vitamin D deficiency had a higher mMRC score and modified Reiff scores compared to vitamin D non-deficient BR patients.

Epidemiological studies suggest that in many countries vitamin D deficiency is prevalent through all age groups, as well as healthy subjects (15). In the National Health and Nutrition Examination Survey 2005 to 2006, 41.6% of adult participants had vitamin D deficiency (19). Vitamin D deficiency is a common problem in Turkey, especially in women, and the elderly (19,20). Some studies reported that the vitamin D concentrations was in the range of  $16.9 \pm 13.09$  (18) to  $21.0 \pm 20.7$  ng/ml in Turkish populations (21). In our study, we found similar mean 25(OH)D concentrations in the healthy control group, but the adult BR patients had lower mean 25(OH)D levels to those reported.

Previous studies have looked at the impact of vitamin D on asthma, chronic obstructive pulmonary diseases (COPD) and tuberculosis (22). One study reported that the prevalence of vitamin D insufficiency was 76% and the deficiency was 23% in adult cystic fibrosis patients (23). Chalmers's et al. investigated 402 adult BR patients and reported that 50% of BR patients were vitamin D deficient, and 43% were insufficient. In a recent study on advanced COPD patients, the prevalence of vitamin D deficiency was between 33% and 77% (24). Monaldi's study showed that serum 25(OH)D levels may be related to low FEV<sub>1</sub> in patients with COPD (24). Another study reported a greater decline in FEV<sub>1</sub>% predicted in the three-year follow-up period in a vitamin D deficient adult BR group compared with a sufficient group (4). Data from the 3<sup>rd</sup> National Health and Nutrition Examinations Survey (n = 14,091) reported that vitamin D levels were related to FEV<sub>1</sub> and FVC (26). Salas et al. showed that vitamin D sufficiency was associated with a reduction in the total number of asthma exacerbations (27). In a recent study, serum vitamin D levels were correlated with low FEV<sub>1</sub>, and FEV<sub>1</sub>% predicted in adult asthma patients. Also, lower vitamin D levels have been linked with uncontrolled asthma (28). There have been no enough studies investigating pulmonary

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100

©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

function tests and vitamin D level in adult BR. Chalmer's et al. showed that the median FEV<sub>1</sub>% predicted value was 68% in a vitamin D deficient group and this result was lower than vitamin D insufficient/sufficient non-CF BR patients (median FEV<sub>1</sub>% predicted value 68% vs. 74.2% vs. 72.2%, p=0.02, respectively) (4). They also reported that FEV<sub>1</sub> decline was higher in a vitamin D deficient group than insufficient/sufficient non-CF BR patients (4). On the other hand, in a recent study from New Zeland, no significant correlation between vitamin D level and FEV<sub>1</sub> or FVC was detected in 32 adult BR patients (9). In our study, reduced FVC% predicted value was associated with lower 25(OH)D concentrations in adult BR patients. But, there was no relationship between reduced FEV<sub>1</sub>% predicted value and vitamin D deficiency.

Chalmers's et al. looked at the relationship between vitamin D deficiency and chronic colonization and disease severity in 402 adult BR patients. The vitamin D deficient group was more frequently chronically colonized with bacteria, especially *Pseudomonas aeruginosa* (4). They also reported that these patients had more frequent exacerbations and worse health-related quality of life. In our study group, 95 patients had sputum culture. There were no significant differences in *Pseudomonas aeruginosa* colonization between the vitamin D deficient and sufficient groups. But in this study, the difference in our study may be due to the numbers of cases.

A randomized controlled trial was to assess the clinical effect of single high dose vitamin D administration in patients with CF hospitalized for exacerbation (29). There was increased one-year survival, hospital-free days and antibiotic therapy-free days in the vitamin D group.

