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Insights into the Clinical and Laboratory Characteristics of Pediatric Cystic Fibrosis Patients: a single-center study

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A B S T R A C T

Background: Cystic fibrosis (CF) in children is an inherited disorder that causes thick mucus to build up in body and leads to damage various organs, especially the digestive system and lungs. The predicted incidence of cystic fibrosis fluctuates among ethnic groups, with Caucasians having the greatest prevalence.

Objective: The objective of the study was to explore the clinical and laboratory profile of children with Cystic Fibrosis.

Methodology: The current retrospective study was piloted at the paediatric Medicine department of Qazi Hussain Ahmad Medical Complex, Nowshera from august 2021 to January 2022. This research involved subjects who had cystic fibrosis on the basis of positive sweat chloride test and clinical features from birth to fifteen years of age, regardless of gender. Analyses of the identified Delta F-508 mutations were observed. Analysis of the data was done with SPSS version 20.

Results: A total of 47 children were enrolled in the study according to the inclusion criteria. The most prevalent symptoms among the study cases were chronic cough (70%). Respiratory features that was most common in our study on chest HRCT included bronchiectasis and hyperinflation (38%). Radiological examination evaluated 27% consolidation. Culture investigation showed that most prevalent bacteria was Pseudomonas (27%). Gastroenterological features like steatorrhea were seen in 6 (12.7%) patients.

Conclusion: In children diagnosed with cystic fibrosis, respiratory symptoms were found to be more prevalent compared to gastrointestinal symptoms. When analyzing their chest CT scans, nearly half of the examined cases showed bronchiectatic changes. Among those investigated, 27% exhibited pseudomonas colonization in their airways.

Keywords: Cystic Fibrosis; Sweat Chloride Test; Delta F508; Genetic Mutations Analysis

Introduction

Cystic fibrosis (CF) is life threating hereditary disease that is mostly common in Europe and Australia [1,2] The mutation in the CF transmembrane conductance regulator (CFTR) leads to the desiccation of secretions in the respiratory airways, hepatobiliary-pancreatic ducts, and other tissue linings, resulting in gradual and irreversible damage to the organs.[3] Cystic fibrosis is anticipated to affect different racial groups at different rates, with Europeans anticipated to have the highest prevalence (1 per 2,500). The estimated prevalence of CF among South Asian immigrants living in the United Kingdom ranges from 1:10,000 to 1:12, 000.[4] In Pakistan, one of the diseases that is underd-iagnosed is cystic fibrosis.[5]The prognosis and behavior of people with CF are greatly influenced by the genetic diagnosis. Although the precise occurrence in Pakistan is unclear, given the high number of cousin marriages, it is anticipated to be significant. Because there are no diagnostic tools available in Pakistan to confirm CF diagnosis, the illness is thought to be underdiagnosed there. Suggested clinical characteristics are used to diagnosis the majority of the cases that have been documented. A proper diagnosis depends on the identification of the case based on the history, physical examination, and relevant laboratory observations. During the first two years of life, patients with cystic fibrosis (CF) often have stunted development, recurrent pneumonia, persistent productive cough, resistant asthma, chronic diarrhoea (steattorhea), and dehydration. In affluent nations, a program called Neonatal Screening has been implemented to identify possible patients at an early age by detecting the level of active serum trypsinogen. Screening program are unavailable in developing nations, and the majority of cases are identified based solely on clinical presentation, with additional support from genetic analysis and sweat chloride testing. The prognosis and behavior of CF are largely determined by the genetic diagnosis. The most often documented genetic mutation associated with cystic fibrosis (CF) amongst Europeans is Delta F-508.[6] Data on mutations in Pakistani CF patients presented in a few studies indicated that the mutation of D -F508 is uncommon in this community.[5] This is in contrast to a couple of studies that demonstrated the prevalence of this mutation in the CF group in Pakistan.[7,8] Cystic fibrosis is a common problem in our country and no attention has been given to this problem. Based on literature, no such study has been carried out on cystic fibrosis. This study was therefore carried out to find out clinical and laboratory profile of children with Cystic fibrosis.

