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Article

Role of Anemia as a Modifier in Cystic and Non-Cystic Fibrosis Patients with Bronchiectasis Concomitant Obstructive Sleep Apnea

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Abstract

(1) **Background:** Anemia and obstructive sleep apnea (OSA) are prevalent comorbidities in bronchiectasis and may share overlapping pathophysiological mechanisms. However, their combined impact on clinical outcomes in bronchiectasis remains underexplored. We aimed to investigate the associations between anemia, OSA, and clinical characteristics in patients with bronchiectasis, including cystic fibrosis (CF) and non-CF subtypes. (2) **Methods:** 70 adults with bronchiectasis (35 CF-related, 35 non-CF) underwent polysomnography. Anemia was defined using standard hemoglobin <13 g/dL for men and <12 g/dL for women. Clinical, nutritional, and sleep-related variables were assessed, and associations with anemia were evaluated. (3) **Results:** Anemia was present in 24.3% of participants. Compared to non-anemic patients, those with anemia had significantly higher rates of female sex (38.5% vs. 6.5%, $p=0.002$), nutritional problems (47.1% vs. 20.8%, $p=0.034$), OSA prevalence (94.1% vs. 54.7%, $p=0.003$), and annual hospitalizations (1.41 ± 0.41 vs. 0.43 ± 0.10 , $p=0.002$). In multivariate analysis, female sex (OR: 12.32; 95% CI: 3.12–45.96; $p=0.002$) and OSA (OR: 4.70; 95% CI: 2.67–45.29; $p=0.007$) remained independent predictors of anemia. Subgroup analysis showed a significant univariate association between OSA and anemia in CF patients ($p=0.045$), while hospitalization frequency was an independent predictor of anemia in non-CF bronchiectasis ($p=0.040$). (4) **Conclusions:** Anemia in bronchiectasis is independently associated with female sex and OSA, with additional subgroup-specific associations. These findings suggest that OSA may contribute to the systemic burden of disease in bronchiectasis and highlight the importance of integrated management strategies.

Keywords: anemia; bronchiectasis; obstructive sleep apnea; cystic fibrosis (CF); clinical outcomes

1. Introduction

Obstructive sleep apnea (OSA) is a prevalent sleep disorder characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to intermittent hypoxia, sympathetic activation, and sleep fragmentation [1,2]. In recent years, there has been growing interest in the prevalence and consequences of OSA in patients with chronic pulmonary diseases, particularly those with bronchiectasis, a condition marked by permanent dilation of bronchi, impaired mucociliary clearance, and chronic airway inflammation [3,4].

Among bronchiectasis subtypes, both cystic fibrosis (CF)-related and non-CF bronchiectasis have been associated with an increased risk of sleep-disordered breathing (SDB) [5]. Structural lung damage,

mucus plugging, and airflow obstruction can compromise nocturnal ventilation and gas exchange, predisposing patients to more severe desaturation events during sleep [6,7]. Prior studies have demonstrated a high prevalence of OSA in these populations, often exceeding that in the general population [8,9].

Furthermore, the pathophysiological burden of OSA may be exacerbated by comorbid systemic conditions such as anemia, which is frequently observed in bronchiectasis patients due to chronic inflammation, recurrent infections, nutritional deficiencies, and in the case of CF, malabsorption syndromes [10,11]. Anemia reduces the blood’s oxygen carrying capacity, which may compound the deleterious effects of OSA-related intermittent hypoxia [10,12,13].

Despite this reasonable pathophysiological synergy, the interaction between anemia and OSA severity on nocturnal hypoxemia in bronchiectasis remains underexplored. Most existing studies have examined these factors in isolation, without evaluating their combined impact on sleep-related oxygenation. Understanding this relationship is crucial, as it may help refine risk stratification and identify novel therapeutic targets to improve sleep and respiratory outcomes in this vulnerable patient group.

