Investigation of the Prevalence of Microbial Agents and Antibacterial Response in Pediatric with Cystic Fibrosis

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Abstract

Background: No definitive cure for cystic fibrosis (CF) has been established to date. The prolonged use of antibiotics in managing CF has contributed to the emergence of antibiotic resistance. Investigating bacterial profiles in CF is, therefore, critical for advancing treatment strategies.

Objectives: This study aimed to comprehensively identify the common microbial pathogens present in pediatric patients diagnosed with CF and to evaluate their patterns of resistance and susceptibility to various antibacterial agents.

Methods: This cross-sectional study investigated the patterns of microbial sensitivity and antibiotic resistance in 99 children with CF treated at Ali Asghar Hospital in Zahedan between 2023 and 2024. Data were retrospectively collected from available medical records, using a simple and convenient sampling method. The study focused on analyzing microbial pathogens isolated from sputum samples and assessing their antibiotic resistance profiles. Data analysis was performed using descriptive statistics and the chi-square test in SPSS version 26.

Results: The study revealed that *Staphylococcus aureus* was the most prevalent microbial agent, identified in 31 children (31.3%), followed by *Pseudomonas aeruginosa*, detected in 29 children (29.3%), and *Acinetobacter*, found in 6 children (6.1%). The distribution of microbial agents was not significantly associated with the age or sex of the children. Furthermore, *S. aureus* exhibited the highest sensitivity to vancomycin (74.2%) and the highest resistance to erythromycin (90.3%).

Conclusions: The study concluded that *S. aureus* is the most prevalent microbial agent in children with CF, and the distribution of microbial agents is independent of age and sex. Given the potential for resistant strains of *P. aeruginosa*, it is recommended that children with CF be admitted to separate wards to minimize the risk of cross-infection and improve clinical outcomes.

Keywords: Cystic Fibrosis, Antibiotic Sensitivity, Microbial Response

1. Background

Cystic fibrosis (CF) is a recessive autosomal disorder characterized by defective mucus secretion within the respiratory, digestive, and reproductive systems. Over 90% of individuals with CF have a chromosome 7 long arm defect, which leads to a deletion of phenylalanine at position 508 in the CFTR channel protein sequence (1, 2). This channel is located in epithelial tissues and is a chloride channel, which facilitates the outflow of chloride and water from the cell (3). This channel plays a role not only in epithelial surface homeostasis regulation but also in the regulation of other chloride and organic anion transporters, such as sodium and glutathione (4).

People with CF exhibit an insensitivity of the epithelial membrane to chloride ions. It is impermeable, which results in the imbalance between Cl ion extrusion due to CFTR and Na ion influx due to ENaC, ultimately resulting in the deficiency of fluid volume on the epithelial surface (5), which results in the secretion of thick mucous membranous tissue (3, 6). This causes the attachment and colonization of some bacteria on the thick and sticky mucus, especially in the respiratory tract, which is associated with chronic infections, progressive diseases, and even airway obstruction and often death in patients with CF (7, 8).

The sweat test is the most common test in the diagnosis of CF patients. This test measures the amount of sodium chloride (salt) in the sweat. In CF patients, the chloride ion concentration in sweat is greater than 60 mmol/L (9). The CF is a genetic disorder with a reported prevalence of approximately 1 in 2,500 to 3,500 births in the United States. However, its prevalence varies significantly across different ethnic groups, with lower rates observed among African Americans (1 in 17,000) and Asians (1 in 31,000) (10). The average life expectancy for individuals with CF is around 30 years, although advancements in therapeutic and maintenance interventions have contributed to an increase in life expectancy in recent years.

The spectrum of infectious agents in CF patients is relatively limited and primarily includes bacteria, viruses, and fungi. Among these, *Staphylococcus aureus* and *Haemophilus influenzae* are the most significant microbial agents, often colonizing patients early in life (11). Following these, bacteria such as *Pseudomonas aeruginosa*, *P. cepacia*, *Stenotrophomonas maltophilia*, *Alcaligenes xyloxidans*, and non-tuberculous mycobacteria are commonly identified in adulthood (11). Additionally, fungal agents such as *Aspergillus fumigatus* and *Candida* species are also prevalent in CF patients (12).