Objective

The objective of the study was to explore the clinical and laboratory profile of children with Cystic Fibrosis.

Methodology

The current retrospective study was piloted at the paediatric Medicine department of Qazi Hussain Ahmad Medical Complex, Nowshera from august 2021 to January 2022. This research involved subjects who had cystic fibrosis on the basis of positive sweat chloride test and clinical features from birth to fifteen years of age, regardless of gender. These individuals were divided in to 5 groups on the basis of age and symptoms. More investigation was done on these CF patients. For their first clinical indications or symptoms, these CF patients underwent more investigation. The standard deviation and mean value of the sweat chloride readings were recorded. Pilocarpine iontophoresis was used to induce perspiration. Wescor macroduct sweat collecting equipment was used for collecting the sweat. Patients were classified as confirmed with a CF diagnosis if their sweat chloride assessments were more than 60 mmol/L. Each individual who diagnosed positive for sweat chloride had their genetic mutation Delta F-508 assessed. Individuals who tested positive for the Delta F-508 mutation in the gene were divided into homozygous and heterozygous groups. Parents with consanguineous relationships were identified, as well as a family history or previous occurrences of cystic fibrosis (CF) among siblings. Standard physical examination results as well as general body characteristics were noted. Symptoms of heart problems, digestive disorders, respiratory disorders, and other diseases were noted for these kids. The complete blood count, fat globules, electrolytes, and outcomes of the X-rays, blood culture, and stool examination were recorded. HRCT (Chest high-resolution computed tomography) was performed at the time of examination. Based on radiological findings, study cases were categorized into six groups. Sputum samples were also analyzed for organism growth to identify the initial colonization of the airways. Data analysis was performed using SPSS version 20, organizing variables by mean, standard deviation, numbers, and percentages.

Results

A total of 47 children with cystic fibrosis were enrolled in this study**.** The Mean age of the study cases was 57.00 ± 33.72 months (4.7 years). The male patients in our study were 27 (54.4%) while female patients were 20 (42.5%). The ratio of male to female was 1.3:1. The mean study duration was 14.41 ± 26.18 months. Over 50% of the individuals in our study obtained a diagnosis after three years of life. Even though most of the individuals experienced clinical signs in their first year of life (Table 1). Based on history, 5 children (10%) have a positive family history and 26 (53.31%) of them have consanguineous parents. The occurrence symptoms of based on age were observed as, 10% in neonatal age, 65% in postnatal age

Table 1. Demographic features and general parameters of study cases

Gender	Frequency (%)
Male	27 (54.4)
Female	20 (42.5)
Male to female ratio	1.3:1
Onset of symptoms Mean age	14.41 ± 26.18 months
At diagnosis Mean age	47.20 ± 45.80 months
Height below 3rd centile (short stature)	26 (55.3)
Weight below 3rd centile	36 (76.5)

while after 5 years there was no case. Figure 1 compares the development of signs across various age groups. Based on diagnostic test in children with CF, the mean chloride test results were 82.70 with Std. Deviation of ± 22.74. The outcomes of a number of diagnostic procedures performed on the individuals we treated are shown in Table 2. In our study, the most typical first clinical sign was a chronic cough (70%) followed by Steatorrhea (12.7%) as displayed in table 3. In sputum culture in our study participants exhibited about 27.6% growth of pseudomonas aeruginosa followed by S. aureus (14.8%). The mean hemoglobin level among the study cases was 8.6 ± 3.41. Additionally, electrolyte levels differed, with sodium levels averaging 135.22 ± 2.21 mEq/L. Blood cultures conducted during the study indicated that 68.0% of cases showed no growth, whereas in sputum or tracheal cultures, this rate was 25.5% among the study cases. Pseudomonas aeruginosa was the most prevalent organism (12.7%) among blood culture samples, and in sputum and tracheal cultures, Pseudomonas aeruginosa prevalence was even higher at 27.6%. Radiological findings on chest X-rays revealed that 40.4% of cases showed honeycombing in their chest, while high-resolution CT scans showed radiological features of bronchiectasis and hyperinflation in 38.2% of cases (Table 4).