This study aims to investigate whether anemia modifies the relationship between OSA and sleep-related hypoxemia in patients with bronchiectasis, hypothesizing that the presence of anemia amplifies nocturnal oxygen desaturation in those with coexisting OSA.

2. Materials and Methods

2.1. Study Design and Participants

This prospective, cross-sectional investigation was carried out between April 2019 and December 2021. Adult patients (aged ≥18 years) diagnosed with bronchiectasis, either CF-related or non-CF—were recruited from the Adult Chest Diseases Outpatient Clinic at Marmara University Pendik Training and Research Hospital (Figure 1). Of the 104 initially eligible individuals, 34 were excluded due to lack of consent for further evaluation, death, or active respiratory infection during the follow-up period. The final study cohort included 70 participants, evenly divided between CF (n=35) and non-CF (n=35) bronchiectasis cases. Anemia was defined using standard hemoglobin thresholds: <13 g/dL for men and <12 g/dL for women. The study received approval from the Marmara University Institutional Ethics Committee (protocol number: 09.2019.503) and adhered to the ethical standards outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants.

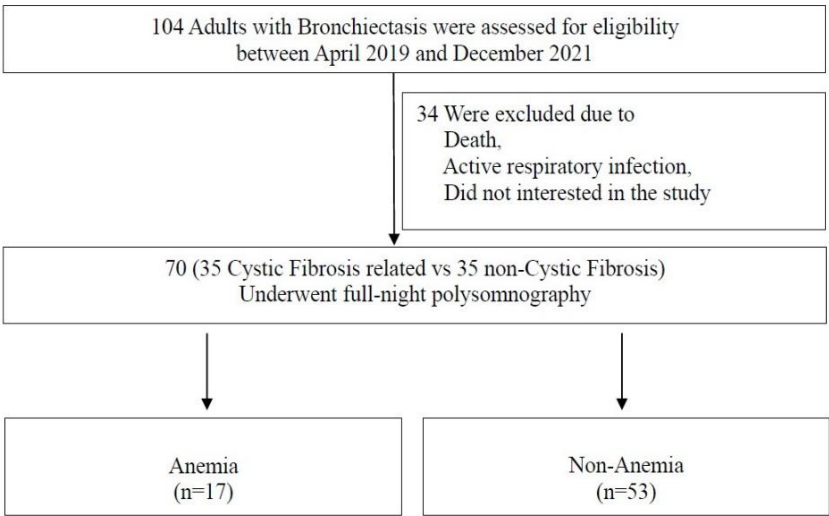


Figure 1. This is a figure. Schemes follow the same formatting.

2.2. Polysomnographic Evaluation

All subjects underwent overnight attended polysomnography (PSG) using the Embletta device (Natus Medical Incorporated, Orlando, USA). The PSG recordings included data on sleep architecture, total sleep duration, nasal airflow, thoracoabdominal movements, body posture, heart rate, oxygen saturation (SpO₂), leg muscle activity, periodic limb movements, and snoring events. In cases where total sleep time was less than 240 minutes, a repeat PSG was offered. Scoring and interpretation were performed according to the American Academy of Sleep Medicine (AASM) criteria by a single trained physician (B.B) to ensure consistency across assessments [14].

2.3. Participant Stratification

As shown in Figure 1, 104 adult patients were screened for eligibility. Following exclusion criteria, 70 patients were included in the analysis, of whom 17 were identified as anemic. All included patients completed an in-laboratory full-night PSG, and only those with a total sleep time exceeding 4 hours were retained for final analysis.

2.4. Assessment Tools

2.4.1. Epworth Sleepiness Scale (ESS)

Daytime sleepiness was evaluated using the validated Turkish version of the ESS, a self-report questionnaire composed of eight items scored from 0 to 3. The cumulative score ranges from 0 to 24, with scores ≥ 11 indicating excessive daytime sleepiness (EDS) [15].