Pseudomonas aeruginosa is considered the most critical pathogen in CF, particularly due to its mucoid alginate-producing strains, which are highly resistant and challenging to eradicate from CF patients (13, 14). Currently, there is no definitive cure for CF, and treatment strategies primarily focus on managing symptoms resulting from CFTR deficiency. These include physical therapy to facilitate mucus clearance, antibiotic therapy for respiratory infections, and anti-inflammatory treatments such as macrolides (15). The prolonged and continuous use of antibiotics in pediatric patients with CF has contributed to the emergence and spread of antibiotic-resistant strains of microorganisms. This growing resistance poses significant challenges to effective treatment and long-term disease management. Therefore, understanding the current microbial profile and resistance patterns is essential.

2. Objectives

This study aimed to comprehensively identify the common microbial pathogens found in children diagnosed with CF and to evaluate their resistance and susceptibility patterns to commonly used antibacterial agents. By analyzing these patterns, the study seeks to provide insights that can support more effective, targeted, and sustainable antibiotic therapy in this vulnerable population.

3. Methods

3.1. Study Design

This study employed a cross-sectional design to investigate microbial organisms and antibacterial sensitivity and resistance patterns in children with CF. The study population consisted of 99 children with CF who were referred to the clinic of Ali Ebn Abitalib Hospital in Zahedan between 2023 and 2024. The hospital serves as a major referral center for CF patients in the region, making it an appropriate setting for this study. Children with a confirmed diagnosis of CF based on clinical and laboratory criteria, and availability of complete and relevant information on antibiotic resistance and sensitivity profiles, were included in the study. Children who did not meet these criteria were excluded from the study to ensure the accuracy and reliability of the findings.

3.2. Data Collection

For this retrospective study, we analyzed medical records of pediatric CF patients, focusing on microbiological culture results, antibiotic susceptibility patterns, and demographic data. To identify the bacterial causes of pharyngeal infections and evaluate antibiotic resistance, we examined throat swab samples collected from these patients. During sample collection, clinicians carefully obtained throat swabs using sterile cotton swabs, avoiding contact with the tongue, cheeks,

and teeth to prevent contamination. These swabs were promptly streaked onto blood agar (to isolate Gram-positive bacteria like *Streptococcus pyogenes*) and cchocolate agar (to support fastidious Gram-negatives like *Haemophilus influenzae*). The cultures were then incubated at 35 - 37°C for 24 - 48 hours in a 5% CO_2 atmosphere. After incubation, we examined microbial growth based on colony morphology, hemolysis patterns, and Gram stain results. For antibiotic susceptibility testing, we used the Kirby-Bauer disk diffusion method on Mueller-Hinton agar, measuring inhibition zone diameters and interpreting them per CLSI guidelines. The results classified bacterial isolates as sensitive or resistant to the antibiotics included in our study.

3.3. Data Analysis

The data were analyzed using SPSS 26 (IBM Corp., Armonk, NY, USA) and presented by descriptive statistics, such as frequencies, percentages, means, and standard deviations, to summarize the demographic characteristics of the study population, the prevalence of microbial organisms, and antibiotic resistance patterns.

4. Results

In this study, 99 children with CF who visited Ali Asghar Clinic in Zahedan between 2023 and 2024 were evaluated for microbial organisms and their response to antibacterial treatments. The analysis, as presented in Table 1, showed that out of 99 samples, the prevalence of pathogens was highest in *S. aureus*, 31 (31.3%), followed by *P. aeruginosa*, 29 (29.3%), and *Acinetobacter*, 6 (6.1%), respectively, while normal (no growth) cultures were 33 (33.3%). The table also revealed that *P. aeruginosa* was more prevalent in children over 10 years old (32.6%) compared to those under 10 years old (26.8%). In contrast, *S. aureus* was more common in children under 10 years old (37.5%) than in those over 10 years old (23.3%).