Discussion

Cystic fibrosis is a hereditary disorder remains undiagnosed in developing countries. Its signs and symptoms often resemble to those of gastrointestinal and respiratory diseases such as pneumonia, malabsorption disorders and asthma. Children with CF frequently experience diarrhea and respiratory illnesses.[8] Cystic fibrosis is an inherited condition that remains undiagnosed in developing countries. Its symptoms often resemble those of gastrointestinal and respiratory disorders, such as pneumonia, malabsorption syndromes, and asthma. Children with cystic fibrosis frequently experience diarrhea and respiratory illnesses. Delay diagnosis of CF in children increase the risk of mortality and morbidity. Over 50% of the individuals in our study obtained a diagnosis after three years of life. Even though most of the individuals experienced clinical signs in their first year of life. This differs from data from the USA and Europe, where CF patients are often identified in their first year of life. Similar findings were reported by El-Falaki et al., who

Table 2. Diagnostic tests in CF Children

Sweat chloride test results	Mean Value
Gene analyses for Delta F-508	13 (27.6%)
Negative for Delta F-508	32 (68%)
Heterozygous	6 (12.7%)
Homozygous	8 (17%)

Table 3. Major clinical manifestations experienced by study cases (N=47)

Clinical Manifestations	Frequency (%)
Delayed passage of Meconium or Meconium ileus	5 (10.6%)
Prolonged Cholestatic Jaundice	2 (4.2%)
Chronic cough	31 (70%)
Steatorrhea	6(12.7%)
Failure to thrive only	1 (2.1%)
Pseudobarter syndrome with electrolyte imbalance	2 (4.2%)

found that most individuals showed symptoms in their first year of life and were diagnosed in their second year.[9] The inability of the medical expert to justify CF is one of the reasons for this delay considered a vital differential diagnosis and in part due to the lack of resources supporting early identification.[10] Over 50% of the individuals in our group were born into consanguineous marriages. It is comparable to the prevalence of consanguineous marriage documented in the CF population by Desgeorges and colleagues in Lebanon [11]

A total of 13 patients (27.6%) in our research tested positive for the genetic mutation designated as Delta F-508. Among them, 6 (12.7%) were heterozygous and 8 (17%) were homozygous. These findings align with those reported by Kabra et al.[8] and Naguib et al[12] which demonstrated comparable rates of Delta F508 mutations, with percentages ranging from 19% to 25%in their respective studies. In a similar study previously conducted in Pakistan found that Pakistani CF children had a lower prevalence of the delta F508 mutation than reported in the Caucasian society.[13]

In the present study, the most prevalent symptom was chronic cough 31(70%) followed by diarrhea. Without any concomitant respiratory or gastrointestinal symptoms, one patient merely showed signs of failure to grow. Five patients (10.6%) presented with meconium-related symptoms in the early stages of childhood. Meconium ileus is frequently referenced as vital medical proof for cystic fibrosis (CF) as reported by previous study.[14,15] So screening the newborns is vital as soon as possible. Two

