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Vitamin D deficiency as a sign of severity in bronchiectasis

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Abstract

Bronchiectasis is a chronic heterogeneous lung disease with poorly understood pathogenic processes and variable contributing factors. The aim of this study is to assess the prevalence and the impact of vitamin D deficiency in bronchiectasis patients. A cross-sectional study of 40 Baghdad teaching hospital respiratory diseases consultant outpatient clinic patients with verified bronchiectasis was undertaken between 2022 and 2023. 40 healthy, demographically matched controls were also studied. A detailed history, comprehensive physical examination with respiratory emphasis, and vitamin D level evaluation were done. Vitamin D levels were categorized as deficient (< 20 ng/ml), insufficiency (20–29.9 ng/ml), and adequate (≥ 30 ng/ml). Patients were categorized as frequent exacerbates (≥3 times/year) or non-frequent exacerbates (<3 times/year). Symptom intensity was further divided into mild, moderate, and severe. We studied 40 bronchiectasis patients, 21 of them were male and 7 had comorbidities. The mean age, BMI, ESR, and CRP for included patients were 39 years, 23.945 kg/m2, 9.65 ml/hr, and 0.234 mg/dL. Group vitamin levels averaged 19.68 ng/ml. Average annual exacerbation, BSI, Bhalla, and FEV1 scores were 1.95, 6.325, 14.275, and 85.8%. Bronchiectasis patients and healthy controls had similar demographic and clinical features except for vitamin D and CRP. Exacerbation number, BSI score, Bhalla score, and FEV1 correlated with vitamin D but not ESR or CRP. In conclusion, Vitamin D insufficiency is common in bronchiectasis patients and healthy people and is linked to poor symptom severity, radiological abnormalities, and lung function.

Keywords: Bronchiectasis, Vitamin D, Exacerbation, severity, Deficiency

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Introduction

Bronchiectasis is a chronic and complex respiratory condition first described by Laennec in the early 19th century [1-3]. It involves the permanent enlargement and weakening of the bronchial tubes, leading to impaired mucociliary clearance, recurrent infections, and progressive lung damage. This condition results from a vicious cycle of airway inflammation, typically initiated by infection in genetically susceptible individuals, leading to airway destruction, abnormal mucus clearance, and further infection. The disease is characterized by neutrophilic inflammation, with human neutrophil elastase (HNE) playing a central role in tissue damage, and is exacerbated by factors such as

bacterial pathogens and the body's immune response to these pathogens, including the formation of biofilms and neutrophil-mediated damage [4]. The pathogenesis of bronchiectasis remains poorly understood, partly due to the lack of animal models, and is believed to involve interactions between the host's immune system, pathogens, and environmental factors [4]. Notably, vitamin D has been identified as having significant immunomodulatory effects that may influence the disease's progression, including the regulation of pro-inflammatory cytokines and the production of antimicrobial peptides [5,6]. The incidence and prevalence of bronchiectasis have seen a significant increase worldwide over the past decade, with current estimates suggesting varying rates across different populations, age groups, and genders, highlighting its growing impact on global health [7,8]. The disease manifests heterogeneously, with numerous potential causes ranging from infections (bacterial, viral, fungal) to congenital or genetic factors (e.g., cystic fibrosis, primary ciliary dyskinesia), immune disorders, and environmental exposures [9]. The diagnosis of bronchiectasis requires a comprehensive evaluation, including a detailed clinical history, imaging studies (notably high-resolution computed tomography or HRCT), and laboratory tests to identify underlying causes and assess disease severity [10,11]. Management of bronchiectasis is multifaceted and includes antimicrobial therapy to treat acute exacerbations and chronic infection, airway clearance techniques, anti-inflammatory treatments, and in some cases, surgical intervention [12,13]. Despite these approaches, there are no specific therapies approved for bronchiectasis, and treatment guidelines are based on limited evidence [12]. The use of aerosolized antibiotics, though controversial, has been explored for its potential benefits in reducing bacterial load and exacerbations [14,15]. Airway clearance techniques and pharmacologic agents like hyperosmolar solutions and macrolides offer symptomatic relief and may impact disease progression [16,17]. Anti-inflammatory therapies, including novel agents such as brensocatib, are under investigation for their potential to reduce exacerbation rates [18]. The prognosis of bronchiectasis varies widely, influenced by factors such as age, lung function, the presence of chronic infections (notably Pseudomonas aeruginosa), and comorbid conditions [19,20]. Mortality rates in patients with bronchiectasis are higher than those in age-matched controls, with respiratory causes being the predominant factor [44]. Predictive tools like the Bronchiectasis Severity Index (BSI) and FACED score have been developed to assess disease severity and guide management decisions, underscoring the importance of tailored approaches to treatment [19]. **Aim of the study:** To assess the prevalence and the impact of vitamin D deficiency in bronchiectasis patients.