The proportion of normal cultures (no bacterial growth) was higher in children over 10 years old (39.5%) than in those under 10 years old (28.6%). Additionally, *P. aeruginosa* was more frequently observed in boys (35.7%) than in girls (24.6%), while *S. aureus* was equally distributed between boys and girls (35.7% and 28.1%, respectively). *Acinetobacter*, a group of bacteria, had the lowest frequency among the samples. The proportion of normal cultures was higher in girls (43.9%) than in boys (19.0%).

Table 2 highlighted the antibiotic susceptibility patterns of the identified pathogens. *P. aeruginosa* showed the highest susceptibility to ciprofloxacin (72.4%) and tobramycin (65.5%), making these the most effective antibiotics against this pathogen. However, it demonstrated no susceptibility to clindamycin and vancomycin, rendering these ineffective. Moderate susceptibility was observed for amikacin and gentamicin (62.1% each), suggesting they could serve as secondary treatment options. For *S. aureus*, vancomycin (74.2%) was the most effective antibiotic, underscoring its critical role in treating infections caused by this pathogen.

Moderate susceptibility was noted for ciprofloxacin (54.8%) and cotrimoxazole (38.7%), while most other antibiotics showed very low susceptibility (≤ 6.7%), limiting their utility. In the case of *Acinetobacter*, the highest susceptibility was observed for ciprofloxacin and imipenem (66.7% each), making them the preferred choices. No susceptibility was found for clindamycin, cotrimoxazole, and vancomycin, indicating these were ineffective. Moderate susceptibility was seen for amikacin, ceftazidime, gentamicin, and tobramycin (33.3% each), suggesting they may serve as alternative options in specific cases.

Table 3 outlined the resistance patterns of the pathogens. *P. aeruginosa* exhibited the highest resistance to imipenem (51.7%) and gentamicin (37.9%), indicating significant challenges in treating infections with these antibiotics. Moderate resistance levels were observed for amikacin (34.5%) and ceftazidime (20.7%), suggesting limited efficacy. Lower resistance rates were noted for tobramycin (17.2%), cotrimoxazole (10.3%), and ciprofloxacin (10.3%), while no resistance was detected against tetracycline, penicillin, erythromycin, and clindamycin, highlighting their potential utility. For *S. aureus*, extremely high resistance rates were observed for erythromycin (90.3%) and clindamycin (64.5%), underscoring their ineffectiveness. Moderate resistance was noted for cotrimoxazole (32.3%), ciprofloxacin (32.3%), and penicillin (25.8%), indicating limited therapeutic options. Low resistance levels were found for tetracycline (9.7%) and tobramycin (3.2%), while no resistance was detected against imipenem, gentamicin, ceftazidime, and amikacin, making these antibiotics more reliable for treatment.

Table 1. Distribution of Bacterial Isolates by Age Group and Gender in Children [a]

Category	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Acinetobacter*	Normal (No Growth)	Total
Age group (y)					
< 10	15 (26.8)	21 (37.5)	4 (7.1)	16 (28.6)	56 100)
> 10	14 (32.6)	10 (23.3)	2 (4.7)	17 (39.5)	43 (100)
Gender					
Girls	14 (24.6)	16 (28.1)	2 (3.5)	25 (43.9)	57 (100)
Boys	15 (35.7)	15 (35.7)	4 (9.5)	8 (19.0)	42 (100)
Total	29 (29.3)	31 (31.3)	6 (6.1)	33 (33.3)	99 (100)

[a] Values are expressed as No. (%).

In the case of *Acinetobacter*, high resistance rates were observed for tobramycin, gentamicin, clindamycin, ceftazidime, and amikacin (66.7% each), reflecting significant treatment challenges. Moderate resistance was noted for imipenem (33.3%) and cotrimoxazole (50%), while low resistance was observed for ciprofloxacin (16.7%). No resistance was detected against tetracycline, penicillin, and erythromycin, suggesting these antibiotics may serve as potential alternatives in specific cases.

Table 4 summarized the antibiotic sensitivity and resistance patterns of *P. aeruginosa*, *S. aureus*, and *Acinetobacter* spp. *P. aeruginosa* showed sensitivity to amikacin, ciprofloxacin, ceftazidime, gentamicin, and tobramycin. *S. aureus* was sensitive to ciprofloxacin, cotrimoxazole, and vancomycin but resistant to clindamycin and imipenem. *Acinetobacter* spp showed sensitivity to amikacin, ceftazidime, and imipenem, but resistance to clindamycin, cotrimoxazole, and vancomycin.

