Clinical profile and outcome of Childhood Interstitial Lung Disease (chILD) Syndrome in a tertiary pediatric hospital: a 10-year review (2013-2022)

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OBJECTIVE: This study described childhood interstitial lung disease profiles at the Philippine Children's Medical Center (2013-2022).

MATERIALS AND METHODS: A retrospective chart review at PCMC analyzed pediatric interstitial lung disease cases (Jan 2013-Dec 2022). Included were patients aged 0-18 with childhood interstitial lung disease. Excluded were those with specific conditions. Data included clinical course, tests, therapeutic management, and short-term outcomes based on a previous study.

RESULTS: Twenty-three patients were included in this study. Most (52.17%) were diagnosed between 2013-2017, and were within the ages of 0-2 years. Majority of patients had normal nutritional status (52.17%). Common clinical presentation on admission included breathing difficulties, with chest retractions, crackles, and hypoxemia. Few had a family history of chronic lung disease. Comorbidities included pulmonary hypertension (30.43%) and pulmonary tuberculosis (21.74%). Chest radiography revealed infiltrates in all cases, and HRCT scans showed ground glass opacities in 82.61%. Prednisone was the primary treatment (86.96%). Lung biopsy results (43.48%) were mostly unclassified or nondiagnostic, with lymphoid interstitial pneumonia as the predominant diagnosis (20%). Improvement of signs and symptoms was seen in 39.13% of cases, whereas death occurred in 21.74%. Furthermore, the outcome remained undetermined in as much as 34.78% of cases due to inadequate follow-up.

CONCLUSION: This retrospective study emphasizes chILD's prevalence in infants under 2 years, with male predominance. Nutritional variations underscore the need for supplementation. Various common signs include crackles, retractions, and hypoxemia, with breathing difficulty as a frequent symptom. The diagnostic process involves imaging and ancillary tests, advocating a systematic approach with noninvasive methods like CXR and HRCT, reserving lung biopsy for inconclusive cases. Corticosteroids, whether used alone or in combination, prove beneficial in managing chILD by suppressing inflammation.

KEYWORDS: Childhood interstitial lung disease, clinical profiles, treatment outcome

INTRODUCTION

Childhood interstitial lung disease (chILD) is a heterogeneous group of rare pulmonary disorders, comprising approximately more than 200 immune- and nonimmune-mediated respiratory conditions presenting with impaired gas exchange and diffuse radiologic infiltrates on plain radiographs [1,2,5]. chILD is associated with high morbidity and mortality, and it depends on the specific type of chILD disorder [1,3]. Reports on its mortality rates, incidence and prevalence vary are relatively underrepresented in and pulmonary research as compared to adult data [1]. A study done at the Philippine Children's Medical Center (PCMC) last 2019 assessed the association of chest high resolution CT scan, histopathology findings and severity illness score to the survival rate of patients with chILD in our institution [6]. Although this study included demographic data and survival rates of chILD patients, it underestimated the total population of chILD in our institution by excluding patients who did not undergo biopsy. Biopsy is just one of the ways in which a diagnosis can be made. Biopsy is routinely requested for all patients labeled as chILD, but due to the invasiveness of the procedure, securing consent is difficult. The global thrust now is to utilize other non-invasive modalities before resorting to biopsy. According to the American Thoracic Society, fulfilling three out of the four criteria of chILD makes

physicians diagnose patients as having chILD Syndrome already. These include respiratory symptoms, such as cough, rapid and/or difficult breathing, or exercise intolerance; respiratory signs like tachypnea, adventitious sounds, retractions, digital clubbing, failure to thrive, or respiratory failure; hypoxemia; and diffuse abnormalities on a chest radiograph (CXR) or computed tomography (CT) scan [4]. Clinical profiles and outcomes of chILD vary by age at presentation [1]. Despite the heterogeneity of these disorders, such as age of presentation, genetic mutations, disease course, international studies have posited overlapping clinical manifestations [2]. This review explored these issues to better elucidate the different clinical presentations of chILD in Filipino children, and their outcomes for recommendations for future research and treatment advancement. This study included patients who have and have not undergone pulmonary biopsy for histopathologic confirmation. Apart from these, this study can potentially increase international relations and partnerships with companies or pharmaceutical industries for possible funding of resources such as medications for patients with chILD.

Childhood interstitial lung disease is a rare group of pulmonary diseases, characterized by a disordered exchange of gases attributable to different pathological mechanisms [1,5]. The exact incidence of chILD is unknown, and different studies have reported varying statistics which may be due

