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Antimicrobial Sensitivity Patterns Among Pediatric Cystic Fibrosis Patients: Implications for Effective Treatment Strategies

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A B S T R A C T

Background: Patients with cystic fibrosis (CF) who have recurrent bacterial lung infections eventually develop respiratory incompetency, which increases morbidity and death. It's important to treat these patients promptly to achieve positive results.

Objective: To explore the Antimicrobial sensitivity pattern of pediatric cystic fibrosis patients.

Methodology: This observational study was conducted form April 2022 to September 2022 at the Department of Paediatric Medicine, Qazi Hussain Ahmad Medical Complex, Nowshera, Pakistan. The health status of the pediatric CF patients, extensive evaluations were conducted as part of the diagnostic evaluation and data gathering procedure for this study. Physical examination and laboratory testing like culture and sensitivity were performed. To evaluate the antimicrobial sensitivity pattern Kirby Bauer modified disc diffusion method was used. Version 26 of the SPSS software was used to carry out the statistical analysis. The p-value level of 0.05 has been defined as a measure of statistical significance.

Results: A total of 84 children with CF symptoms were included in the research. Of these patients, there were 28 females (33.3%) and 56 boys (66.6%). Among the respiratory samples taken from pediatric CF patients, the most prevalent isolated bacteria was Pseudomonas aeruginosa (36%) followed by Klebsiella pneumonia (22.9%). Among all bacterial strains, Ciprofloxacin and Levofloxacin had the highest levels of antimicrobial sensitivity, whereas Amoxicillin, Erythromycin, and Rifampicin shown significant resistance.

Conclusion: Our study concludes that the P. aeruginosa was the most prevalent isolated bacteria followed by Klebsiella pneumonia in patients with cystic fibrosis. The most effective antimicrobial agents in our study were ciprofloxacin and levofloxacin.

Keywords: Cystic Fibrosis; Pediatric Patients; Antibiogram

Introduction

Patients with cystic fibrosis (CF) who have recurrent bacterial lung infections eventually develop respiratory incompetency, which increases morbidity and death.[1,2] Cystic fibrosis occurs due to mutation in CFTR gene which destroys the part of the innate immunity, including the mucociliary clearance mechanism. As a result, lungs are colonized by a diverse group of microorganisms which leads to lungs diseases.[3] Almost one-third of CF patients have lung issues that start in early childhood and show radiological indications of bronchiectasis.[4] Pseudomonas aeruginosa becomes the most common and well-known causative agent for CF. In the beginning, Hemophilus influenzae and Staphylococcus aureus are the main causative agents.[5,6] Furthermore, exacerbations of respiratory symptoms can also be attributed to other opportunistic bacteria such as Burkholderia cepacia, Achromobacter, and Stenotrophomonas maltophilia.[7,8]

The estimated frequency of cystic fibrosis varies among ethnic groups, with Caucasians having the greatest prevalence (1 in 2,500). Incidence of CF among South Asian immigrants living in the UK is estimated to be between 1:10,000 and 1:12,000.[4] In Pakistan, CF is one of the diseases that is underdiagnosed.[5]

According to study, vancomycin was found to be highly resistant (87.5%) against S. aureus. Only fluoroquinolones such as levofloxacin, ciprofloxacin, and fourth-generation cephalosporine (cefepime) were found to be effective against these strains. All beta-lactam antibiotics were resistant to E. coli. Only levofloxacin and linezolid were effective against it.[9]

Moreover, repeated treatment with antibiotics promotes the development of antibiotic resistance and changes the diversity of the microbiome in the infected pulmonary environment as the individuals getting old. However, recently emerging pathogens are displacing traditional microorganisms, and benign colonizers are becoming the ones responsible for the spread of illness.[9,10] Therefore, it is frequently challenging to treat CF airway infection considering such a dynamic micro-biome.[11]

In our setup, no such study has been carried out on the antibiogram assay of microorganism isolated from the pediatric patients with pediatric cystic fibrosis. The current study was therefore conducted to explore the Antimicrobial sensitivity pattern of pediatric cystic fibrosis patients.

Objective

The present study was conducted with the aim to explore the Antimicrobial sensitivity pattern of pediatric cystic fibrosis patients.