5. Discussion

This study examined microbial agents and antibiotic resistance patterns in children with CF. The findings revealed that *S. aureus* was the most commonly identified microorganism, followed by *P. aeruginosa* and *Acinetobacter*. A portion of the patients also showed no bacterial growth in their cultures. These findings align with those reported by Kodori et al. (15) in Tehran and Khan et al. (16) in Pakistan. The prevalence of *S. aureus* as the primary microbial agent in bacterial infections among children with CF in southeastern Iran highlights the need for clinicians to consider this in treatment plans. Only one-third of the children had normal microbial cultures, indicating a high percentage of

bacterial infections. Studies by Erfanimanesh et al. (17) in Tehran, Fazeli et al. (18) in Isfahan, and Perikleous et al. (19) in Greece demonstrated that these children are prone to bacterial infections, which may be due to a weakened immune system and living conditions. Therefore, preventive measures by healthcare providers should be strongly recommended to avoid further complications in these children. A study conducted in India reported bacterial growth in 246 samples (55%), with 48 samples (19.5%) exhibiting mixed infections, particularly in older children.

The highest positive culture rate (62.5%) was observed in children aged 3 - 6 months, with *P. aeruginosa* (52.6%) and *S. aureus* being the most frequently identified organisms. These findings are somewhat consistent with the microbial distribution observed in the present study. In the current study, *P. aeruginosa* was more prevalent among children over ten years of age (32.6%), whereas *S. aureus* was more frequently detected in children under ten years of age (37.5%). However, statistical analysis using the chi-square test revealed no significant association between microbial distribution and age.

This result is in accordance with the findings of Perikleous et al. (19) in Greece, where, despite the highest prevalence occurring in the 1 - 12-year age group, no statistically significant differences were observed in the age distribution of microbial agents. These findings suggest that the main factor influencing microbial infections in children with CF may not be their age, but rather how well they follow preventive measures and the general health challenges linked to the disease, which make them more vulnerable to infections. This result is consistent with the study by Erfanimanesh et al. (17) in Tehran but not with Perikleous et al. (19) in Greece, where bacterial infections were more prevalent

Table 2. Distribution of Antibiotic Sensitivity Across Different Microbial Agents [a]

Type of Antibiotic (Microbial Agents)	Yes	No
Amikacin		
Pseudomonas aeruginosa	18 (62.1)	11 (37.9)
Staphylococcus aureus	2 (6.7)	29 (93.3)
Acinetobacter	2 (33.3)	4 (66.7)
Clindamycin		
P. aeruginosa	0 (0)	29 (100)
S. aureus	8 (25.8)	23 (74.2)
Acinetobacter	0 (0)	6 (100)
Ciprofloxacin		
P. aeruginosa	21 (72.4)	7 (27.6)
S. aureus	17 (54.8)	14 (45.2)
Acinetobacter	4 (66.7)	2 (33.3)
Ceftazidime		
P. aeruginosa	16 (55.2)	13 (44.8)
S. aureus	2 (6.5)	29 (93.5)
Acinetobacter	2 (33.4)	4 (66.6)
Cotrimoxazole		
P. aeruginosa	1 (3.4)	28 (96.6)
S. aureus	12 (38.7)	19 (61.3)
Acinetobacter	0 (0)	6 (100)
Gentamicin		
P. aeruginosa	18 (62.1)	11 (37.9)
S. aureus	2 (6.5)	29 (93.5)
Acinetobacter	2 (33.3)	4 (66.7)
Vancomycin		
P. aeruginosa	0 (0)	29 (100)
S. aureus	23 (74.2)	8 (25.8)
Acinetobacter	0 (0)	6 (100)
Tobramycin		
P. aeruginosa	19 (65.5)	10 (34.5)
S. aureus	1 (3.2)	30 (96.8)
Acinetobacter	2 (33.3)	4 (66.7)
Imipenem		
P. aeruginosa	11 (37.9)	18 (62.1)
S. aureus	2 (6.5)	29 (93.5)
Acinetobacter	4 (66.7)	2 (33.3)

[a] Values are expressed as No. (%).

in boys than in girls, indicating greater susceptibility in boys, especially at younger ages. Discrepancies with some studies may be due to study methods, sample sizes, and diagnostic laboratory conditions, warranting further research in this area.

