JOURNAL OF HEALTHCARE SCIENCES
Volume 1 Issue 5 2021, Article ID: JOHS2021000266
http://dx.doi.org/10.52533/JOHS.2021.1405
ISSN: 1658-8967

Original Article

Primary Ciliary Dyskinesia in Taif, Saudi Arabia: A Retrospective Study

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Received: 16 July 2021, Revised: 23 July 2021, Accepted: 23 July 2021, Published: 10 August 2021

Abstract

Introduction: Primary ciliary dyskinesia, also known as immotile-cilia syndrome, is a rare genetic disease that is inherited in an autosomal recessive manner, unfortunately there are no studies for primary ciliary dyskinesia in Taif region, yet much is still lacking in terms of identifying the different characteristics of this disease. In this paper, we aim to briefly cover those studies published about primary ciliary dyskinesia in Taif region, as well as to provide recommendations and guidelines for future studies.

Methods: This is a retrospective chart review study that was conducted by reviewing the case records of children attending primary care in one of the children's hospitals in Taif city. Children diagnosed with bronchiectasis with primary ciliary dyskinesia were included in the study. Children with other respiratory diseases were excluded from the study. The bronchiectasis diagnosis was made using a high-resolution chest computed tomography scan.

Results: A total of 10 patients were included in the study with a mean age of 4.3 ± 2.9 years. Gender had even distribution with five males and five females. It was observed that six patients had bronchopulmonary manifestations in which five patients showed asthma and one patient had pnuemopathies. The bronchopulmonary manifestations were comparatively observed more in female patients (50%) where only one of the male patients had such manifestations (p=0.010).

Conclusion: Rhinosinusitis is found to be a major clinical manifestation in primary ciliary dyskinesia patients and the prevalence of other bronchopulmonary manifestations. The management of primary ciliary dyskinesia has become challenging and in future primary ciliary dyskinesia studies in diagnosis management should utilize more collaborative partnerships between different healthcare disciplinaries.

Keywords: primary ciliary dyskinesia, immotile-cilia syndrome, kartagener syndrome,

Introduction

Bronchiectasis is a chronic progressive lung disease affecting the airways, and it still remains one of the most neglected respiratory diseases among children (1). Epidemiological data show that the incidence of bronchiectasis has increased over the past years, and this may create a substantial healthcare burden on the parents and health sector (2). Some of the causes of bronchiectasis include Cystic fibrosis, Allergic bronchopulmonary aspergillosis, Alpha1-antitrypsin deficiency, Primary ciliary dyskinesia (PCD), Autoimmune/connective tissue diseases (rheumatoid arthritis, Systemic Lupus Erythematous), Aspiration, Inflammatory bowel diseases, Congenital malformations such as Williams–Campbell syndrome (bronchomalacia), Mounier-Kuhn syndrome (tracheobronchomegaly) and lung sequestration, Humoral immunodeficiency and postinfectious (pneumonia, Bordetella pertussis, Mycobacterium tuberculosis, nontuberculous mycobacteria) (3-8). Among these causes, Primary ciliary dyskinesia (PCD) is one of the main causes of bronchiectasis, a rare genetic disorder with an autosomal recessive trait that causes defects in the cilia structure leading to dysfunction in the mucociliary clearance (9).

The mean incidence of PCD in bronchiectasis cases varies from 2.0-10.3%, and the estimated overall incidence is reported to be 1 per 10,000–20,000 births (10, 11). The inadequacy in the diagnostic methods used often makes it difficult to estimate the prevalence of PCD (12). In patients with PCD, the cilia cells lining in the nasopharynx, middle ear, paranasal sinuses, the lower respiratory tract, and the reproductive tract are disordered and dysfunctional, leading to its clinical manifestations. In children with PCD, symptoms often appear at birth or after some weeks, which is characterized by respiratory distress, abnormalities in chest x-ray, atelectasis in particular, and hypoxia (13, 14). In a newborn child, Continuous rhinorrhea, respiratory distress, or neonatal pneumonia could increase the suspicion of the presence of PCD (13), whereas, in childhood, the symptoms often include chronic productive cough, atypical asthma unresponsive to treatment, rhinosinusitis, idiopathic, bronchiectasis and recurrent otitis (15). The clinical phenotype of PCD is very wide irrespective of any age, and in children, it is often challenging to recognize respiratory exacerbations even when they have a persistent wet cough. In healthy children, most of the symptoms or signs of respiratory diseases are very common, and this makes the diagnosis of PCD often difficult, which is usually made beyond infancy or childhood that may delay the start of appropriate treatment (16, 17). The main respiratory manifestation in PCD patients usually consists of recurrent to chromic upper and lower respiratory tract infections that often get complicated with bronchiectasis as they get older (18). It is reasonable to assume that the prevalence of bronchiectasis due to PCD might be variable and local data would be required to define national health policy priorities in Saudi Arabia. So far, no epidemiological data have been conducted in the Taif region in inpatient and outpatient hospital settings. In addition, the co-existence of bronchiectasis with other obstructive pulmonary diseases, such as asthma and other pulmonary diseases, might hinder the precise assessment of bronchiectasis epidemiology; by now, no studies have evaluated prevalence and incidence in a population of patients with only bronchiectasis and no concomitant diagnosis of other chronic respiratory diseases. This study aims to estimate the prevalence and causes of bronchiectasis due to PCD in the Taif region in the children followed up by primary care physicians.