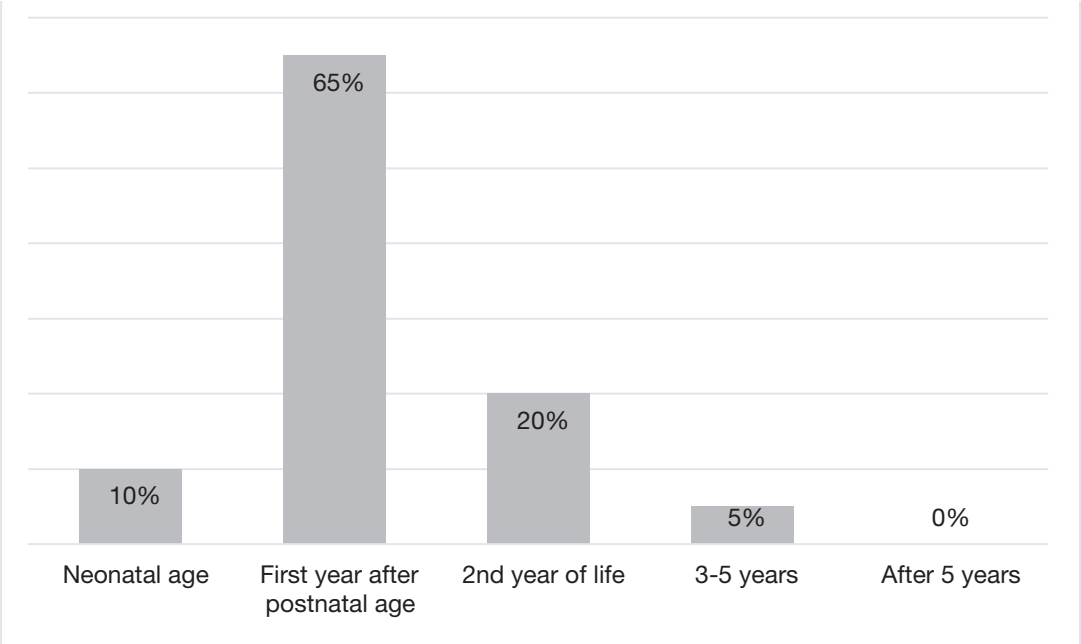

Figure 1. Comparison of occurrence of symptoms within different age groups among study cases

Table 4. Radiological and laboratory examination of CP participants of the study

Full Blood Count	Mean value with STD	Electrolytes	Mean value with STD
Hemoglobin (g/L)	8.67 ± 3.41	Sodium (mEq/L	135.22 ± 2.21
White blood count (X 10E9/L)	13.23 ± 4.88	Potassium (mEq/L)	3.39 ± 1.57
Platelets (X 10E9/L)	265.31 ± 127.15	Chloride (mEq/L)	95.21 ± 3.81
CRP (mg/dl)	6.21 ± 5.64	Bicarbonate (mEq/L)	22.45 ± 2.25
Blood Culture	N=47 (%)	Sputum / Tracheal Culture	N=47(%)
No growth	32 (68)	No growth	12 (25.5)
Methicillin resistant Staphylococcus aureus	2 (4.2)	Pseudomonas aeruginosa	13 (27.6)
Methicillin Sensitive Staphylococcus aureus	4 (8.5)	S. aureus	7 (14.8)
Pseudomonas aeruginosa	6 (12.7)	K. Pneumonia	4 (8.5)
Escherichia Coli	1 (2.1)	Streptococcus species	3 (6.3
Streptococcus pneumonia	1 (2.1)	Haemophilus influenza	2 (4.2)
Burkholderia Cepacia	1 (2.1)	Burkholderia Cepacia	2 (4.2)
Radiology features on X-ray Chest	N =47 (%)	Radiology features on HRCT Chest	N=47 (%)
Normal	2 (4.2)	Normal	8 (17)
Not done	0 (0)	Not done	5 (10.6)
Consolidation	13 (27)	Consolidation only	6 (12.7)
Hyperinflation	6 (12.7)	Consolidation with hyperinflation	5 (10.6)
Prominent Broncho vascular markings	4 (8.5)	Consolidation with collapse	3 (6.3)
Perihilar infiltrates	2 (4.2)	Consolidation collapse and hyperinflation	2 (4.2)
Honey combing	19 (40.4)	Bronchiectasis and hyperinflation	18 (38.2)

patients (4.2%) had an electrolyte imbalance while they first enrolled with their initial characteristic that defines CF being pseudo-barter syndrome. The occurrence of metabolic alkalosis and electrolyte imbalance is a notable clinical presentation in children with cystic fibrosis. Particularly in humid environments, and urgent examinations can aid in establishing the proper diagnosis.[16]