The highest sensitivity to antibiotics such as amikacin, clindamycin, ciprofloxacin, ceftazidime, cotrimoxazole, gentamicin, vancomycin, tobramycin, and imipenem was observed in *P. aeruginosa* (62.1%), *S. aureus* (25.8%), *P. aeruginosa* (72.4%), *P. aeruginosa* (52.2%),

S. aureus (38.7%), *P. aeruginosa* (62.1%), *S. aureus* (74.2%), *P. aeruginosa* (65.5%), and *Acinetobacter* (66.7%) respectively. This result partially aligns with the distribution of microbial agents found in the study by Bashir et al. ([20]) in India. In that study, *P. aeruginosa* strains were highly sensitive to all aminoglycosides, piperacillin-tazobactam, and polymyxin, while Enterococcus strains showed similar sensitivity to methicillin-sensitive *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) to vancomycin, linezolid, and teicoplanin.

Table 3. Distribution of Antibiotic Resistance Across Different Microbial Agents [a]

Type of Antibiotic (Microbial Agents)	Yes	No
Tetracycline		
Pseudomonas aeruginosa	0 (0)	29 (100)
Staphylococcus aureus	3 (9.7)	28 (90.3)
Acinetobacter	0 (0)	6 (100)
Tobramycin		
P. aeruginosa	5 (17.2)	24 (82.8)
S. aureus	1 (3.2)	30 (96.8)
Acinetobacter	4 (66.7)	2 (33.3)
Imipenem		
P. aeruginosa	15 (51.7)	14 (48.3)
S. aureus	0 (0)	31 (100)
Acinetobacter	2 (33.3)	4 (66.7)
Penicillin		
P. aeruginosa	0 (0)	29 (100)
S. aureus	8 (25.8)	23 (74.2)
Acinetobacter	0 (0)	6 (100)
Cotrimoxazole		
P. aeruginosa	3 (10.3)	26 (89.7)
S. aureus	10 (32.3)	21 (67.7)
Acinetobacter	3 (50)	3 (50)
Erythromycin		
P. aeruginosa	0 (0)	29 (100)
S. aureus	28 (90.3)	3 (9.7)
Acinetobacter	0 (0)	6 (100)
Gentamicin		
P. aeruginosa	11 (37.9)	18 (62.1)
S. aureus	0 (0)	31 (100)
Acinetobacter	4 (66.7)	2 (33.3)
Clindamycin		
P. aeruginosa	0 (0)	29 (100)
S. aureus	20 (64.5)	11 (35.5)
Acinetobacter	0 (0)	6 (100)
Ciprofloxacin		
P. aeruginosa	3 (10.63)	26 (89.37)
S. aureus	10 (32.3)	21 (67.7)
Acinetobacter	1 (16.7)	5 (83.3)
Ceftazidime		
P. aeruginosa	6 (20.7)	23 (79.3)
S. aureus	0 (0)	31 (100)
Acinetobacter	4 (66.7)	2 (33.3)
Amikacin		
P. aeruginosa	10 (34.5)	19 (65.5)
S. aureus	0 (0)	31 (100)
Acinetobacter	4 (66.7)	2 (33.3)

[a] Values are expressed as No. (%).

Overall, 61% of cultures were positive, with *S. aureus* being the most common organism, and *P. aeruginosa* isolates being largely sensitive to aminoglycosides, carbapenems, and polymyxin. In a study by Kodori et al.