2.4.2. Charlson Comorbidity Index

This scoring system was applied to quantify each participant's comorbid burden, serving as a predictor of 1-year mortality risk. Higher scores represent more severe comorbid conditions [16].

2.4.3. Modified Medical Research Council (mMRC) Dyspnea Scale

Participants' perceptions of breathlessness were assessed using the mMRC scale, a 5-point tool ranging from 0 (no breathlessness) to 4 (severe dyspnea during minimal exertion) [17].

2.4.4. Zung Self-Rating Depression Scale (SDS)

The presence of depressive symptoms was determined at baseline using the Turkish version of the Zung SDS [18]. This self-administered instrument contains 20 items, each rated on a 4-point scale from 1 ("a little of the time") to 4 ("most of the time"). Reverse scoring was applied to items 2, 5, 6, 11, 12, 14, 16, 17, 18, and 20. Scores ≥ 40 were considered indicative of depression. All responses were entered into the study database by a designated investigator.

2.5. Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean $\pm$ standard deviation (SD) if normally distributed or as median with interquartile range (IQR) if not. Categorical data were expressed as counts and percentages, along with 95% confidence intervals (CI). Comparisons between groups were conducted using the t-test for normally distributed continuous variables, the Mann-Whitney U test for non-normally distributed data, and the chi-square test (or Fisher's exact test when appropriate) for categorical variables. Logistic regression models were employed to examine associations between sleep apnea and clinical variables, with results reported as odds ratios (ORs) and 95% confidence intervals. All tests were two-tailed, and statistical significance was defined as a p-value < 0.05 .

3. Results

3.1. Demographics, Clinical, and Sleep Related Characteristics

As shown in Table 1, 17 participants had anemia, while 53 did not. Notably, the proportion of female participants was significantly higher in the anemia group compared to the non-anemia group (38.5% vs. 6.5%; $p=0.002$). Furthermore, nutritional problems were more frequently reported by patients with anemia (47.1% vs. 20.8%; $p=0.034$). The prevalence of OSA was also significantly greater in the anemia group (94.1% vs. 54.7%; $p=0.003$). Additionally, hospitalization rates per year were markedly higher among anemic patients (1.41 ± 0.41 vs. 0.43 ± 0.10 ; $p=0.002$). In contrast, the mean age was nearly identical between the two groups, and there was no significant difference in body mass index (BMI) or smoking status. Comorbidities such as diabetes, pancreatic disease, cardiac disease, and oxygen supplementation use were similar between groups. Measures of daytime sleepiness also did not differ significantly; although the anemia group had a higher mean ESS score, this difference did not reach statistical significance, and subjective sleepiness was also comparable. There were no significant group differences in dyspnea severity MMRC, Charlson Comorbidity Index, or disease duration. Although patients with anemia experienced more frequent exacerbations per year, the difference was not statistically significant. Similarly, depressive symptoms measured by the SDS score were higher in the anemia group but not significantly so. Polysomnographic parameters, including total sleep time, sleep efficiency, sleep latency, and REM latency were not significantly different between the groups. Similarly, no significant AHI, ODI, average and lowest oxygen saturation, or the duration and percentage of time spent with $SpO_2 < 90\%$. Finally, although the average heart rate tended to be higher in the anemia group this did not reach statistical significance.

Table 1. Comparison of the evaluated variables among the bronchiectasis adults with and without anemia (n=70).