In a recent study, 32 adult BR patients had higher 25(OH) vitamin D level than New Zeland adult population (9). They also investigated vitamin D<sub>3</sub> supplementation and measuring time to first exacerbation and exacerbation frequency. Although the sample size was limited, there was no association between vitamin D levels and exacerbation (9). In this study, we evaluated the relationship between vitamin D deficiency and exacerbation of BR in the previous year and hospitalization in the previous two years. We did not detect any association between vitamin D deficiency and previous exacerbation or hospitalization of BR patients.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

Obesity is a risk factor for vitamin D deficiency because it is a fat-soluble vitamin that is stored in adipose tissue. Adipose tissue reduces the release of vitamin D from the skin into circulation in obese individuals (30). Some studies have noted lower serum vitamin D levels in obese persons and other studies report vitamin D deficiency related to acute coronary syndrome, hypertension, and hyperlipidemia (18,31,32). In the current study, we did not find an association between BMI, comorbidity and vitamin D deficiency.

The mechanisms underlying the role of vitamin D in the pathogenesis of bronchiectasis are unclear. Vitamin D may affect immunity via local pro-inflammatory microenvironment, anti-infective, and anti-inflammatory properties in the airways. Therefore, vitamin D deficiency may play a role in the etiopathogenesis of impaired mucociliary activity, chronic colonization and recurrent infection of airways, namely the “vicious circle hypothesis” (33). Our results show that vitamin D deficient adult BR patients have higher modified Reiff scores indicating that these patients have more severe radiological findings compared to vitamin D non-deficient BR patients. Also, it was found that the mMRC scores increased in BR patients with vitamin D deficiency. Patients with severe disease and more symptoms may have decreased physical activity and tend to spend less time for outdoor activities which in turn may lead to reduce vitamin D production. On the other hand, low vitamin D level is a known factor for impaired immunity, which can contribute to development of recurrent infections in the lung and therefore, BR. However, it’s difficult to explain the association between vitamin D deficiency and the development of BR in adults, as vitamin D level measured at one point in time does not reflect the levels all year around.

In this study, we would like to emphasize that vitamin D insufficiency/deficiency can be detected in chronic respiratory diseases such as BR. Although the role of vitamin D in the pathogenesis of BR is unclear, it may affect clinical and radiological parameters of BR patients. It is important to detect the presence of vitamin D insufficiency/deficiency in BR patients, and proper treatment should be given for these patients. Besides, clinicians may advise expanded sun exposure and increased physical activity to BR patients.

### **Limitations**

There are some limitations to this study. Firstly, the study was conducted in a single center.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

Secondly, some factors that may affect serum vitamin D levels, such as dietary patterns, dressing style, and sun exposure, could not be evaluated.

## **Conclusion**

This study showed that serum vitamin D levels in bronchiectasis patients were less than healthy controls. We found that vitamin D deficiency was commonly seen in adult bronchiectasis patients in a stable period and it might be related to severe radiological findings on chest CT and poorer lung function.

**Acknowledgement:** None

**Author contributions:** Concept-E.Y.N, L.K, M.A.U; Design-E.Y.N, L.K, B.Y, M.A.U; Supervision-G.Ç, M.A.U; Resource-E.Y.N, D.B, B.Y; Materials-E.Y.N, L.K, D.B; Data collection and/or Processing- E.Y.N, D.B; Analysis and/or interpretation- E.Y.N, M.A.U, D.B; Literature Search- E.Y.N, L.K, B.Y; Writing-E.Y.N, L.K, M.A.U; Critical reviews- G.Ç, M.A.U.

**Conflict of interest:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** None

## **References**

1. Wang TT, Nestel FP, Bourdeau V, et al. Cutting edge: 1,25-Dihydroxyvitamin D3 is a direct inducer of antimicrobial peptide gene expression. *J Immunol* 2004;173:2909-2912.
2. Searing DA, Leung DYM. Vitamin D in atopic dermatitis, asthma, and allergic diseases. *Immunol Allergy Clin North Am* 2010;30(3):397-409.
3. Persson LJP, Aanerud M, Hiemstra PS, et al. Chronic obstructive pulmonary disease is associated with low levels of vitamin D. *PLoS One*. 2012;7:e38934. DOI: 10.1371/journal.pone.0038934.
4. Chalmers JD, McHugh BJ, Docherty C, et al. Vitamin D deficiency is associated with chronic bacterial colonization and disease severity in bronchiectasis. *Thorax* 2013;68(1):39-47.
5. Black PN, Scragg R. Relationship between serum 25-hydroxyvitamin d and pulmonary function in the third national health and nutrition examination survey. *Chest* 2005;128:3792-3798.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. *Turk Thorac J* 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