Methodology

This is a retrospective chart review study that was conducted by reviewing the case records of children attending primary care in Children's Hospital at Taif, Saudi Arabia. Children diagnosed with bronchiectasis with PCD were included in the study. Children with other respiratory diseases were excluded from the study. The bronchiectasis diagnosis was made using a high-resolution chest computed tomography (CT) scan. A convenience sampling method was used to collect the data based on the availability during the study period (October 2020- March 2021). A standardized proforma was used to collect the information from the case records, which recorded the children's age, gender, and data on conditions associated with bronchiectasis, including bronchopulmonary manifestations, ENT events, presence of complete situs inversus and Incomplete situs inversus, dextrocardia, Urogenital events, sensory impairment, and Family history respiratory disorders. All the collected information was tabulated on a Microsoft Excel sheet and transferred to IBM Statistical Package for Social Sciences, Version 23 (SPSS Inc., Chicago, IL, USA) for analysis. Descriptive statistics in the form of frequencies and percentages using suitable tables and figures were used to represent categorical data.

http://dx.doi.org/10.52533/JOHS.2021.1501

Results

In this hospital based retrospective study we included 10 children who attended the hospital due to bronchiectasis with PCD. The mean age of the patients was found to be 4.3 ± 2.9 years and the gender distribution showed that 50% (n=5) were males and 50% (n=5) were females. It was observed that 60% (n=6) had bronchopulmonary manifestations in which five patients showed asthma and one patient had pnuemopathies.

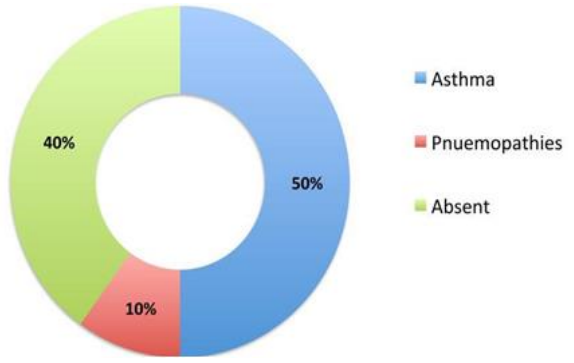

Figure 1. Bronchopulmonary manifestation (n=10)

The bronchopulmonary manifestations were comparatively more observed in female patients (50%) where only one of the male patients had such manifestations (p=0.010) **(Table 1, Figure 1).**

The prevalence of Rhinosinusitis was found in 50% (n=5) of the patients, which didn't show any statistically significant association with gender of the patients (p=0.527). The prevalence of other ENT events showed that 3 patients had history of Neonatal respiratory distress syndrome (neonatal RDS) and one patient had polydactyly. Out of 10 patients one male patient had shown Complete situs inversus and there were no incomplete situs inversus reported. Dextrocardia was present in one male patient and two male patients showed urogenital events, which was mild hydronephrosis and polycystic kidney (p=0.114). When we assessed the family history of any respiratory or ENT events in child's parents it was found that three patients reported Rhinosinusitis and one patient had Asthma **(Table 1)**.

Table 1: Causes and events based on gender of the patient and their relation

			Gender		Total	P-value
			Female	Male		
Bronchopulmonary manifestations	Present	N	5	1	6	0.010*
		%	83.3%	16.7%	60.0%	
	Absent	N	0	4	4	
		%	0.0%	100.0%	40.0%	
Rhinosinusitis	Present	N	2	3	5	0.527
		%	40.0%	60.0%	50.0%	
	Absent	N	3	2	5	
		%	60.0%	40.0%	50.0%	
Other ENT Events	Present	N	2	2	4	1.000
		%	50.0%	50.0%	40.0%	
	Absent	N	3	3	6	
		%	50.0%	50.0%	60.0%	
Complete situs inversus	Present	N	0	1	1	0.292
		%	0.0%	100.0%	10.0%	
	Absent	N	5	4	9	
		%	55.6%	44.4%	90.0%	
Incomplete situs inversus	Present	N	0	0	0	--
		%	0.0%	0.0%	0.0%	
	Absent	N	5	5	100	
		%	50.0%	50.0%	100.0%	
Dextrocardia	Present	N	0	1	1	0.292
		%	0.0%	100.0%	10.0%	
	Absent	N	5	4	9	
		%	55.6%	44.4%	90.0%	
Urogenital events	Present	N	0	2	2	0.114
		%	0.0%	100.0%	20.0%	
	Absent	N	5	3	8	
		%	62.5%	37.5%	80.0%	
Family history of Respiratory/ENT disorders	Present	N	1	3	4	0.197
		%	25.0%	75.0%	40.0%	
	Absent	N	4	2	6	
		%	66.7%	33.3%	60.0%	

