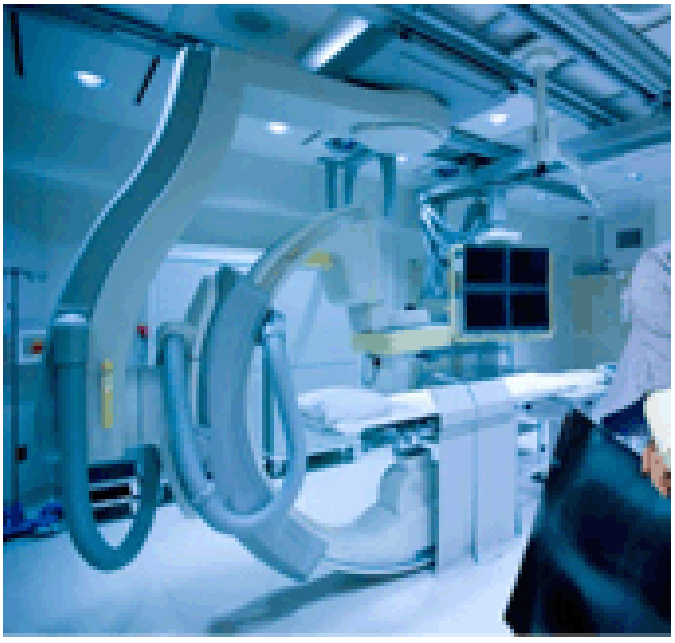

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Oropharyngeal Microbiota Composition and Antibiotic Resistance Patterns in Patients with Chronic Obstructive Pulmonary Disease: A Single-Center Study

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Abstract **Background:** Chronic obstructive pulmonary disease (COPD) is associated with dysbiosis of the respiratory microbiota, which may drive airway inflammation and antimicrobial resistance. Regional data from Central Asia remain scarce. **Objective:** To characterize the oropharyngeal microbiota composition and antibiotic resistance profiles in hospitalized COPD patients at a tertiary center in Uzbekistan. **Methods:** A cross-sectional descriptive study was conducted in 41 COPD patients (mean age 61.4 ± 12.0 years; range 36-86 years; 61.0% male) admitted to the Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation, Tashkent, from January 2023 through March 2026. Oropharyngeal swabs were analyzed by standard culture and MALDI-TOF MS identification; antibiotic susceptibility was tested by disk diffusion according to EUCAST criteria. Antibiotics were selected to represent locally used empirical agents for respiratory infections and major antimicrobial classes relevant for Gram-positive and Gram-negative respiratory pathogens. **Results:** Pathogenic flora was detected in 35/41 patients (85.4%); 10 (24.4%) had polymicrobial infection (≥2 organisms). A total of 46 isolates were identified: *Streptococcus mitis* (n=22; 47.8%), *Staphylococcus aureus* (n=14; 30.4%), *Streptococcus pneumoniae* (n=3; 6.5%), *Klebsiella pneumoniae* (n=3; 6.5%), *Gemella haemolysans* (n=2; 4.3%), *Candida albicans* (n=1), and *Pseudomonas aeruginosa* (n=1). *Streptococcus mitis* showed 100% resistance to ceftazidime, gentamicin, amikacin, and ciprofloxacin, and 95% to co-trimoxazole, with retained susceptibility to chloramphenicol, vancomycin, and tetracyclines (100%, 100%, and 91%, respectively). *Staphylococcus aureus* demonstrated universal penicillin resistance and high macrolide resistance (71%), while remaining fully susceptible to vancomycin. **Conclusions:** Hospitalized COPD patients at this Uzbek tertiary center harbored a high burden of oropharyngeal pathogenic microbiota with clinically important multidrug resistance, particularly to aminoglycosides, fluoroquinolones, cephalosporins, and macrolides. Because this was a single-center descriptive study with a small and heterogeneous sample, the findings should be interpreted as local and hypothesis-generating. Microbiological surveillance and antibiotic stewardship are urgently needed.