Method

A cross-sectional study conducted between 2022 and 2023 at Baghdad Teaching Hospital's respiratory diseases consultant outpatient clinic analyzed 40 patients with confirmed bronchiectasis and 40 demographically matched healthy controls. The study received approval from the Iraqi Board of Medical Specializations' respiratory diseases department. Participants aged 10 to 70 years with a confirmed diagnosis of bronchiectasis through chronic sputum production, frequent respiratory exacerbations, and high-resolution chest CT scan findings were included. Exclusions were applied

for those outside the age range, unwilling participants, unstable patients, smokers, individuals with severe comorbidities, or those who had taken vitamin D supplements within the last six months. Following informed consent, a detailed history and physical examination focused on the respiratory system were conducted for both patients and controls, along with vitamin D level assessment through fluorescence immunoassay technique, CRP, and ESR evaluations. Vitamin D levels were categorized into deficiency (<20 ng/ml), insufficiency (20–29.9 ng/ml), and sufficiency (≥30 ng/ml) [21]. Patients were classified into frequent exacerbators (≥3 times/year) and non-frequent exacerbators (<3 times/year), with symptom severity assessed using the Bronchiectasis Severity Index (BSI) through an online tool. Radiological findings from high-resolution chest CT scans were scored according to the Bhalla scoring system, and pulmonary function was evaluated by measuring FEV1 and FVC [22]. Statistical analysis involved the Shapiro–Wilk test for data distribution, with mean, ranges, and frequencies for quantitative and qualitative variables, respectively. The Mann-Whitney U and Chi-square tests compared quantitative and qualitative parameters, while the Pearson correlation test assessed parameter associations. One-way ANOVA with post-hoc analysis compared the three groups of bronchiectasis patients. Significance was set at $p<0.05$. Data processing used Microsoft Excel 2010 and SPSS 26.

Results

The study included 40 bronchiectasis patients, comprising 21 males, with 7 presenting comorbid conditions. The average age was 39 years, with a mean Body Mass Index (BMI) of 23.945 kg/m^2, an average Erythrocyte Sedimentation Rate (ESR) of 9.65 ml/hr, and a mean C-Reactive Protein (CRP) level of 0.234 mg/dL. The mean vitamin D concentration among the participants was 19.68 ng/ml. The group's average exacerbation frequency was 1.95 times per year, with a mean Bronchiectasis Severity Index (BSI) score of 6.325, an average Bhalla score of 14.275, and a mean Forced Expiratory Volume in 1 second (FEV1) of 85.8%. Table 1 presents the demographic and laboratory details of the patients enrolled. Significant differences were observed between bronchiectasis patients and healthy controls in terms of vitamin D and CRP levels, with patients showing lower average vitamin D levels (19.68 ng/ml vs. 33.73 ng/ml, p-value = 0.01) and higher CRP levels (0.529 mg/dL vs. 0.187 mg/dL, p-value = 0.002), as illustrated in Table 2 and Figure 1. A noteworthy correlation was identified between the number of exacerbations, BSI score, Bhalla score, and FEV1 with vitamin D levels, whereas no significant correlation was found with ESR or CRP, as detailed in Table 3.