Methodology

This observational study was conducted form April 2022 to September 2022 at the Department of Paediatric Medicine, Qazi Hussain Ahmad Medical Complex, Nowshera, Pakistan after taking the approval from the ethical committee of the institute. Individuals with a clinical diagnosis of cystic fibrosis (CF) aged 0-18 years who had a measured sweat chloride level of > 90 mmol/L were included. The study excluded participants with clinical characteristics suggestive of congenital diaphragmatic hernia, aspiration pneumonia, foreign body aspiration, congenital lobar emphysema, pulmonary tuberculosis, asthma, primary immunodeficiency, congenital heart disease, and pulmonary abscess. In order to make sure an accurate representation of the health state of the pediatric CF patients, extensive evaluations were conducted as part of the diagnostic evaluation and data gathering procedure for this study. Medical evaluations and testing were performed, such as sputum and random sugar level (RBS) measurements, antibiotic sensitivity from pharyngeal swabs, Mantoux tests, whole blood counts and chest X-rays. Samples of sputum were collected, put into lab-provided sterile containers, fastened with screws, and labelled. With the support of their parents or by asking the child to open their lips, participants who were unable generate saliva on their own had oropharyngeal swabs taken. A sterile cotton swab stick was then carefully swiped over the pharynx wall and placed in a sterile plastic bottle. Samples were obtained and within an hour brought to the microbiological lab. Samples were inoculated in Blood agar, MacConkey, and chocolate agar cultures, and incubated for 48 hours at 37°C. After that microbial growth were detected colonies were isolated and cultured on deferential media for biochemical tests for further confirmation. To evaluate the antimicrobial sensitivity pattern Kirby Bauer modified disc diffusion method was used. Various antibiotic discs used in our study were Ceftazidime, Vancomycin, Amoxicillin, Imipenem, Cefepime, Rifampicin, Ciprofloxacin, Levofloxacin, Gentamicin, Linezolid, Meropenem ,Cotrimoxazole, Erythromycin and Amikacin. Version 26 of the SPSS software was used to carry out the statistical analysis. The mean and standard deviation, which demonstrate both the variability in the data and an average value, were used to represent continuous variables. Certain data sets were analyzed using Fischer exact tests. The p-value level of 0.05 has been defined as a measure of statistical significance, indicating that outcome with a p-value of less than or equivalent to 0.05 considered to be statistically significant.

Results

A total of 84 children with CF symptoms were included in the research. Of these patients, there were 28 females

Table 1. Demographic Characteristics of the study cases

Characteristics	Frequency (%)	P-value
Gender		
Male	56 (66.6)	0.002
Female	28 (33.3)	
Age in years		
≤1	14 (16.6)	0.465
>1 to 12	46 (54.7)	
>12 to 18	24 (28.5)	
Parental consanguinity in marriage		
Absent	23 (27.3)	0.0004
Present	61 (72.6)	
CF in the family history		
No	31 (36.9)	0.021
Yes	53 (63)	

(33.3%) and 56 boys (66.6%). Based on the age distribution, it was found that twenty-four participants (28.5%) were between the ages of 12 and 18 years, 46 patients (54.7%) were between the ages of 1 and 12, and 14 of the patients (16.6%) were less than 1 year. Regarding parent-child consanguinity,61 patients (72.6%) had parents who were married in a consanguineous manner, whereas 23 patients (27.3%) were married in a non-consanguineous manner. In terms of family history, 31 patients (36.9%) had no family history, whereas 53 patients (63%) had a positive family history of CF (Table 1). There was a positive microbiological presence in72.6% of the children (n=61) whose respiratory specimens from pediatric CF patients were examined. Of the sixty-one individuals, 47 (77.1%) showed the presence of a single microbe, and 14 (22.9%) showed the presence of two different microorganisms. In particular, 84.61% of participants (n = 12) with kids below 1 year old confirmed positive for microorganisms, 68.89% (n = 32) with children over 1 and under 12 years old, and 77.27% (n = 17) with those over 12 and under 18 years old tested positive. Nevertheless, there was no statistically significant difference in the presence of microorganisms across the various age groups (p=0.362). Among the respiratory samples taken from pediatric CF patients, the most prevalent isolated bacteria was Pseudomonas aeruginosa 22(36%), Klebsiella pneumonia 14 (22.9%), Staphylococcus aureus10 (16%), Escherichiacoli8 (13.1), Acinetobacter Species 4 (6.5%) and Streptococcus Pneumoniae 3 (4.9%) (Figure 1).

Table 2 displays the antibiotic sensitivity patterns of microorganisms obtained from respiratory system samples of children with cystic fibrosis. Among all bacterial strains, Ciprofloxacin and Levofloxacin had the highest levels of antimicrobial sensitivity, whereas Amoxicillin, Erythromycin, and Rifampicin shown significant resistance. Furthermore, vancomycin frequently presented sensitivity against S. pneumoniae and S. aureus. While Ceftazidime and Meropenem showed varying degrees of sensitivity against different types of bacteria, they were very efficient against P. aeruginosa. Furthermore, imipenem and cotrimoxazole exhibited comparatively good sensitivity profiles for a variety of species, especially for S. Pneumoniae and Acinetobacter species. The results of chi-square tests are displayed in table 3, which demonstrating the statistical relationships between different bacterial species (P.aeruginosa, S. Pneumoniae, K. pneumoniae, E. Coli, S.aureus, and Acinetobacter) and the patterns of antibiotic sensitivity that correspond with those relationships.