Keywords COPD, Oropharyngeal microbiota, Antibiotic resistance, *Streptococcus mitis*, *Staphylococcus aureus*, MALDI-TOF, Uzbekistan, Central Asia

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity, hospitalization, and premature death globally, affecting an estimated 391 million adults and accounting for approximately 3.2 million deaths annually [1]. In low- and middle-income countries, including those of Central Asia, COPD prevalence is driven by a high burden of tobacco smoking, occupational exposures to dust and biomass fumes, and suboptimal access to pulmonary function testing and specialist care [2,3].

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The role of the respiratory microbiome in COPD pathogenesis has received increasing attention over the past decade. The lungs are not sterile organs; microbial communities inhabiting the oropharynx can be aspirated into the lower airways, contributing to the persistent low-grade inflammation that characterizes COPD [4,5]. During acute exacerbations of COPD (AECOPD), which account for the majority of disease-related hospitalizations and costs, bacterial colonization and infection are implicated in a substantial proportion of episodes [6]. Identifying etiological agents and their resistance profiles is essential for guiding empirical antibiotic therapy.

The oropharynx serves as a microbiological interface between the oral cavity and the lower respiratory tract. In health, it harbors a diverse commensal flora dominated by viridans streptococci, *Neisseria spp.*, *Haemophilus spp.*,

and other oral organisms [7]. In COPD, chronic inflammation, mucociliary dysfunction, corticosteroid exposure, and recurrent antibiotic courses may promote an ecological shift toward potentially pathogenic species including *Streptococcus pneumoniae*, *Staphylococcus aureus*, Gram-negative enteric bacilli, and *Pseudomonas aeruginosa* [8,9]. This dysbiosis may contribute to exacerbation risk and may select for antibiotic-resistant organisms, threatening the efficacy of standard treatment.

Despite its clinical relevance, microbiological data on oropharyngeal flora in COPD patients from Uzbekistan and Central Asia are limited in the international literature. Understanding local pathogen ecology and resistance patterns is critical for developing local empirical-treatment policies. This study therefore aimed to characterize the composition and antibiotic resistance profiles of oropharyngeal microbiota in hospitalized COPD patients at a tertiary referral center in Tashkent, Uzbekistan. The findings are intended to describe this single-center cohort and should not be generalized to all populations without confirmation in larger multicenter studies.

2. Materials and Methods

2.1. Study Design and Setting

A single-center, cross-sectional descriptive study was conducted at the Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation (RSSPMC), Tashkent, Uzbekistan, a national tertiary referral hospital for pulmonology and internal medicine. Consecutive eligible admissions from January 2023 through March 2026 were reviewed. The period is presented with full years to avoid ambiguity in the date range.

2.2. Study Population

Inclusion criteria were adult patients (≥18 years) with a physician-confirmed diagnosis of COPD admitted to the pulmonology department during the study period and available oropharyngeal microbiological sampling at admission. Exclusion criteria were systemic antibiotic therapy within 4 weeks preceding admission, concurrent active pulmonary tuberculosis or lung malignancy, absence of microbiological data, and age <18 years. A total of 41 patients met the inclusion criteria and were enrolled consecutively. Patients were not selected or matched by sex; therefore, sex distribution was reported descriptively only, and no male-versus-female inferential comparison was performed.

2.3. Clinical Data

Data were retrieved from the institutional electronic patient database and discharge summaries. Variables collected included age, sex, smoking status (active smoker, ex-smoker, or never-smoker) and pack-year index, COPD phenotype (bronchitic, emphysematous, or mixed), GOLD stage when spirometry was available, exacerbation phase, degree of respiratory failure, comorbidities (ischemic heart disease [IHD], arterial hypertension [AH], diabetes mellitus [DM]), left ventricular ejection fraction (LVEF) by echocardiography, peripheral oxygen saturation (SpO_2), and respiratory rate (RR) at admission. Spirometric data (FEV_1, FVC, FEV_1/FVC, and PEF) were collected where available, and COPD staging followed GOLD recommendations [23].