6. Polverino E, Goeminne PC, McDonnell MJ, et al. European Respiratory Guidelines for the management of adult bronchiectasis. *Eur Respir J* 2017;50(3). DOI: 10.1183/13993003.00629-2017.
7. Bartley J, Garrett J, Grant CC, et al. Could vitamin d have potential anti-inflammatory and anti-infective role in bronchiectasis? *Curr Infect Dis Rep* 2013;15:148-157.
8. Herscovitch K, Dauletbaev N, Lands LC. Vitamin D as an anti-microbial and anti-inflammatory therapy for cystic fibrosis. *Paediatr Respir Rev* 2014;15:154-162.
9. Bartley J, Garrett J, Camargo Jr CA, et al. Vitamin D<sub>3</sub> supplementation in adults with bronchiectasis: a pilot study. *Chronic Respir Dis* 2018;15(4):384-392. ).
10. White AJ, Gompertz S, Bayley DL, et al. Resolution of bronchial inflammation is related to bacterial eradication following treatment of exacerbations of chronic bronchitis. *Thorax* 2003;58(8):680-685.
11. Farrell PM, Rosenstein BJ, White TB, et al. Guidelines for diagnosis of cystic fibrosis in newborn through older adults: Cystic Fibrosis Foundation Report. *J Pediatr*. 2008;153(2):4-14.
12. Reiff DB, Wells AU, Carr DH, et al. CT findings in bronchiectasis: limited value in distinguishing between idiopathic and specific types. *AJR Am J Roentgenol* 1995;165:261-267.
13. Chalmers JD, Goeminne P, Aliberti S, et al. The bronchiectasis severity index. *Am J Respir Crit Care Med* 2014;189(5):576-585.
14. McDonnell MJ, Aliberti S, Goeminne PC, et al. Comorbidities and the risk of mortality in patients with bronchiectasis: an international multicenter cohort study. *Lancet Respir Med* 2016;4(12):969-979.
15. Holick MF. Vitamin D deficiency *N Engl J Med* 2007;357:266-281.
16. Gönen MS, Yavuz DG. Osteoporoz ve metabolic kemik hastalıkları tanı ve tedavi klavuzu Bayt Bilimsel Araştırmalar Basın Yayın 2017 Ankara sf119.
17. Satman I, Colak Ozbey N, Boztepe H, et al. (2012). Prevalence and of vitamin D deficiency and association factors in Turkey. *Endocr Rev* 2012;33:349. <http://endocrine-abstracts.org/ea/0032/eposters/ea032p135>.
18. Forrest KY, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. *Nutr Res* 2011;31:48-54.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. *Turk Thorac J* 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