Table 2. Antimicrobial susceptibility pattern of bacteria isolated from children with cystic fibrosis

Drugs		S. aeruginosa	S. pneumoniae	K. pneumoniae	E. coli	S. aureus	Acinetobacter Species
Ceftazidime	S	15	00	6	2	2	2
	R	5	3	8	5	5	3
	I	2	00	00	1	2	00
Vancomycin	S	9	4	2	3	7	1
	R	11	00	9	5	2	4
	I	2	00	1	00	00	00
Amoxicillin	S	00	00	00	00	00	00
	R	22	4	13	8	9	5
	I	00	00	00	00	00	00
Imipenem	S	8	4	5	2	3	3
	R	9	00	6	5	5	0
	I	5	0	2	1	1	2
Cefepime	S	7	00	2	4	3	1
	R	14	2	9	2	6	0
	I	2	1	1	2	0	3
Rifampicin	S	00	00	00	00	00	00
	R	19	4	9	4	8	2
	I	3	0	4	4	1	3
Ciprofloxacin	S	22	4	13	8	9	5
	R	00	00	00	00	00	00
	I	3	0	4	4	1	3
Levofloxacin	S	21	4	11	6	8	4
	R	1	0	2	2	1	1
	I	00	00	00	00	00	00

Gentamicin	S	6	1	4	3	3	2
	R	14	2	8	4	6	3
	I	3	1	00	00	00	00
Linezolid	S	8	4	4	5	4	2
	R	14	5	3	3	4	3
	I	00	1	3	1	00	00
Meropenem	S	19	3	5	6	5	3
	R	00	2	5	2	1	00
	I	00	00	3	3	2	2
Cotrimoxazole	S	7	4	2	3	0	5
	R	20	2	13	7	9	4
	I	3	1	4	3	4	1
Erythromycin	S	00	00	00	00	00	00
	R	20	4	12	8	9	4
	I	1	1	1	0	0	1
Amikacin	S	13	3	4	4	6	3
	R	8	2	8	5	2	3
	I	00	00	00	00	00	00
S. Sensitive			R. Resistant			I. intermediate	

Discussion

One of the hereditary illnesses that is underdiagnosed in poor nations is cystic fibrosis (CF). Clinical signs of cystic fibrosis (CF) resemble those of common gastrointestinal and respiratory disorders and can be confused with asthma, pneumonia, and malabsorption syndromes. Simultaneously, our region's high under-five death rates have made it difficult to rule out CF as a differential diagnosis in children who appear with respiratory infections and diarrhoea.[8] Due to the delayed diagnosis, these children are at a higher risk of morbidity and death. The study aimed to evaluate the pattern of antibiotic sensitivity in children with cystic fibrosis. It is hereditary illness that affects the digestive and respiratory systems significantly. It frequently results in recurrent respiratory infections because of inadequate mucus clearance and bacterial proliferation. Given the vitality of successful antibiotic therapy in managing infections associated to cystic fibrosis (CF), being aware of common bacteria' antibiotic susceptibility is essential for determining strategies for treatment. The study's key finding that a significant frequency of consanguinity 61 (72.6%) exists among CF patients in the Pakistani community put light on a surprising aspect of the disease. These findings of are similar with previous study that was carried out in Iran.[12]But the outcomes of our study were not similar to the study conducted in India which reported only 19 percent cases showed higher incidence of consanguinity.[13] Comparisons with previous research indicate that Pakistan has higher rates of consanguinity than other countries.[14,15] The evidence shows that Pakistan's greater incidence of cystic fibrosis (CF) may be due to hereditary

Table 3. Chi-square test outcomes for the relationship between bacterial species and antibiogram

Variables	P. aeruginosa	S. pneumoniae	K. pneumoniae	E. coli	S. aureus	Acinetobacter
Chi-Square	24.857	25.428	21.144	11.715	23.239	15.428
Degree of freedom	18	4	12	7	9	5
Asymptotic significance	.099	.0002	.048	0.12	.007	.008

and environmental factors as well as social beliefs around consanguineous marriages.