2.4. Microbiological Sampling, Culture, and Identification

Oropharyngeal swabs were collected from the posterior pharyngeal wall and tonsillar area by trained staff under aseptic conditions at hospital admission, before in-hospital antibiotic administration. Specimens were transported to the laboratory within 2 hours of collection and inoculated onto blood agar, chocolate agar, and MacConkey agar plates (Himedia Laboratories, India), following standard clinical microbiology procedures [25]. Plates were incubated aerobically at 37 ℃ for 24-48 hours. Colony morphology, hemolysis pattern, and Gram staining were used for preliminary characterization.

Species-level identification was performed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker MALDI Biotyper, Germany). Briefly, isolated colonies were applied to a target plate, overlaid with matrix solution according to the manufacturer protocol, air-dried, and analyzed against the Bruker reference database. When direct smear identification was insufficient, an on-target formic acid extraction step was used. Identification was accepted at the species level when the manufacturer-recommended score threshold was reached; lower-score results were repeated or interpreted only at the genus level. Only isolates present at concentrations $\geq 10^3$ CFU/mL and judged clinically relevant in the context of COPD exacerbation were included in the analysis [24,25].

2.5. Antibiotic Panel Selection and Susceptibility Testing

Antibiotic susceptibility testing was performed using the Kirby-Bauer disk-diffusion method on Mueller-Hinton agar according to the EUCAST disk-diffusion methodology and EUCAST Clinical Breakpoint Tables v14.0 (2024) [21,22]. Results were categorized as susceptible (S), susceptible with increased exposure/intermediate (I), or resistant (R).

The antibiotic panel was selected for three reasons: (1) to represent drug classes commonly used or considered for empirical treatment of respiratory infections and AECOPD in local hospital practice; (2) to cover major antimicrobial classes relevant to the organisms isolated in this cohort, including penicillins, beta-lactam/beta-lactamase inhibitor combinations, cephalosporins, aminoglycosides, macrolides, tetracyclines, fluoroquinolones, sulfonamides, amphenicols, and glycopeptides; and (3) to screen for clinically important resistance phenotypes in both Gram-positive and Gram-negative respiratory pathogens. The tested panel included 21 agents where clinically applicable. For organism-drug

combinations without organism-specific EUCAST clinical breakpoints, results were interpreted descriptively and with caution, rather than as definitive treatment recommendations. Antifungal susceptibility (nystatin, fluconazole, ketoconazole, nitrofurantoin, and clotrimazole) was additionally tested for the *Candida albicans* isolate.

2.6. Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) with range. Categorical variables are reported as absolute numbers with percentages. Microbiological results are reported at two levels: patient level (colonization prevalence) and isolate level (resistance rates per total number of tested isolates). Because of the limited sample size, unequal sex distribution (25 male and 16 female patients), and wide adult age range (36-86 years), the analysis was descriptive; no between-sex or age-stratified statistical hypothesis testing was performed, and no claim of statistical significance is made for sex or age subgroups. All analyses were performed using Python 3.12 with scipy, pandas, and numpy libraries.

2.7. Ethics

The study was conducted in accordance with the Declaration of Helsinki and its amendments. Ethical approval was obtained from the Ethics Committee of Tashkent Pediatric Medical Institute (Protocol No. 14, January 25, 2025). Written informed consent was obtained from all participants prior to enrollment.

3. Results

3.1. Patient Characteristics

A total of 41 patients with COPD were included (Table 1). The mean age was 61.4 ± 12.0 years (range 36-86 years); 25 patients (61.0%) were male and 16 (39.0%) were female. Sex distribution is reported only as a baseline characteristic, not as a comparative statistical variable. COPD stage was documented in 21 patients: Stage II, 7 (17.1%); Stage III, 10 (24.4%); and Stage IV, 4 (9.8%). The bronchitic phenotype predominated (33/41; 80.5%). Respiratory failure was present in 35 patients (85.4%). SpO_2 at admission was 92.3 ± 3.9% (range 82-97%); mean RR was 22.4 ± 4.1 breaths/min. Active smoking was recorded in 8 patients (19.5%), ex-smoking in 18 (43.9%), and never-smoking in 15 (36.6%). Comorbidity was common: IHD in 20 (48.8%), hypertension in 28 (68.3%), and DM in 6 (14.6%). Mean LVEF was 56.7 ± 4.9%.