19. Cigerli O, Parildar H, Unal AD, et al. Vitamin D is a problem for adult out-patients? A university hospital sample in Istanbul, Turkey. *Public Health Nutr* 2013;16(7):1306-1313.
20. Hekimsoy Z, Dinç G, Kafesçiler S, et al. Vitamin D status among adults in the Aegean region of Turkey. *BMC Public Health* 2010;10:782.
21. Meral G, Guven A, Uslu A, et al. The prevalence of vitamin D deficiency in children, adolescents and adults in a sample of Turkish population. *Ethno Med* 2016;10(1):71-5. DOI:10.1080/09735070.2016.11905494.
22. Hejazi ME, Modarresi-Ghazani F, Entezari-Maleki T. A review of vitamin D effects on common respiratory diseases: Asthma, chronic obstructive pulmonary diseases and tuberculosis. *J Res Pharm Pract.* 2016;5(1):7-15.
23. Wolfenden LL, Judd SE, Shah R, et al. Vitamin D and bone health in adults with cystic fibrosis. *Clin Endocrinol (Oxf)*. 2008;69(3):374-381.
24. Janssens W, Bouillon R, Claes B, et al. Vitamin D deficiency is highly prevalent in COPD and correlates with variants in the vitamin D-binding gene. *Thorax* 2010;65:215-220.
25. Monadi M, Heidari B, Asghatpour M, et al. Relationship between serum vitamin D and forced expiratory volume in patients with COPD. *Caspian J Intern Med* 2012;3:451-455.
26. Black PN, Scragg R. Relationship between serum 25-hydroxyvitamin D and pulmonary function in the third national health and nutrition examination survey. *Chest* 2005;128:3792-3798.
27. Salas NM, Luo L, Harkins MS. Vitamin D deficiency and adult asthma exacerbations. *J Asthma* 2014;51(9):950-955.
28. Beyhan-Sagmen S, Baykan O, Balcan B, et al. Association between severe vitamin D deficiency, lung function and asthma control. *Arch Bronconeumol* 2017;53(4):186-191.
29. Grossmann RE, Zughaier SM, Kumari M, et al. Pilot study of vitamin D supplementation in adults with cystic fibrosis pulmonary exacerbation: A randomized, controlled trial. *Dermato-Endocrinology* 2012;4:191-197.)
30. Wortsman J, Atsuoka LY, Chen TC, et al. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr.* 2000;72(3):690-693.
31. Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin proc* 2006;81:353-373.

This article has been accepted for publication<sup>12</sup> and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlioğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. *Turk Thorac J* 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

32. Knezevic Pravecek M, Vukovic-Arar Z, Miskic B, et al. Vitamin D deficiency in acute coronary syndrome-Clinically relevant or incidental findings? Cent Eur J Public Health 2017;25(3):185-190.

33. Ishak A, Everard ML. Persistent and recurrent bacterial bronchitis-a paradigm shift in our understanding of chronic respiratory disease. Front Pediatr. 2017;5:19.

Table 1: Baseline characteristics of the study population

	Case Group (n=130)	Control Group (n=73)	p
Age, years	41.9±9.1	45.5±16.7	0.062
Female/ Male	66/64	39/34	0.666
BMI, kg/m <sup>2</sup> *	25.7±2.7	25.4±5.4	0.764
25OH-vitamin D**	14.7±9.6	19.8±6.9	<b>0.001</b>
Vitamin D level***			<b>0.016</b>
Normal	8 (6.2)	6 (8.2)	
Insufficieny	27 (20.8)	27 (37)	
Deficiency	95 (73.1)	40 (54.8)	

\*: Body mass index, \*\*: 25-hydroxyvitamin D, ng/ml, \*\*\*: number (%)

Table 2: Assessment of the clinical, radiological factors in all BR group and 25(OH)D vitamin deficient and sufficient groups.

Items	All BR Patients (n=130)	25(OH)D vitamin ≥20ng/ml (n=35)	25(OH)D vitamin <20ng/ml (n=95)	P
Age, years	41.9±9.1	48.1±16.5	44.7±16.8	0.804
Female/Male,	66/64	19/16	47/48	0.566
BMI, kg/m <sup>2</sup>	25.7±2.7	26.6±5.5	25.1±5.4	0.794
Smoking history				0.099
Non-smoker	80 (61.5)	20 (57.1)	60 (63.2)	
Smoker	23 (17.7)	6 (17.1)	17 (17.9)	
Exsmoker	27 (20.8)	9 (25.7)	18 (18.9)	
Smoking, packs-year	26.5±16.5	29.7±17.6	25.5±16.4	0.421
Comorbidity	39 (30)	12 (34.3)	27 (28.4)	0.514
Dyspnea	112 (88.5)	26 (74.3)	86 (90.5)	0.217

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıoğlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
 ©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)