to differences in the population included in these studies. Ferraro and associates have reported an estimate of 0.13 to 16.2 cases of chILD per 100,000 children per year [2]. In the Philippines alone, studies regarding its incidence or prevalence are lacking. Etiologies of chILD were broadly grouped in studies into those occurring in patients less than 2 years old (or ILD specific to infancy), those occurring in ages 2-18, which may be related to a primary systemic disease or follow a harmful exposure to irritable antigens [2,3]. According to a Japanese study by Kitazawa and Kure, chILD occurring in infancy are а result of congenital malformations, genetic mutations, or chronic damage of the lung due to premature birth or other congenital anomalies [2]. Diagnosis of chILD was consistent with all studies which used different clinical parameters including history and physical examination, chest radiography, high resolution chest CT, pulmonary function testing, bronchoscopy with BAL, echocardiography, genetic testing, and/or lung biopsy, which remains to be the gold standard. But according to the American Thoracic Society Clinical Practice Guidelines, the diagnosis of chILD requires that all neonates and infants below 2 years old presenting with diffuse lung disease known to have been caused by common diseases in this age group are excluded. These include cystic fibrosis, congenital or acquired immunodeficiency, congenital heart disease, bronchopulmonary dysplasia, pulmonary

infection, primary ciliary dyskinesia presenting with newborn respiratory distress, and recurrent aspiration. Once these common diseases that can cause DLD have been eliminated, a neonate or infant with DLD is regarded as having "chILD syndrome" if at least three of the following four criteria are present: (a) Respiratory symptoms (cough, rapid and/or difficult breathing, or exercise intolerance); (b) respiratory signs (tachypnea, sounds, retractions, adventitious digital clubbing, failure to thrive, or respiratory failure); (c) hypoxemia; and (d) diffuse abnormalities on a chest radiograph (CXR) or computed tomography (CT) scan [4]. There is a highly variable severity of chILD at initial presentation. Some present with mild nonspecific symptoms, while others present with a very severe clinical picture at the onset [2]. Sankar and associates included an assessment of disease severity by assigning an illness score based on data gathered from the patient records at the time of their initial evaluation [5]. Ferraro, et.al. identified the common clinical manifestations of chILD depending on the age of presentation. According to this study, chILD may present shortly after birth with unexplained respiratory distress in term neonates, who can rapidly require intubation and ventilation. Preterm infants may present with an acute respiratory distress which is more severe than would be expected because of prematurity [2]. During the first two years of life, the clinical symptomatology vary from having no Two studies from Italy and India have reported the older children present with various nonspecific respiratory manifestations, such as dyspnea, polypnea, dry cough, wheezing, recurrent respiratory infections and exercise intolerance, including other more severe signs and symptoms like hemoptysis, pallor, clubbing, crepitation, and murmur [2,5]. In the study of Sankar et.al., the outcomes assessed included death and symptomatic improvement in dyspnea, hypoxemia and/or lung function tests. It also evaluated the determinants of poor outcomes other than the abnormalities on plain radiographs and chest CT scan, which include the effect of severe hematological investigations at presentation such as total leucocyte count, and liver function tests at presentation such as serum glutamic oxalacetic transaminase. serum glutamic pyruvic transaminase, and alkaline phosphatase (ALP) [5]. In this study, the investigators found out that apart from having a disease severity of graded 3 or higher at initial presentation, lower median serum ALP levels correlated to poorer outcomes.

This study aims to provide a comprehensive description of the clinical profiles and outcomes of pediatric patients with interstitial lung disease admitted to the Philippine Children's Medical Center (PCMC) from 2013 to 2022. Furthermore, it will likewise include determining the age and gender distribution of chILD patients admitted

to PCMC, identifying common sym toms, and evaluating the diagnostics and therapeutics used in their management. Additionally, the study aims to assess the clinical outcomes of chILD patients admitted to PCMC during the specified period from 2013 to 2022.

MATERIALS AND METHODS

The investigator employed a retrospective chart review of children admitted in PCMC who were discharged with a final diagnosis of interstitial lung disease between January 2013 until December 2022. This study was approved by the Philippine Children's Medical Center Institutional Review Board.

Included in the study are patients who met the following criteria: 1) patients ages 0 to 18 admitted from January 2013 until December 2022 with childhood interstitial lung disease syndrome; 2) patients without lung biopsy diagnosed with childhood interstitial lung disease on the basis of clinical signs and symptoms, presence of hypoxemia and characteristic findings on chest x-ray or high-resolution CT scan; 3) patients who underwent lung biopsy with findings suggestive of childhood interstitial lung disease. Children with bronchopulmonary dysplasia (BPD), cystic fibrosis, malignancy, primary or acquired immunodeficiency, coagulation disorders, vasculitis, celiac disease and vascular malformations were excluded from the study.

Case records of children diagnosed with chILD were obtained from the Medical Records Section of our institution for patients who were admitted for collection of data regarding the clinical course, ancillary tests used such as plain chest radiographs, chest high resolution CT scan, bronchospcopy and bronchoalveolar lavage (BAL) analysis. Data regarding the therapeutic management received and follow-up after hospital discharge of these children were also retrieved from patient records. Demographic data and symptomatology of each patients were collected, including laboratory findings and

RESULTS

A total of 23 patients were included in the study. Out of the 23 patients, 65.22% (n = 15) cases were diagnosed between 2013 to 2017,

results of all diagnostic imaging used. Identifying the short-term outcomes was patterned from the study of Sankar, et.al. The variables which were assessed included death and improvement of symptoms—improvement in dyspnea, hypoxemia and/or lung function tests—at follow up from after 3 months of starting therapy until the time of last follow up record available [4]. Outpatient records from the Section of Pediatric Pulmonology were obtained to gather data on these immediate outcomes. In our study, the collected data were presented as frequency (f) or percentage (%) as appropriate.

and 34.78% (n = 8) cases between 2018 to 2022. Table 1 shows the clinical characteristics of these patients.