Table 1. Baseline clinical characteristics of the study population (n=41)

Characteristic	n (%) or Mean ± SD
Age, years	61.4 ± 12.0 (range 36-86)
Male sex	25 (61.0%)
Female sex	16 (39.0%)
COPD Stage II / III / IV	7 (17.1%) / 10 (24.4%) / 4 (9.8%)
Bronchitic phenotype	33 (80.5%)
Acute exacerbation phase	37 (90.2%)
Respiratory failure, any degree	35 (85.4%)
SpO_2 at admission (%)	92.3 ± 3.9
Respiratory rate, /min	22.4 ± 4.1
LVEF, %	56.7 ± 4.9
Ischemic heart disease	20 (48.8%)
Arterial hypertension	28 (68.3%)
Diabetes mellitus	6 (14.6%)
Active smoker	8 (19.5%)
Ex-smoker	18 (43.9%)
Never smoked	15 (36.6%)
COVID-19 history	9 (22.0%)
Serum creatinine, μmol/L	86.4 ± 31.2
Fasting glucose, mmol/L	5.6 ± 1.1

LVEF = left ventricular ejection fraction; SpO_2 = peripheral oxygen saturation.

Table 2. Oropharyngeal microbial isolates in COPD patients (n=41; 46 isolates total)

Microorganism	Isolates, n (%)	Patients colonized, n (%)	Notes
Streptococcus mitis	22 (47.8%)	22 (53.7%)	Dominant isolate; titers 10^4-10^6 CFU/mL
Staphylococcus aureus	14 (30.4%)	14 (34.1%)	Beta-lactam-resistant phenotype in subset; methicillin resistance was not confirmed molecularly
Streptococcus pneumoniae	3 (6.5%)	3 (7.3%)	Macrolide-resistant in 2/3
Klebsiella pneumoniae	3 (6.5%)	3 (7.3%)	ESBL phenotype suspected in 2/3; not molecularly confirmed
Gemella haemolysans	2 (4.3%)	2 (4.9%)	Opportunistic organism; beta-lactam resistance observed
Candida albicans	1 (2.2%)	1 (2.4%)	Susceptible to nystatin/fluconazole
Pseudomonas aeruginosa	1 (2.2%)	1 (2.4%)	Multidrug-resistant phenotype; COPD Stage IV
TOTAL	46 (100%)	35 (85.4%)	10 patients (24.4%) polymicrobial

Percentages for patients are based on total n=41; isolate percentages are based on 46 total isolates.
ESBL = extended-spectrum beta-lactamase.

3.2. Oropharyngeal Microbiota: Prevalence and Spectrum

Pathogenic oropharyngeal flora was detected in 35 of 41 patients (85.4%). The remaining 6 patients (14.6%) harbored only commensal organisms (*Streptococcus vestibularis*, *Neisseria spp.*, and/or *Streptococcus salivarius* in physiological titers $\leq 10^3$ CFU/mL). A total of 46 microbial isolates were cultured from the 35 colonized patients. Polymicrobial colonization with two or more pathogenic organisms was observed in 10 patients (24.4%): 9 patients yielded two co-isolated pathogens, and 1 patient had three simultaneously isolated organisms (*Streptococcus mitis* + *Staphylococcus aureus* + *Klebsiella pneumoniae*). The most frequent co-isolated pair was *Streptococcus mitis* + *Staphylococcus aureus* (n=8 patients).

Streptococcus mitis was the most common pathogen, isolated in 22 patients (53.7% of all 41 patients), constituting 47.8% of all isolates. *Staphylococcus aureus* ranked second (14 isolates; 34.1% of patients; 30.4% of isolates). *Streptococcus pneumoniae* and *Klebsiella pneumoniae* were each identified in 3 patients (7.3%/6.5%, respectively). *Gemella haemolysans* was found in 2 patients (4.9%), and *Pseudomonas aeruginosa* and *Candida albicans* were isolated in 1 patient each (2.4%). The complete isolate distribution is shown in Table 2.