The most common clinical manifestation in our study cohort was a persistent productive cough, which was obvious in the individuals we studied. Wheezing during childhood in people with cystic fibrosis (CF) is prevalent and has been associated to reduced lung function in adulthood.[17] Children with cystic fibrosis (CF) are more likely to develop nasal polyps and rhinosinusitis.[18] In our study Bronchiectasis and hyperinflation was reported in 18 (38.2%). Patients with cystic fibrosis (CF), particularly those whose condition progresses, have a significantly elevated risk of death when they have pulmonary hypertension.[19,20] Several significant mutations are linked to the gastrointestinal symptoms of cystic fibrosis (CF). A number of distinct genetic changes have distinguished both its onset and its presence or absence.[21] In our study, we identified 6 (12.7%) recipients experienced steatorrhea as the first distinguishing symptom of cystic fibrosis (CF), and about 24 (51%) individuals had this presentation at some point during their diagnosis of CF. These results are comparable to those of Kawoosa et al., who reported that 50% of patients had both diarrhea and sterorrhea.[22] A computed tomography examination of the chest revealed some degree of bronchiectasis alterations of the studied participants. A number of studies promote the use of CT scans as a means of identifying pulmonary deterioration early on. They also found that while serial CT scans showed early deterioration, serial pulmonary function tests performed at the same time in children with cystic fibrosis (CF) either showed no change or declined more gradually.[24] In sputum culture in our study participants exhibited about 27.6% growth of pseudomonas aeruginosa followed by S. aureus (14.8%). Pseudomonas aeruginosa usually constitutes the second bacteria that is identified in the early stages of CF patients following S. aureus.[25]

The findings from our study underscore the complex clinical presentation of cystic fibrosis (CF) and the challenges associated with its diagnosis, particularly in developing countries. Delayed diagnosis, often attributed to the resemblance of CF symptoms to other respiratory and gastrointestinal conditions, significantly increases the risk of morbidity and mortality in affected individuals. Consistent with previous research, our study highlights the importance of early screening, especially in regions where resources for medical diagnosis may be limited.

Furthermore, our research adds to the existing body of literature regarding the genetic mutations associated with CF, with the Delta F508 mutation being the most prevalent in our cohort. However, it's notable that the prevalence of certain mutations may vary across different ethnic groups and populations, as evidenced by comparisons with studies conducted in other regions.

The diverse spectrum of clinical manifestations observed in our study, ranging from chronic cough and diarrhea to meconium-related symptoms and electrolyte imbalances, emphasizes the multisystem nature of CF. Additionally, the high prevalence of bronchiectasis and pulmonary complications underscores the importance of early detection and intervention to mitigate long-term respiratory complications.

Moving forward, efforts to enhance awareness among healthcare providers, improve access to diagnostic tools, and implement newborn screening programs can contribute to earlier detection and improved outcomes for individuals with CF, particularly in resource-limited settings. Collaborative research endeavors aimed at understanding the genetic and environmental factors influencing CF presentation and progression will further inform strategies for timely diagnosis and comprehensive management of this challenging condition.

Conclusion

In conclusion, the present study showed that the clinical complexities and diagnostic challenges associated with cystic fibrosis (CF), particularly in developing countries where resources may be limited. The delay in diagnosis observed in a significant proportion of our cohort underscores the urgent need for increased awareness and access to screening programs, especially in regions with a high prevalence of consanguineous marriages. This study also points out that Genetic mutations such as Delta F508 play a crucial role in CF, highlighting the importance of genetic testing in diagnosis and management. The diverse range of symptoms observed underscores the multisystem nature of CF, necessitating a comprehensive approach to diagnosis and treatment. In children diagnosed with cystic fibrosis, respiratory symptoms were found to be more prevalent compared to gastrointestinal symptoms. When analyzing their chest CT scans, nearly half of the examined cases showed bronchiectatic changes. Among those investigated, 27% exhibited pseudomonas colonization in their airways. In the present study, the delta F-508 mutation was identified as rare.

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