When categorizing bronchiectasis patients based on their vitamin D levels, it was found that those with levels below 20 ng/ml experienced significantly more exacerbations annually (2.75/year) compared to those with levels between 20 ng/ml and 29.9 ng/ml (1.73/year) and those with levels of 30 ng/ml or higher (0.88/year), p-value = 0.0006. Similarly, patients with lower vitamin D levels had higher average BSI scores (8.75) compared to those in the intermediate (5.46) and higher vitamin D categories (4.66), p-value = 0.0001. Furthermore, lower Bhalla scores were observed in the deficient group (11.43) compared to the insufficient (15.73) and sufficient groups (16.88), p-value = 0.02. The

mean FEV1 was also lower in patients with vitamin D deficiency (75.56%) compared to those with insufficient (91.53%) and sufficient levels (94.44%), p-value = 0.0002. Other parameters did not show significant differences among these subgroups, as shown in Table 4.

Table 1.

(Demographics and laboratory parameters of the patients)

Variable	Bronchiectasis patients (n=40) Mean(range)
Age (years) Mean (range)	39(14-70)
Sex (male/female)	21/19
BMI (kg/m^2) Mean (range)	23.945(17-33)
Comorbid diseases (yes/no)	7/33
Vitamin D level (ng/mL) Mean (range)	19.68(6.4-87)
ESR (ml/hr) Mean (range)	11.22(0-55)
CRP (mg/dL) Mean (range)	0.529(0.05-3.1)
Excerabation/year Mean (range)	1.95(0-4)
BSI score Mean (range)	6.325(2-13)
Bhalla score Mean (range)	14.275(3-24)
FEV1 Mean(range)	85.8(62-111)

** BMI; body mass index, ESR; erythrocyte sedimentation rate, CRP; C-reactive protein, BSI; bronchiectasis severity index, FEV1; forced expiratory volume in 1 second*

Table 2.

(Comparison of cases and controls).

Variable	Controls (n=40)	Cases (n=40)	*p*-value
Age(years) Mean(range)	37.8(18-64)	39(14-70)	0.75
Sex (male/female)	20/20	21/19	0.82
BMI(kg/m^2) Mean(range)	24.8(20-30)	23.945(17-33)	0.07
Comorbid diseases (yes/no)	8/32	7/33	0.77
Vitamin D level(ng/mL) Mean(range)	33.73(8-127)	19.68(6.4-87)	0.01
ESR(ml/hr) Mean(range)	9.1(0-45)	11.22(0-55)	0.36
CRP(mg/dL) Mean(range)	0.187(0.03-0.8)	0.529(0.05-3.1)	0.002

**p-value significant less 0.05, BMI; body mass index, ESR; erythrocyte sedimentation rate, CRP; C-reactive protein.*

Figure 1.

(Mean vitamin D levels in bronchiectasis-patients and controls)