3.3. Antibiotic Resistance Profiles

3.3.1. Streptococcus mitis (n=22 isolates)

Table 3. Antibiotic susceptibility of *Streptococcus mitis* isolates (n=22)

Antibiotic (class)	S, n (%)	I, n (%)	R, n (%)
Penicillin (penicillin)	11 (50%)	0	11 (50%)
Ampicillin (penicillin)	21 (95%)	0	1 (5%)
Amoxicillin/clavulanate	21 (95%)	0	1 (5%)
Cefuroxime (CS-II)	11 (50%)	0	11 (50%)
Cefotaxime (CS-III)	12 (55%)	0	10 (45%)
Ceftriaxone (CS-III)	12 (55%)	0	10 (45%)
Ceftazidime (CS-III)	0 (0%)	0	20 (100%)
Cefepime (CS-IV)	12 (55%)	0	10 (45%)
Gentamicin (AG)	0 (0%)	0	20 (100%)
Amikacin (AG)	0 (0%)	0	20 (100%)
Erythromycin (macrolide)	9 (41%)	1 (5%)	12 (55%)
Azithromycin (macrolide)	9 (41%)	1 (5%)	12 (55%)
Clarithromycin (macrolide)	9 (41%)	1 (5%)	12 (55%)
Tetracycline	20 (91%)	1 (5%)	1 (5%)
Doxycycline	20 (91%)	1 (5%)	1 (5%)
Levofloxacin (FQ)	7 (32%)	1 (5%)	14 (64%)
Ciprofloxacin (FQ)	0 (0%)	0	22 (100%)
Moxifloxacin (FQ)	16 (73%)	1 (5%)	5 (23%)
Co-trimoxazole	1 (5%)	0	21 (95%)
Chloramphenicol	22 (100%)	0	0 (0%)
Vancomycin (glycopeptide)	22 (100%)	0	0 (0%)

CS = cephalosporin generation; AG = aminoglycoside; FQ = fluoroquinolone; S = susceptible; I = susceptible with increased exposure/intermediate; R = resistant.

Streptococcus mitis exhibited a clinically concerning resistance pattern (Table 3). Complete resistance (100%) was documented for ceftazidime, gentamicin, amikacin, and ciprofloxacin across all tested isolates. Very high resistance was also noted to co-trimoxazole (95%), levofloxacin (64%), macrolides (erythromycin/azithromycin/clarithromycin, 54-55% each), and cefuroxime (50%). Moderate-to-high resistance was found to cefotaxime, ceftriaxone, and cefepime (45% each) and to penicillin (50%). Because aminoglycosides are not generally used as monotherapy for streptococcal infections and organism-specific interpretive issues may apply, aminoglycoside results are reported descriptively.

In contrast, *Streptococcus mitis* isolates retained full susceptibility to chloramphenicol and vancomycin (100%), with high susceptibility to tetracycline and doxycycline (91%), moxifloxacin (73%), and ampicillin/amoxicillin-clavulanate (95%).

3.3.2. Staphylococcus aureus (n=14 isolates)

Table 4. Antibiotic susceptibility of *Staphylococcus aureus* isolates (n=14)

Antibiotic (class)	S, n (%)	I, n (%)	R, n (%)
Penicillin	0 (0%)	0	14 (100%)
Ampicillin	0 (0%)	0	14 (100%)
Amoxicillin/clavulanate	8 (57%)	0	6 (43%)
Cefuroxime (CS-II)	8 (57%)	0	6 (43%)
Cefotaxime (CS-III)	8 (57%)	0	6 (43%)
Ceftriaxone (CS-III)	8 (57%)	0	6 (43%)
Ceftazidime (CS-III)	4 (29%)	0	10 (71%)
Cefepime (CS-IV)	8 (57%)	0	6 (43%)
Gentamicin (AG)	12 (86%)	0	2 (14%)
Amikacin (AG)	12 (86%)	0	2 (14%)
Erythromycin (macrolide)	4 (29%)	0	10 (71%)
Azithromycin (macrolide)	4 (29%)	0	10 (71%)
Clarithromycin (macrolide)	4 (29%)	0	10 (71%)
Tetracycline	9 (64%)	0	5 (36%)
Doxycycline	9 (64%)	0	5 (36%)
Levofloxacin (FQ)	10 (71%)	0	4 (29%)
Ciprofloxacin (FQ)	8 (57%)	2 (14%)	4 (29%)
Moxifloxacin (FQ)	12 (86%)	0	2 (14%)
Co-trimoxazole	10 (71%)	0	4 (29%)
Chloramphenicol	11 (79%)	0	3 (21%)
Vancomycin (glycopeptide)	14 (100%)	0	0 (0%)