Variables	Anemia (17)	Non-Anemia (53)	<i>p Value</i>
Age	29.65 ± 9.12	29.81 ± 9.12	0.960
Female sex, %	38.5	6.5	0.002
BMI, kg/m ²	21.13 ± 4.16	22.91 ± 4.18	0.131
Current or former smoker,%	5.9	15.1	0.323
Nutrition support, %	47.1	20.8	0.034
Diabetes Mellitus, %	17.6	13.2	0.649
Pancreatic disease, %	47.1	37.7	0.495
Cardiac disease, %	0.0	3.8	0.416
Oxygen supply, %	5.9	3.8	0.709
ESS	5.65 ± 3.93	3.87 ± 3.35	0.072
Sleepy, %	11.8	5.7	0.395
OSA, %	94.1	54.7	0.003
mMRC	1.29 ± 0.47	1.32 ± 0.51	0.849
Charlson	0.29 ± 0.18	0.71 ± 0.09	0.683
Exacerbation count/year	2.12 ± 1.57	1.49 ± 1.25	0.096
Hospitalization /year	1.41 ± 0.41	0.43 ± 0.10	0.002
Duration	17.71 ± 9.06	17.79 ± 8.21	0.971
Zung SDS score	44.24 ± 13.21	40.85 ± 10.43	0.280
TST	349.41 ± 71.23	360.90 ± 68.59	0.565
Sleep efficiency	78.47 ± 11.68	80.48 ± 13.26	0.579
Sleep latency	44.06 ± 15.01	29.80 ± 3.54	0.178
REM latency	155.29 ± 62.93	138.46	0.413
AHI	9.08 ± 5.50	7.24 ± 6.40	0.289
ODI	7.54 ± 5.93	5.83 ± 5.18	0.829
Average Saturation	92.73 ± 3.45	93.29 ± 3.09	0.528
Lowest saturation	86.41 ± 4.47	87.67 ± 5.71	0.407
SpO ₂ < 90%, perc	15.57 ± 7.86	12.41 ± 3.84	0.699
SpO ₂ < 90%, min	33.35 ± 18.32	24.32 ± 7.81	0.722
Average heart rate	71.89 ± 9.60	67.66 ± 8.56	0.090

Definition of abbreviations: AHI=apnea-hypopnea-index; BMI=body mass index; ESS=Epworth sleepiness scale; mMMRC= modified medical research council; ODI=oxygen desaturation index; OSA=obstructive sleep apnea; REM=rapid eye movements; SDS=self-related depression score; TST=total sleep time.

3.2. Factors Associated with Anemia in Adults with Bronchiectasis

As presented in Table 2, In the univariate analysis, female gender was strongly associated with anemia (OR: 9.06; 95% CI: 1.88–43.62; p=0.006). In addition, hospitalization frequency was significantly associated with anemia (OR:1.99; 95% CI: 1.21–3.23; p=0.006). Nutritional support also showed a significant association (OR: 3.39; 95% CI: 1.06–10.83; p=0.039). Lastly, OSA was significantly associated with anemia (OR: 3.42; 95% CI: 1.64–7.21; p=0.015). Several other variables were not significantly associated with anemia in either model. These included age, BMI, and smoking status. Neither CF status nor pancreatic disease showed significant associations. Disease duration, MMRC dyspnea score, Charlson Comorbidity Index, and comorbidities such as diabetes mellitus and oxygen therapy use were also not significantly linked to anemia. Although ESS score and average heart rate showed a trend toward association (ESS: OR: 1.14; p = 0.080; heart rate: OR: 1.05; p = 0.095), these did not reach statistical significance. Additionally, no significant associations were found for polysomnographic parameters, including total sleep time, sleep efficiency, sleep latency, AHI, ODI, average or lowest oxygen saturation, or duration of desaturation below 90%. In the multivariate analysis, after adjusting for potential confounders, female gender remained a independent predictor of anemia (OR: 12.32; 95% CI: 3.12–45.96; p=0.002). Similarly, OSA continued to be significantly associated with anemia (OR: 4.70; 95% CI: 2.67–45.29; p=0.007). Hospitalization and nutritional support, while significant in univariate analysis, did not retain significance after adjustment.

Table 2. Associates of anemia in the participants with bronchiectasis (n=70).