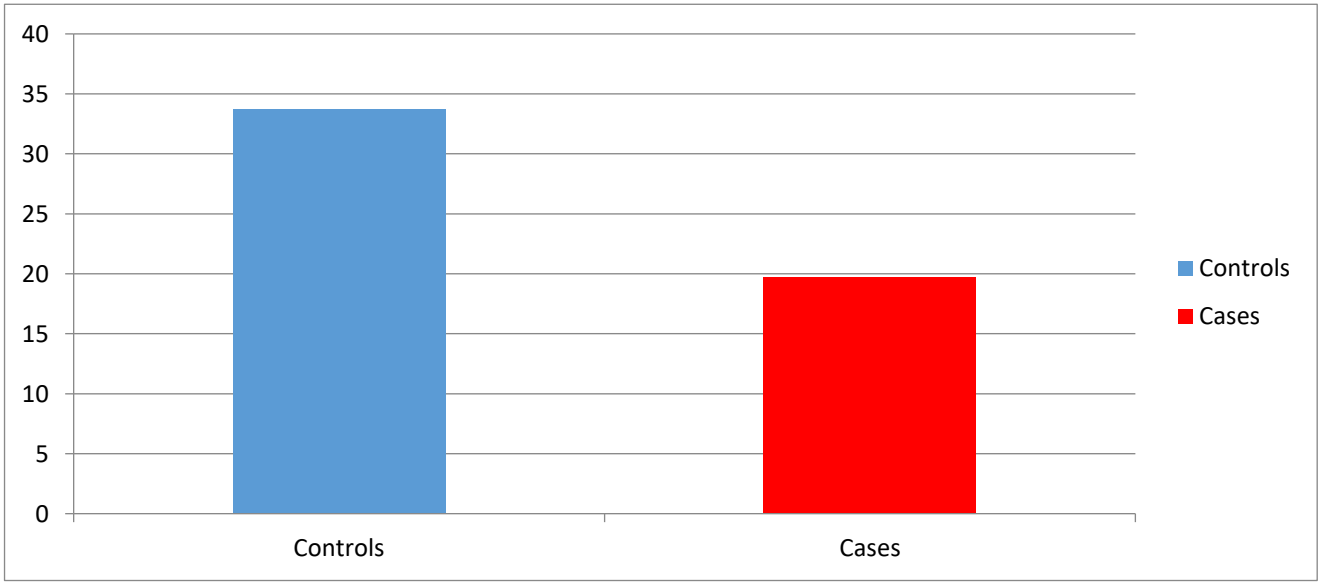

Table 3.

(Pearson correlation for parameters under study)

Variable	Excerabation (R , *p*-value)	BCI score (R , *p*-value)	Bhalla (R , *p*-value)	FEV1 (R , *p*-value)
Vitamin D	-0.4793, 0.001	-0.3328, 0.03	0.3396, 0.03	0.4453, 0.003
ESR	-0.0415, 0.80	0.0988, 0.54	-0.0700, 0 .66	0.1066, 0.51
CRP	-0.2634, 0.10	0.0332, 0.83	0.1943, 0.23	-0.0073, 0.96

**p-value significant less 0.05, , ESR; erythrocyte sedimentation rate, CRP; C-reactive protein*

Table 4.

(Classification of the sample and comparison of subgroups).

Variable	Vitamin D level (ng/mL)			*p*-value
	< 20 (n=16)	≥ 20 to < 30 (n=15)	≥ 30 (n=9)	
Age Mean(range)	43(14-65)	37.33(17-68)	34.55(21-50)	0.34
Sex (male/female)	6/10	11/4	4/5	0.11
BMI Mean(range)	22.48(17-33)	24.66(17-33)	25.33(21-33)	0.24
Comorbid diseases (yes/no)	3/13	2/13	5/4	0.052
ESR Mean(range)	6.875(0-55)	8.6(0-26)	16.33(2-36)	0.12
CRP Mean(range)	0.1975(0.05-0.33)	0.25(0.05-0.45)	0.26(0.15-0.45)	0.36
Exacerbation/year Mean(range)	2.75(1-4)	1.73(0-4)	0.88(0-3)	0.0006(I vs III)
BSI score Mean(range)	8..75(3-13)	5.46(2-11)	4.66(2-9)	0.0001 (I vs II, I vs III)
Bhalla score Mean(range)	11.43(3-24)	15.73(8-21)	16.88(6-22)	0.02(I vs III)
FEV1 Mean(range)	75.56(62-104)	91.53(75-111)	94.44(69-111)	0.0002 (I vs II, I vs III)