AG = aminoglycoside; FQ = fluoroquinolone; CS = cephalosporin generation.

All 14 *Staphylococcus aureus* isolates were resistant to penicillin and ampicillin (100%), consistent with beta-lactamase -mediated resistance. Broad resistance was also found to macrolides (71%), ceftazidime (71%), and tetracyclines (36%). Importantly, all isolates retained full susceptibility to vancomycin (100%). Moxifloxacin and aminoglycosides (gentamicin, amikacin) also showed high activity (86%). The study did not include cefoxitin/oxacillin screening or mecA testing; therefore, methicillin-resistant *Staphylococcus aureus* was not confirmed. The overall *Staphylococcus aureus*

resistance profile is detailed in Table 4.

3.3.3. Other Pathogens

Streptococcus pneumoniae (n=3) was susceptible to penicillins and cefotaxime/ceftriaxone in all 3 isolates but exhibited macrolide resistance in 2/3 (67%), ciprofloxacin resistance in 2/3, and co-trimoxazole resistance in 2/3. All 3 isolates were susceptible to vancomycin.

Klebsiella pneumoniae (n=3) showed broad-spectrum resistance to penicillins in all isolates. Two of three isolates demonstrated phenotypic resistance patterns suggestive of ESBL production (resistance to penicillins and several cephalosporins), but ESBL genes were not tested, and carbapenem susceptibility was not assessed in this panel. All *Klebsiella pneumoniae* isolates were susceptible to cefepime in the tested panel.

The single *Pseudomonas aeruginosa* isolate (from a Stage IV COPD patient with bronchiectasis) was multidrug-resistant, showing susceptibility only to cefoperazone/sulbactam, cefepime, gentamicin, amikacin, and ciprofloxacin among the tested panel. *Gemella haemolysans* (n=2) was susceptible to macrolides, tetracyclines, and vancomycin but resistant to most beta-lactams and aminoglycosides. The single *Candida albicans* isolate was susceptible to nystatin, fluconazole, nitrofurantoin, and clotrimazole, with intermediate susceptibility to ketoconazole.

4. Discussion

This single-center study provides a descriptive characterization of oropharyngeal pathogenic microbiota and antibiotic resistance profiles in hospitalized COPD patients from a tertiary center in Uzbekistan. The principal findings are: (i) a high prevalence of pathogenic oropharyngeal colonization (85.4%); (ii) *Streptococcus mitis* as the predominant isolate, detected in more than half of all patients; (iii) polymicrobial infection in nearly one-quarter of cases; and (iv) high-level resistance to key antibiotic classes including aminoglycosides, fluoroquinolones, cephalosporins, and macrolides in both streptococcal and staphylococcal isolates.

The predominance of *Streptococcus mitis* in this cohort is notable. While traditionally regarded as a commensal viridans streptococcus, *Streptococcus mitis* is increasingly recognized as a clinically significant opportunistic pathogen in immunocompromised or chronically inflamed hosts, capable of forming biofilms on respiratory epithelium and producing hydrogen peroxide that damages mucosal barriers [10,11]. The high isolation rates at titers of 10^4-10^6 CFU/mL in patients with active COPD exacerbations suggest a possible transition from commensal carriage to opportunistic pathogenicity. This finding requires confirmation in larger studies that include healthy controls and lower-airway sampling.