	OR	95 % CI	p Value
<i>Univariate</i>			
Age, years	0.99	0.95 – 1.08	0.960
Female gender	9.06	1.88 – 43.62	0.006
Cystic fibrosis	1.60	0.53 – 4.83	0.405
BMI, kg/m ²	0.88	0.76 – 1.04	0.134
Current or former smoker	0.35	0.04 – 3.04	0.342
Disease duration	0.99	0.93 – 1.07	0.970
MMRC score	0.89	0.29 – 2.73	0.847
Charlson score	0.84	0.37 – 1.91	0.679
Exacerbation count	1.39	0.94 – 2.09	0.102
Hospitalization	1.99	1.21 – 3.23	0.006
Nutrition support	3.39	1.06 – 10.83	0.039
Diabetes mellitus	1.40	0.32 – 6.18	0.650
Pancreatic disease	1.46	0.48 – 4.42	0.496
Oxygen supply use	1.59	0.14 – 18.75	0.711
Sleepy (ESS ≥ 10)	2.22	0.34 – 14.56	0.405
ESS score	1.14	0.98 – 1.32	0.080
Zung SDS score	1.03	0.98 – 1.08	0.277
TST	0.99	0.99 – 1.01	0.549
Sleep Efficiency	0.98	0.95 – 1.03	0.574
Sleep latency	1.01	0.99 – 1.02	0.217
AHI	1.05	0.96 – 1.13	0.291
ODI	0.99	0.92 – 1.07	0.890
OSA	3.42	1.64 – 7.21	0.015
Mean saturation	0.95	0.79 – 1.21	0.523
Lowest saturation	0.96	0.87 – 1.06	0.403
O2 saturation < 90%	1.04	0.98 – 1.02	0.694
Heart rate	1.05	0.99 – 1.12	0.095
<i>Multivariate</i>			
Age	0.98	0.93 – 1.05	0.660

Female gender	12.32	3.12 – 45.96	0.002
Hospitalization	1.10	0.49 – 2.42	0.813
Nutrition support	5.48	0.64 – 47.42	0.122
OSA	4.70	2.67 – 45.29	0.007

Definition of abbreviations: AHI=apnea-hypopnea-index; BMI=body mass index; CI=confident interval; ESS=Epworth sleepiness scale; mMMRC= modified medical research council; ODI=oxygen desaturation index; OSA=obstructive sleep apnea; REM=rapid eye movements; SDS=self-related depression score; TST=total sleep time.

3.3. Factors Associated with Anemia in Participants with Cystic Fibrosis

As demonstrated in Table 3, In the univariate analysis, OSA was found to be significantly associated with anemia among CF participants (OR: 1.24; 95% CI: 1.88–12.25; p = 0.045). Female gender was related with anemia, but did not reach statistical significance. Hospitalization frequency (OR: 1.68; p = 0.093) and Zung SDS score for depressive symptoms (OR: 1.06; p = 0.094) also showed borderline associations. Other clinical and demographic characteristics such as age, BMI, smoking status, disease duration, MMRC score, Charlson index, diabetes, and nutritional support were not significantly associated with anemia. Likewise, subjective sleepiness and ESS score itself did not reach statistical significance. Polysomnographic parameters, including total sleep time, sleep efficiency, sleep latency, AHI, ODI, and oxygen saturation metrics, did not show meaningful associations with anemia. In the multivariate model, no variables remained statistically significant. OSA lost its significance (OR: 1.03; 95% CI: 0.98–1.13; p = 0.660), and neither female gender (OR: 1.01; p = 0.217) nor age (OR: 1.27; p = 0.740) independently predicted anemia among CF patients.

Table 3. Associates of anemia in participants with Cystic Fibrosis (n=35).