Cough	106 (81.5)	25 (71.4)	81 (85.3)	0.199
Sputum	83 (63.8)	21 (60)	62 (65.3)	0.535
Haemoptysis	17 (13.1)	5 (14.3)	12 (12.6)	0.771
mMRC	2.3±1.2	1.9±1.1	2.4±1.2	<b>0.036</b>
Duration of diagnosis, years	9.5±7.1	9.1±6.3	9.6±7.3	0.629
BSI	6.9±4.6	6.4±4.8	7.1±4.6	0.926
FEV <sub>1</sub> % predicted	47.8±23.7	54.4±26.3	45.4±22.2	0.051
FVC% predicted	56.0±11.8	62.4±23.1	53.6±21.0	<b>0.021</b>
FEV <sub>1</sub> /FVC	66.3±14.5	65.5±13.7	66.5±14.9	0.678
Modified Reiff score, median (IQR)	6.0(3-9)	4.0 (3-6)	6 (4-9)	<b>0.015</b>
Hemoglobine, g/dL	13.5±1.6	13.6±1.6	1.4±1.5	0.758
Hematocrite, %	41.3±5.5	40.8±7.5	41.5±4.6	0.202
Number of exacerbation in previous year	85 (65.4)	20 (57.1)	65 (68.4)	0.299
Previous hospital admission*	31 (23.8)	7 (20)	24 (25.3)	0.645
Sputum culture positivity**	47/95 (%49.5)	13/23 (%56.5)	34/72 (%47.2)	0.535
P. aeruginosa colonization, n(%)	27 (28.4)	9 (%39.1)	18 (%25)	0.169

Data are represented as means±standard deviation or n (%). BMI: Body mass index, mMRC: Modified Medical Research Council dyspnea scale BSI: Bronchiectasis severity index, IQR: Inter quartile range, \*: Hospitalization with a severe exacerbation in the past 2 years, \*\*: Sputum culture in stable period, 95 BR patients had sputum culture and 48 (50.5%) had negative sputum culture results.

Table 3: Logistic regression analysis for the association between vitamin D deficiency and related factors.

Vitamin D	Odds ratio (95% CI)	p value
Age	1.010 (0.975-1.049)	0.538
Gender (Male)	1.087 (0.307-3.897)	0.960
BSI-mild		0.179
BSI-moderate	0.626 (0.158-2.476)	0.504
BSI-severe	0.223 (0.044-1.144)	0.072
FEV <sub>1</sub> % predicted	1.003 (0.864-1.164)	0.926
FVC% predicted	0.963 (0.845-1.097)	0.600
mMRC		0.365
mMRC (1)	0.452 (0.081-2.521)	0.081
mMRC(2)	7.395 (0.782-69.947)	0.252
mMRC(3)	3.434 (0.416-28.373)	0.252
Modified Reiff Score	1.285 (1.039-1.590)	<b>0.021</b>

BSI: Bronchiectasis severity index, FEV<sub>1</sub>: Forced expiratory volume in 1 second, FVC: Forced vital capacity, mMRC: Modified Medical Research Council Dyspnea Scale.

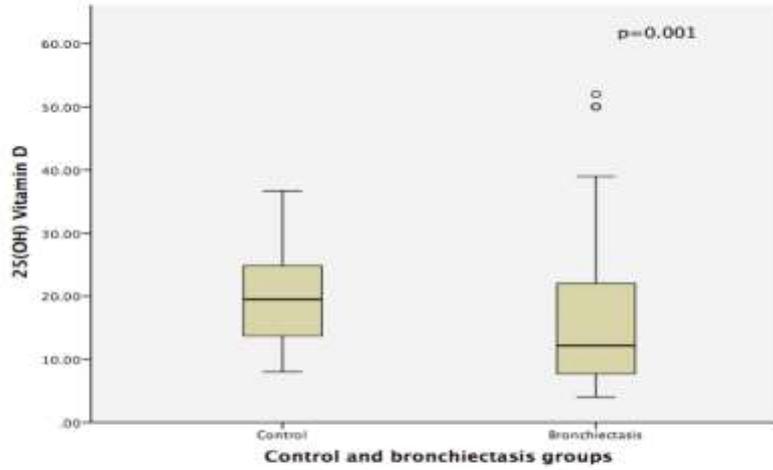


Figure 1: The mean level of 25(OH) vitamin D in control and bronchiectasis groups.