The antibiotic resistance pattern of *Streptococcus mitis* deserves particular attention. The high resistance to ceftazidime, ciprofloxacin, and co-trimoxazole may reflect acquired resistance under antimicrobial selection pressure, while aminoglycoside findings should be interpreted cautiously because these agents have limited activity as monotherapy against streptococci. The preserved susceptibility to tetracyclines, moxifloxacin, chloramphenicol, and vancomycin suggests potential alternatives for selected severe infections, although toxicity profiles, stewardship principles, and organism-specific clinical breakpoints must guide actual treatment decisions.

The *Staphylococcus aureus* data showed universal penicillin resistance and high macrolide resistance, posing a therapeutic challenge. However, methicillin resistance was not confirmed because cefoxitin/oxacillin screening and mecA testing were not performed. The full preservation of vancomycin susceptibility and high activity of moxifloxacin and aminoglycosides are encouraging for severe *Staphylococcus aureus* infections, but these findings should be confirmed by larger surveillance studies. The co-isolation of *Staphylococcus aureus* with *Streptococcus mitis* in 8 patients may indicate complex polymicrobial airway ecology.

The presence of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, pathogens typically associated with advanced COPD, structural lung disease, and prolonged healthcare exposure, signals an important ecological shift in the most severely ill patients [16]. Phenotypically suspected ESBL -producing *Klebsiella pneumoniae* and the multidrug-resistant *Pseudomonas aeruginosa* isolate represent potential treatment challenges in a resource-limited setting. Molecular confirmation of resistance mechanisms was not performed in this study and should be included in future work.

Compared with international data, the present findings show similarities but also notable differences. European and East Asian studies have often identified *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae* as dominant COPD lower respiratory pathogens [17,18]. In contrast, our oropharyngeal samples showed *Streptococcus mitis* predominating over *Streptococcus pneumoniae*. This difference may reflect sampling site (oropharyngeal swab rather than sputum, bronchoalveolar lavage, or protected brush sampling), patient selection, recent antibiotic exposure patterns, or genuine local ecological variation. Therefore, these findings should be interpreted as local data, not as a generalized description of COPD microbiota outside this center.

The study has several limitations. First, the single-center design limits external validity, and the findings cannot be generalized to all COPD patients in Uzbekistan, Central Asia, or other regions without multicenter confirmation. Second, there was no control group of non-COPD respiratory patients or healthy participants from the same region. Third, spirometric staging was not available for approximately half of the cohort, precluding robust stage-stratified microbiological analyses. Fourth, molecular characterization of resistance genes (mecA, blaESBL, erm, and gyrA mutations) was not performed. Fifth, the sample was heterogeneous in age (36-86 years) and had unequal sex distribution (25 male and 16 female patients); therefore, age- or sex-stratified

statistical comparisons were not performed, and no statistical significance is claimed for these subgroups. Finally, sampling was limited to the oropharynx, which may not fully represent lower-airway microbiota. Future multicenter studies incorporating metagenomic sequencing and molecular epidemiology are needed.

5. Conclusions

This single-center descriptive study characterized oropharyngeal microbiota and antibiotic resistance patterns in hospitalized COPD patients at a tertiary center in Tashkent, Uzbekistan. Pathogenic flora was present in 85.4% of patients, with *Streptococcus mitis* (53.7%) and *Staphylococcus aureus* (34.1%) as the dominant organisms, and polymicrobial colonization in 24.4%.

The resistance profiles documented, particularly high resistance to ciprofloxacin, aminoglycosides, and ceftazidime in *Streptococcus mitis* and universal penicillin resistance with high macrolide resistance in *Staphylococcus aureus*, have local implications for empirical antibiotic selection in AECOPD. However, because the sample was small, single-center, heterogeneous in age, and not sex-matched, the results should be interpreted as local surveillance data rather than generalized population-level evidence. These findings support routine microbiological surveillance in hospitalized COPD patients, local antibiotic stewardship programs, and larger multicenter studies to develop region-specific empirical treatment guidelines for AECOPD in Central Asia.

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Authors' contributions: D.S.S.: study conception, data collection, analysis, manuscript writing. All authors approved the final version.

AI assistance disclosure: AI-assisted tools were used to support language editing. All scientific content, interpretation, and conclusions were verified by the authors.

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