	OR	95 % CI	p Value
<i>Univariate</i>			
Age, years	1.09	0.94 – 1.29	0.250
Female gender	4.33	0.76 – 24.61	0.098
BMI, kg/m²	0.91	0.70 – 1.17	0.452
Current or former smoker	2.66	0.15 – 47.30	0.504
Disease duration	0.97	0.87 – 1.08	0.642
MMRC score	1.27	0.29 – 5.49	0.748
Charlson score	0.79	0.13 – 4.79	0.799
Exacerbation count	1.51	0.79 – 2.87	0.206
Hospitalization	1.68	0.91 – 3.08	0.093
Nutrition support	2.25	0.50 – 10.05	0.288
Diabetes mellitus	0.79	0.13 – 4.79	0.799
Sleepy (ESS ≥ 10)	6.00	0.78 – 75.44	0.165
ESS score	1.16	0.95 – 1.40	0.131
Zung SDS score	1.06	0.99 – 1.13	0.094
TST	1.00	0.98 – 1.03	0.884
Sleep Efficiency	1.02	0.95 – 1.06	0.948
Sleep latency	1.01	0.99 – 1.03	0.279
AHI	1.03	0.92 – 1.15	0.555
ODI	1.02	0.93 – 1.08	0.959
OSA	1.24	1.88 – 12.25	0.045
Mean saturation	0.99	0.94 – 1.05	0.874
Lowest saturation	0.96	0.85 – 1.09	0.575
O2 saturation < 90%	1.00	0.98 – 1.03	0.760
<i>Multivariate</i>			
Age	1.27	0.29 – 5.79	0.740
Female Gender	1.01	0.99 – 1.02	0.217
OSA	1.03	0.98 – 1.13	0.660

Definition of abbreviations: AHI=apnea-hypopnea-index; BMI=body mass index; CI=confident interval; ESS=Epworth sleepiness scale; mMMRC= modified medical research council; ODI=oxygen desaturation index; OSA=obstructive sleep apnea; REM=rapid eye movements; SDS=self-related depression score; TST=total sleep time.

3.4. Factors Associated with Anemia in Bronchiectasis Patients (Excluding Cystic Fibrosis)

As shown in Table 4, In the univariate analysis, hospitalization frequency, and OSA (OR: 4.50; 95% CI: 0.47–42.5; p=0.049) was significantly associated with anemia (OR: 2.85; 95% CI: 1.01–8.01; p=0.046). Other variables, including age, female gender, and BMI were not significantly associated with anemia. Additional clinical parameters such as smoking status, disease duration, MMRC score, Charlson index, and diabetes mellitus did not show meaningful associations. While nutritional support showed a trend toward increased anemia risk (OR: 3.80; p=0.091), this did not reach statistical significance. Subjective sleep-related variables like ESS score, and mood symptoms measured via Zung SDS score, were not significantly linked to anemia. Similarly, polysomnographic measures such as total sleep time, sleep efficiency, sleep latency, AHI, ODI, and oxygen saturation metrics did not differ significantly between those with and without anemia. In the multivariate model, after adjusting for age and OSA, hospitalization remained an independent predictor of anemia (OR: 3.69; 95% CI: 1.06–12.84; p=0.040), OSA did not retain significance (OR: 1.12; 95% CI: 0.96–1.31; p=0.136).

Table 4. Associates of anemia in participants with Bronchiectasis patients (n=35).

	OR	95 % CI	p Value
Univariate			
Age, years	0.99	0.94 – 1.05	0.828
Female gender	0.94	0.81 – 1.26	0.987
BMI, kg/m ²	0.88	0.72 – 1.09	0.249
Current or former smoker	0.99	0.82 – 1.76	0.997
Disease duration	0.99	0.90 – 1.09	0.907
MMRC score	0.61	1.02 – 3.76	0.602
Charlson score	0.91	0.35 – 2.37	0.852
Exacerbation count	1.27	0.73 – 2.20	0.381
Hospitalization	2.85	1.01 – 8.01	0.046
Nutrition support	3.80	0.81 – 24.29	0.091
Diabetes mellitus	4.50	0.24 – 82.56	0.311
ESS score	1.10	0.87 – 1.40	0.395
Zung SDS score	0.98	0.90 – 1.07	0.699
TST	0.99	0.98 – 1.01	0.355
Sleep Efficiency	0.97	0.91 – 1.04	0.399
Sleep latency	1.01	0.98 – 1.03	0.682
AHI	1.07	0.93 – 1.22	0.353
ODI	0.91	0.72 – 1.14	0.430
OSA	4.50	0.47 – 42.5	0.049
Mean saturation	1.19	0.79 – 1.80	0.395
Lowest saturation	0.97	0.80 – 1.17	0.773
O2 saturation < 90%	0.98	0.89 – 1.08	0.716
Heart rate	0.96	0.79 – 1.18	0.725
Multivariate			
Age	1.02	0.94 – 1.07	0.947
Hospitalization	3.69	1.06 – 12.84	0.040
OSA	1.12	0.96 – 1.31	0.136