In this study we explored that the most prevalent bacteria isolated from respiratory samples of cystic fibrosis was S. aeruginosa 22 (36%). The results of our study are similar to Nobandegani et al, in which the prevalence of this bacterium was 30%.[16] Nevertheless, the results of this investigation contrast from the findings of the preceding research performed by Valenza et al, [17] in which S. aureus was shown to be particularly prevalent (41%), followed by P. aeruginusa (26%). It is most common cause of long-term lung infections in persons with cystic fibrosis (CF), and its frequency rises with age, reaching more than eighty percent in young adults and 10 - 30% in children.[18] Patients with cystic fibrosis (CF) may experience persistent Pseudomonas aeruginosa in their airways even after receiving intensive antibiotic therapy. Early infection may be treated with antibiotics, but as people age, they are more vulnerable to both chronic and sporadic diseases.[19]

In our study, Klebsiella pneumonia was observed in 14 (22.9%), Staphylococcus aureus in10 (16%), Escherichiacoli in 8 (13.1%), Acinetobacter Species in 4(6.5%) and Streptococcus Pneumoniae in 3(4.9%) patients. These findings were comparable to a previous study done by Valenza et al.[17]

In our study, among all bacterial strains, Ciprofloxacin and Levofloxacin had the highest levels of antimicrobial sensitivity, whereas Amoxicillin, Erythromycin, and Rifampicin shown significant resistance. Furthermore, vancomycin frequently presented sensitivity against S. pneumoniae and S. aureus. While Ceftazidime and Meropenem showed varying degrees of sensitivity against different types of bacteria, they were very efficient against P. aeruginosa. Furthermore, imipenem and cotrimoxazole exhibited comparatively good sensitivity

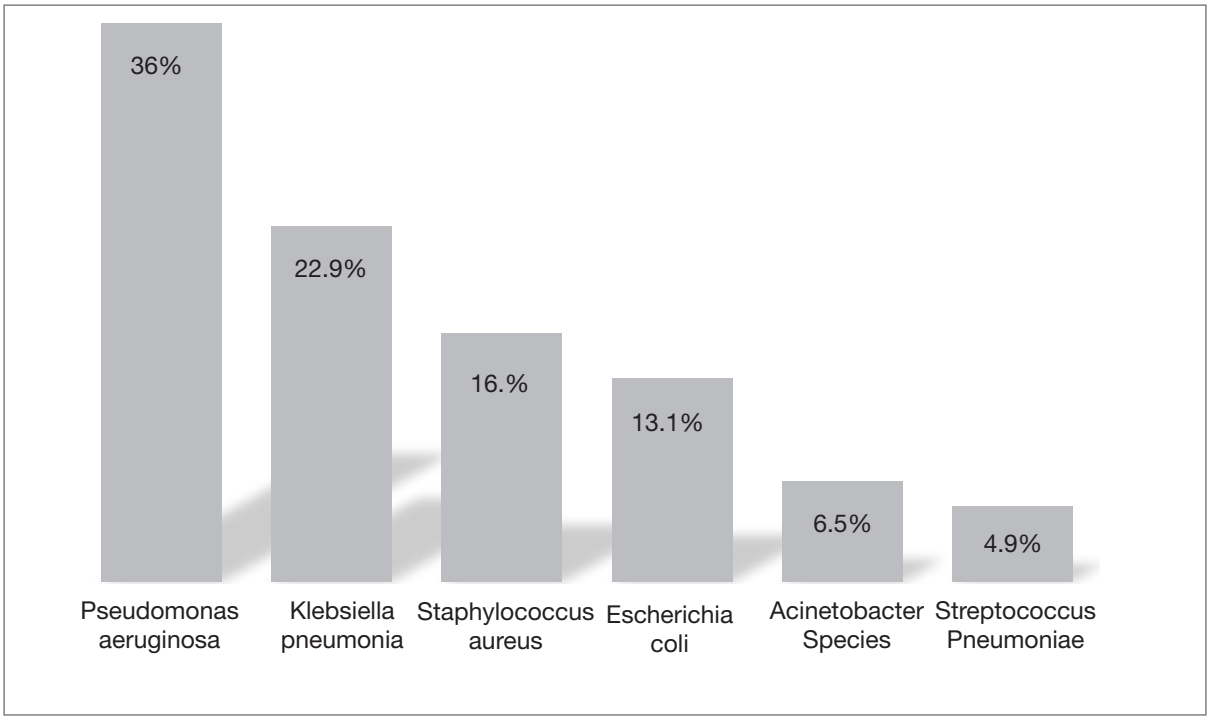

Figure 1. Frequency of bacteria isolated from respiratory samples of CF children

profiles for a variety of species, especially for S. Pneumoniae and Acinetobacter species. Our findings are comparable to previous studies conducted by Chang et al,[20] Hamzah et al.[21] It has been demonstrated that the fast growth of drug-resistant bacteria, some of which exhibit resistance to many treatments, can be due to the excessive use of antibiotics and insufficient patient compliance. This makes it essential to frequently update antibiotic guidance.

Conclusion

Our study concludes that the P. aeruginosa was the most prevalent isolated bacteria followed by Klebsiella pneumonia in patients with cystic fibrosis. The most effective antimicrobial agents in our study were ciprofloxacin and levofloxacin. To enhance the treatment and prognosis of patients with cystic fibrosis, routine promotion of monitoring of microbial isolation and patterns of resistance is necessary.

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