ENT, ears nose and throat, N: numbers

http://dx.doi.org/10.52533/JOHS.2021.1501

Discussion

In infants with PCD, the abnormal ciliary function could gradually lead to respiratory distress, which leads to persistent wet cough, rhinosinusitis, and bronchiectasis (18). In our study, half of the patients had rhinosinusitis, and this may lead to stasis and bacterial colonization that commonly include bacteria such Streptococcus pneumonia, Moraxella catarrhalis, Haemophilus influenzae non–type b, Pseudomonas aeruginosa, and Staphylococcus aureus (19). Genetic studies show that more than 35 cilia-related genes have proven to cause PCD, and experts have the opinion that there are more genes to be discovered for this disorder (20, 21). Thus, minimizing exposure to these respiratory infections and pathogens is crucial in these children when visiting hospitals, schools, or daycare settings. When monitoring PCD in children, the clinical outcomes should give the physician or pediatrician an insight into the patient's current status compared with the previous assessment of the disease's status. The clinician could look into various clinical outcomes such as mortality, exacerbation rate, admission rates in hospitals, growth outcomes (anthropometric measurements of the child, bioelectrical impedance analysis), lung function (Lung Clearance Index, plethysmography, Spirometry), and using age-appropriate questionnaires such as QOL-PCD (22-24).

The current study findings show that only one patient had chronic situs inversus. It is often said that patients having these situs abnormalities have Kartagener syndrome, a triad of chronic sinusitis dextrocardia with situs inversus and bronchiectasis (25). In our study, dextrocardia was present in one patient, and the same patient had chronic sinusitis, which suggests that the patient may have Kartagener syndrome. Chronic obstructive pulmonary disease (COPD) is considered a co-morbidity in patients with bronchiectasis, which is often associated with marked bronchial inflammation, frequent pathogenic colonization, and severe airway obstruction (26).

The diagnosis of PCD is often a complex and challenging process due to its clinical and genetic heterogeneity. The diagnosis is often confirmed by transmission electron microscopy (TEM) for a classic PCD ultra-structural ciliary defect or biallelic mutations in an already identified PCD gene, which again depends on age criteria (27, 28). In the management of PCD, the main aim should be to recover or maintain lung function, which depends on mucus clearance, respiratory infection prevention, and effective antibiotic therapy for bacterial infections (29).

The management is usually symptomatic and depends on specific conditions associated with PCD. In PCD patients, Otitis media (OME) with effusion is a universal finding, and the management of OME is often controversial. Studies have demonstrated that ventilation tube insertion is effective in improving hearing and achieving a dry ear (30, 31). But recent evidence shows that ventilation tubes offer no advantages and could lead to persistent mucous discharge and also could predispose to chronic otorrhoea (16). In PCD patients, chronic sinusitis symptoms are lifelong, and it is the focal point of all respiratory infections. Long-term combinational therapy of antibiotics and steroid nasal sprays could control sinusitis in most PCD cases (32, 33). Even though maintenance therapy using antibiotics has shown clinical effectiveness, it could lead to antibiotic resistance development. Another common finding in PCD patients is Nasal polyposis, and the prevalence of approximately 30% has been reported (34). This condition's treatment involves a combination of medical therapy using corticosteroids and surgical measures after patient assessment (34, 35). In patients with bronchiectasis, antibiotic therapy depending upon the isolated organisms could give symptomatic relief. In some patients, a lobectomy is a therapeutic option; some experts have the opinion that it is rarely needed due to the reasons that the basal defective mechanism is diffuse and is not limited to lobes of the lungs (36). Our study poses some limitations. Firstly, the sample size we included was insufficient for drawing enough conclusions for the prevalence of many risk factors. Secondly, this research was conducted in a single center may have called for bias. A multi-center study involving more patients with PCD is further needed to verify the current findings.

Conclusion

In conclusion, Rhinosinusitis is found to be a major clinical manifestation in PCD patients and the prevalence of other bronchopulmonary manifestations such as asthma and pnuemopathies are not uncommon in PCD patients. The diagnosis and management of PCD in bronchiectasis in patients depends on the clinical presentation and associated comorbidities. Due to the lack clinical trials, the management of PCD has become challenging and in future PCD studies in diagnosis management should utilize more collaborative partnerships between different disciplinarians and countries.

http://dx.doi.org/10.52533/JOHS.2021.1501

Declaration

Statement:

The authors declare no conflict of interest.

Funding:

None

Ethical Consideration:

The study was approved by Taif University Institutional Review Board (IRB) and all data was collected assuring complete confidentiality of the patient's personal information. All methods were performed in accordance with the relevant guidelines and regulations Declaration of Helsinki.

Data Availability:

All data is available withing the article.

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