Definition of abbreviations: AHI=apnea-hypopnea-index; BMI=body mass index; CI=confident interval; ESS=Epworth sleepiness scale; mMMRC= modified medical research council; ODI=oxygen desaturation index; OSA=obstructive sleep apnea; REM=rapid eye movements; SDS=self-related depression score; TST=total sleep time.

4. Discussion

This study reveals important associations between anemia and clinical, nutritional, and sleep-related characteristics in a bronchiectasis cohort. Our findings suggest that anemia may be linked to several adverse outcomes, including a higher prevalence of obstructive sleep apnea (OSA), increased hospitalization rates, and more frequent nutritional challenges.

The significantly higher proportion of female participants in the anemia group aligns with well-established epidemiological data showing that anemia is more prevalent among women due to factors such as menstruation, pregnancy, and iron deficiency [19,20]. This sex-based disparity may also reflect broader biological and sociocultural influences that affect healthcare access and nutritional status. Nutritional deficiencies were more commonly reported among patients with anemia, consistent with the known etiological relationship between inadequate intake or absorption of micronutrients—particularly iron, folate, and vitamin B12—and the development of anemia [21]. In bronchiectasis patients, systemic inflammation and malabsorption may further exacerbate these deficiencies.

One of the most striking findings of our study is the significantly higher prevalence of OSA among patients with anemia and significant association OSA with anemia. This association aligns with prior research, for example, Khan et al. noted that in elderly patients, OSA treatment significantly changed hemoglobin and hematocrit levels, supporting a model where OSA-related hypoxia and inflammation influence erythropoiesis and anemia pathogenesis [22]. Another study demonstrated that serum ferritin—an inflammatory and iron-storage biomarker—correlated positively with OSA severity, independent of BMI, suggesting systemic inflammation and iron dysregulation as meeting points between OSA and anemia [23]. Further, a large NHANES cohort study found a U-shaped association between ferritin levels and OSA risk, supporting the view that both iron deficiency and inflammatory excess contribute to disease interplay in overweight/obese individuals [24]. Finally, emergent research highlights that anemia and OSA may interact synergistically in influencing comorbid conditions like hypertension, rather than a simple unidirectional effect [25]. Together, these lines of evidence support the hypothesis that OSA and anemia are interconnected via mechanisms such as hypoxia-induced erythropoietin alterations, systemic inflammation, and iron metabolism disruption, potentially amplifying each other's clinical impact, all of which can contribute to impaired red blood cell production and anemia [22,26]. Although hospitalization frequency and nutritional support were significantly associated with anemia in univariate analysis, these associations did not persist in the adjusted model. This attenuation may reflect confounding by OSA or sex, or it may indicate that hospitalization and malnutrition act as mediators or downstream consequences rather than independent predictors. Nonetheless, their initial significance highlights the broader systemic impact of anemia in chronic lung disease and warrants further investigation. No significant associations were found between anemia and other clinical parameters as well as polysomnographic indices such as AHI, ODI, or nocturnal desaturation, suggesting that the presence of OSA itself—rather than its severity—may be a more relevant predictor of anemia risk. This supports a potential threshold effect, where even mild OSA may trigger inflammatory and hypoxic processes sufficient to alter erythropoiesis [27].