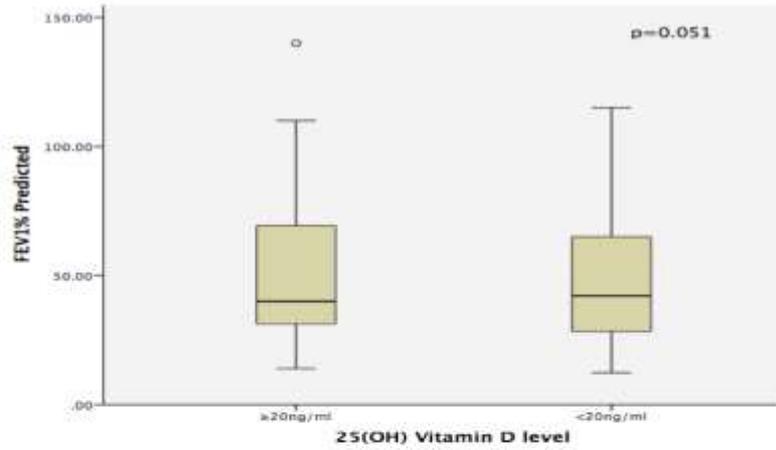


Figure 2: Association between 25(OH) vitamin D level and FEV<sub>1</sub> % predicted values

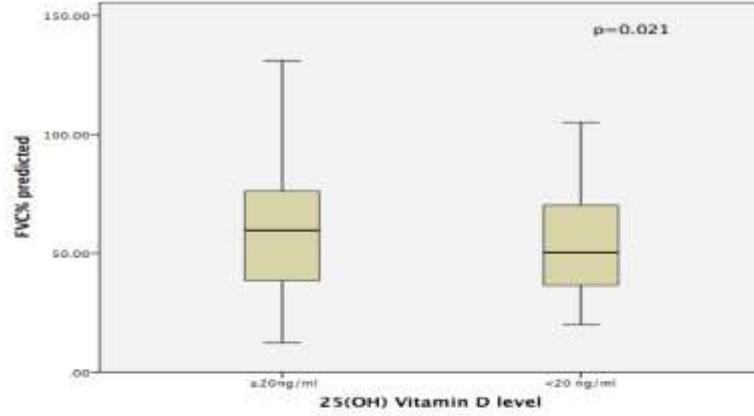


Figure 3: Association between 25(OH) vitamin D level and FVC % predicted values

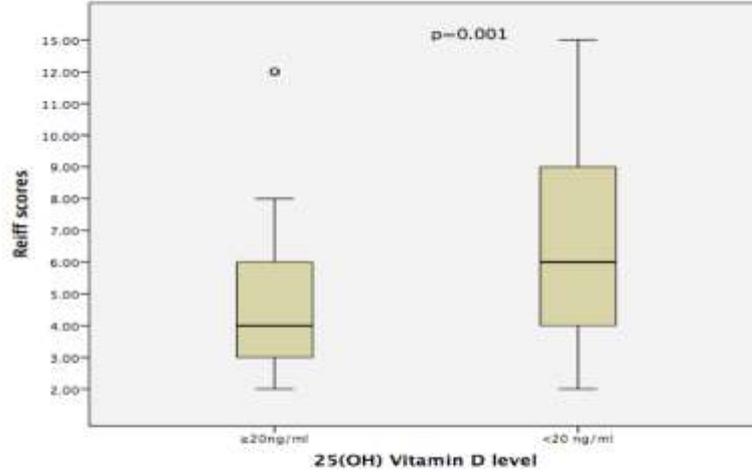


Figure 4: Association between 25(OH) vitamin D level and Reiff scores in bronchiectasis patients.

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Niksarlıođlu EY, Kılıç L, Bilici D, et al. Vitamin D Deficiency and Radiologic Findings in Adult Non-Cystic Fibrosis Bronchiectasis. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2019.18100  
©Copyright 2019 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)