**p-value significant less 0.05, BMI; body mass index, ESR; erythrocyte sedimentation rate, CRP; C-reactive protein, BSI; bronchiectasis severity index, FEV1; forced expiratory volume in 1 second*

Discussion

In this study, we observed a 60% prevalence of vitamin D deficiency among bronchiectasis patients, significantly higher than the 50% observed in healthy controls, underscoring Iraq's high deficiency rates [23]. Notably, 50% of control individuals were vitamin D deficient, with another 10% insufficient. This aligns with various Iraqi studies indicating a deficiency range of 60-80% in different cities [24]. Despite Iraq's ample sunlight, vitamin D deficiency prevails, possibly due to insufficient dietary intake, lack of awareness, and limited outdoor activity due to poor respiratory health [23]. Our findings revealed that 77.5% of bronchiectasis patients had low vitamin D levels, echoing previous studies that report a significant association between vitamin D deficiency and bronchiectasis. For instance, Lokesh KS et al. found a 100% deficiency rate among bronchiectasis patients, while another study indicated a deficiency and insufficiency rate of 93.8% among such patients, compared to 91.7% in healthy individuals [25,26]. These observations suggest a critical link between vitamin D status and bronchiectasis, potentially influenced by factors like elevated matrix metalloproteinases, which may deplete vitamin D, and limited sun exposure due to impaired lung function [27]. Contrary to our results, Ferri et al. reported significant correlations between exacerbation frequency, BSI score, Bhalla score, FEV1%, and levels of ESR/CRP, a discrepancy that could stem from our study's small sample size or selection bias [2]. However, our study aligns with others showing significant associations between vitamin D levels and exacerbations, symptom severity, radiological findings, and lung function [26,28]. For example, Niksarlıoğlu et al. highlighted a higher modified Reiff score among vitamin D-deficient patients, indicating a relationship between deficiency and lung health [26]. The role of vitamin D in bronchiectasis pathogenesis remains partially understood, yet its potential anti-inflammatory and anti-infective properties suggest it could play a crucial role. Vitamin D might mitigate tissue damage by lowering pro-inflammatory cytokines and enhancing immunoregulatory ones like IL-8, besides boosting neutrophil function and antimicrobial peptide secretion [29]. This mechanism could explain the observed improvement in lung function and reduction in exacerbations with vitamin D supplementation [30]. Despite these promising findings, the literature presents mixed outcomes regarding vitamin D supplementation in bronchiectasis management. While some studies report improvements in symptom severity, exacerbation frequency, and lung function following supplementation [31], others like Bartley et al. found no significant benefits [32]. This variability underscores the need for further research to elucidate vitamin D's role in bronchiectasis and determine the efficacy of supplementation as a therapeutic strategy. In summary, our study contributes to the growing body of evidence linking vitamin D deficiency to bronchiectasis, reinforcing the hypothesis that vitamin D plays a significant role in the disease's pathogenesis and progression. Given the high prevalence of deficiency in bronchiectasis patients compared to healthy controls, and the potential therapeutic benefits of vitamin D, our findings highlight the importance of addressing vitamin D status in managing bronchiectasis. Further large-scale, controlled studies are necessary to fully understand the impact of vitamin D supplementation on bronchiectasis outcomes [23].

Conclusion

A deficiency in vitamin D is prevalent among both bronchiectasis patients and healthy individuals. It is also associated with unfavorable outcomes in bronchiectasis in terms of the severity of symptoms, radiological findings, and lung functions. Further multi-center studies with an adequate number of patients and an extended follow-up period are advised in order to comprehensively evaluate the correlation between vitamin D status and bronchiectasis. Furthermore, we advise conducting research to assess the efficacy of Vitamin D supplementation in bronchiectasis patients.

Conflict of Interest

No conflicts of interest were declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Ethics Statement

Approved by local committee.

Authors' contributions

All authors shared in the conception design and interpretation of data, drafting of the manuscript critical revision of the case study for intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

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