Among CF participants, OSA was significantly associated with anemia in univariate analysis (OR: 1.24; $p = 0.045$). While this represents the only univariate predictor reaching significance, it aligns with evidence showing high prevalence of anemia and iron deficiency in adult CF patients—often related to malabsorption and vitamin deficiency (e.g., iron, folate, B₁₂). One study reported anemia in ~33% of CF adults, with 90% of vitamin-deficient patients being anemic ($p = 0.02$), and iron deficiency common in evaluated cases [28]. These findings suggest a potential but not definitive link between OSA and anemia in CF, underscoring the need for larger studies to clarify this relationship.

In non-CF bronchiectasis, both OSA (OR: 2.85; $p = 0.046$) and hospitalization frequency (OR: 4.50; $p = 0.049$) were significantly associated with anemia in univariate analysis. However, only hospitalizations remained an independent predictor in the multivariate model (OR: 3.69; $p = 0.040$), while OSA lost significance. This supports previous observations that anemia in bronchiectasis is linked with greater disease severity and healthcare utilization—studies report anemia prevalence in

bronchiectasis up to ~65%, with associated low serum iron levels and inflammatory markers in affected patients [29,30]. Taken together, increased hospitalizations may serve as a robust indicator of anemia risk in non-CF bronchiectasis populations.

Limitations

Several limitations should be acknowledged. First, the cross-sectional design of the study precludes any causal inference regarding the relationship between anemia and OSA. Longitudinal studies are needed to clarify temporal and directional associations. Second, the sample size—particularly in subgroup analyses—was relatively small, which may have limited the statistical power to detect associations and led to wide confidence intervals in multivariate models. Third, anemia etiology was not specifically stratified (e.g., iron deficiency vs. anemia of chronic disease), and no direct laboratory markers such as ferritin, transferrin saturation, or vitamin B12 were included, which could have strengthened mechanistic interpretation. Additionally, although polysomnographic scoring was conducted by a single trained physician to minimize variability, there remains the possibility of scoring bias. Finally, generalizability may be limited, as all participants were recruited from a single tertiary referral center with advanced bronchiectasis care, possibly reflecting more severe phenotypes.

5. Conclusions

This study provides new insights into the relationship between anemia and obstructive sleep apnea (OSA) in patients with bronchiectasis, including both cystic fibrosis (CF)-related and non-CF etiologies. Anemia was significantly more prevalent in patients with OSA and was independently associated with female sex and OSA in the overall bronchiectasis cohort. In subgroup analyses, OSA was also associated with anemia in patients with CF, while in non-CF bronchiectasis, hospitalization frequency emerged as the strongest independent predictor. These findings highlight the multifactorial nature of anemia in bronchiectasis and underscore the potential contribution of sleep-disordered breathing to its pathogenesis. Clinically, the results suggest that evaluating and addressing OSA may have implications beyond sleep quality, potentially influencing systemic comorbidities such as anemia. Future longitudinal and interventional studies are warranted to determine whether targeted management of OSA or anemia can yield improvements in respiratory, hematologic, and overall functional outcomes in this population.

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Abbreviations

AASM	American Academy of Sleep Medicine
AHI	Apnea–Hypopnea Index

BMI	Body Mass Index
CF	Cystic Fibrosis
CI	Confidence Interval
EDS	Excessive Daytime Sleepiness
ESS	Epworth Sleepiness Scale
g/dL	grams per deciliter
IBM	International Business Machines
IQR	Interquartile Range
mMRC	Modified Medical Research Council
NHANES	National Health and Nutrition Examination Survey
ODI	Oxygen Desaturation Index
OR	Odds Ratio
OSA	Obstructive Sleep Apnea
PSG	Polysomnography
REM	Rapid Eye Movement
SDB	Sleep-Disordered Breathing
SD	Standard Deviation
SDS	Zung Self-Rating Depression Scale
SpO ₂	Peripheral Oxygen Saturation

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