Table 4. Summary of Antibiotic Sensitivity and Resistance Patterns of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Acinetobacter* spp.: Guidance for Empirical Treatment Selection

Types of Antibiotic	Microbial Agent					
	Pseudomonas aeruginosa		*Staphylococcus aureus*		*Acinetobacter* spp	
	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance
Amikacin	✔			✔		✔
Clindamycin		✔		✔		✔
Ciprofloxacin	✔		✔		✔	
Ceftazidime	✔			✔	✔	
Cotrimoxazole		✔	✔			✔
Gentamicin	✔			✔		
Vancomycin		✔	✔			✔
Tobramycin	✔			✔	✔	
Imipenem		✔		✔	✔	

(15) in Tehran, *P. aeruginosa* was the most common bacterium isolated after *S. aureus*, with antibiotic sensitivity tests showing the highest resistance to piperacillin-tazobactam (11.7%) and the lowest resistance to gentamicin (2.3%). Moreover, 83.4% of *S. aureus* strains were sensitive to methicillin, while 16.6% were methicillin-resistant. According to this study, *P. aeruginosa* was the predominant pathogen in children with CF, which is not entirely consistent with the present study's findings.

The present study also indicated that the highest antibiotic resistance to tetracycline, tobramycin, imipenem, penicillin, cotrimoxazole, erythromycin, clindamycin, ciprofloxacin, ceftazidime, and amikacin was observed in *S. aureus* (9.7%), *Acinetobacter* (66.7%), *P. aeruginosa* (51.7%), *S. aureus* (25.8%), *Acinetobacter* (50%), *S. aureus* (90.3%), *Acinetobacter* (66.7%), *S. aureus* (64.5%), *S. aureus* (32.3%), *Acinetobacter* (66.7%), and *Acinetobacter* (66.7%) respectively. This result does not align with the study by Baghbani-Arani et al. (21), which may be due to differences in sample collection methods, equal selection of samples from both genders, and reporting statistics without distinguishing microbial agents. In the mentioned study, 35% of strains exhibited multidrug resistance, and most strains (96%) were resistant to rifampin, with the highest sensitivity to streptomycin (96%), imipenem (93%), and meropenem (94%).

In a study by Gautam et al. (22), children whose initial cultures were positive for *P. aeruginosa* showed mixed microbial cultures in 55% of subsequent cultures. *P. aeruginosa* infections were most sensitive to ciprofloxacin (89%) and piperacillin-tazobactam (88%). Additionally, 38% of *S. aureus* strains were methicillin-

resistant. In a study by Emerson et al. (23) conducted in the United States, sputum samples from 267 participants across 33 CF centers were analyzed. A total of 656 *P. aeruginosa* isolates were identified from 253 culture-positive participants. The study found a significant increase in the prevalence of tobramycin-resistant (11.8% vs. 30.4%) and amikacin-resistant (24.2% vs. 42.7%) *P. aeruginosa* strains over time. However, ciprofloxacin resistance remained stable (34.4% vs. 33.6%, P = 0.81).

The study also explored links between recent antibiotic use and resistance patterns, revealing that intravenous carbapenem exposure was significantly associated with resistance to aztreonam, meropenem, and multidrug resistance. Additionally, the prevalence of *S. aureus*, MRSA, *S. maltophilia*, and *Achromobacter xylosoxidans* increased in the more recent cohort. While this study provides valuable insights into microbial colonization and antibiotic resistance in CF children, several limitations should be acknowledged. The retrospective design may introduce biases related to incomplete or inconsistent record-keeping, and being a single-center study may limit the generalizability of the findings to other populations or settings. Finally, the sample size, though adequate for preliminary analysis, may not be sufficient to detect rare microbial organisms or resistance patterns.

5.1. Conclusions

The study concluded that *S. aureus* and *P. aeruginosa* are the most common microbial agents in CF, with only one-third showing normal microbial cultures. This highlights a high prevalence of bacterial infections,

likely due to weakened immunity and environmental factors. Age and gender did not significantly affect microbial distribution, emphasizing the need for universal preventive measures. Antibiotic sensitivity tests showed *P. aeruginosa* was highly sensitive to ciprofloxacin and ceftazidime, while *S. aureus* exhibited significant resistance to erythromycin and clindamycin. Clinicians should focus on regular microbial monitoring and tailored antibiotic therapy, prioritizing infection prevention and patient education to reduce bacterial infections and resistance.

Acknowledgements

Footnotes

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