Table 1. Clinical Profile of patients diagnosed with chILD admitted from January 2013 to December 2022

| | Demographic Parameters | Frequency (n) | Percent (%) |
|--------------------------|------------------------|---------------|-------------|
| Age at symptom onset | 0 - < 2 years | 15 | 65.22 |
| | 2-5 years | 7 | 30.43 |
| | 6-10 years | - | - |
| | >10 years | 1 | 4.35 |
| Age upon diagnosis | 0 - < 2 years | 12 | 52.17 |
| | 2-5 years | 8 | 34.78 |
| | 6-10 years | 2 | 8.70 |
| | >10 years | 1 | 4.35 |
| Neonatal Maturity | Term | - | - |
| | Preterm | 2 | 8.70 |
| Gender | Male | 13 | 56.52 |
| | Female | 10 | 43.48 |
| Weight-for-length/height | Normal for age | 12 | 52.17 |
| | Z score below -2 | 3 | 13.04 |
| | Z score below -3 | 8 | 34.78 |
| Signs | Hypoxemia | 20 | 86.96 |
| - | Retractions | 22 | 95.65 |
| | Crackles | 21 | 91.30 |
| | Wheezes | 13 | 56.52 |
| | Tachypnea | 17 | 73.91 |
| | Cyanosis | 6 | 26.09 |
| | Hemoptysis | - | - |
| | Clubbing | 3 | 13.04 |

| Symptoms | Cough | 19 | 82.61 |
|-------------------------------|---|----|-------|
| | Difficulty of Breathing | 23 | 100 |
| | Gurgly chest | 1 | 4.35 |
| | Limitation of activity | - | - |
| Family History of Respiratory | None | 17 | 73.91 |
| Disease | With family history of chronic lung disease | 6 | 26.09 |
| Other co-morbidities | Congenital heart disease (VSD, PFO) | 3 | 13.04 |
| | Rheumatic heart disease | 1 | 4.35 |
| | Pulmonary tuberculosis | 5 | 21.74 |
| | Bronchial Asthma | 1 | 4.35 |
| | Pulmonary Hypertension | 7 | 30.43 |
| | Cor Pulmonale | 1 | 4.35 |

Majority of patients had onset of symptoms and were diagnosed between the age of 0-2 years, comprising 65.22% and 52.17% of cases, respectively. Notably, only two cases manifested during the neonatal period, and both were premature births (8.70%). There was also note of slight male predominance.

Around 52.17% of patients had a normal weight-for-length/height. Following this, 34.78% (8 out of 23) of cases are categorized under the nutritional assessment of z < -3, indicating severely wasted when plotted on the World Health Organization Growth Charts.

The most common presenting symptom is difficulty of breathing which was seen in all patients with chILD. On admission, the most common signs collectively noted were chest retractions, crackles, and hypoxemia. None of these cases presented with limitation in activity and hemoptysis. Only 26.09% (n = 6) of the cases reviewed had a family history of chronic lung disease. Family members of these patients were noted to have bronchial asthma. Majority of the patient had no co-morbidities, while 11 were noted to have other medical conditions upon diagnosis. Pulmonary hypertension and pulmonary tuberculosis were the most common co-morbidities noted, presenting at 30.43% and 21.74%, respectively. Seven patients with pulmonary hypertension were classified based on echocardiographic findings as mild pulmonary hypertension (pulmonary arterial pressure = 35-50 mmHg), while 1 was classified as moderate pulmonary hypertension (pulmonary arterial pressure = 50-70 mmHg). Of these patients with pulmonary hypertension, majority had a concomitant pulmonary tuberculosis while the others had congenital heart diseases (i.e. ventricular septal defect and patent foramen ovale)

Table 2 shows the various modalities employed in the diagnosis of these patients.

| | Parameters | Frequency (n) | Percent (%) |
|----------------------|-------------------------------------|---------------|-------------|
| Chest X-ray Findings | Normal | - | - |
| | Infiltrates | 23 | 100 |
| | Hyperaeration | 8 | 34.78 |
| | Consolidation | 6 | 26.09 |
| | Cardiomegaly | 1 | 4.35 |
| High Resolution CT | Ground Glass Opacities | 19 | 82.61 |
| Scan Findings | Consolidation | 4 | 17.39 |
| | Bronchiectasis | 6 | 26.09 |
| | Hyperinflation | - | - |
| | Reticular Opacities | 10 | 43.48 |
| | Nodules/Cysts | 4 | 17.39 |
| | Fibrosis | 6 | 26.09 |
| Other tests done | Echocardiography | 11 | 47.83 |
| | Bronchoscopy | 4 | 17.39 |
| | Bronchoalveolar Lavage | 2 | 8.70 |
| | Spirometry | - | - |
| | Immunodeficiency Panel | 2 | 8.70 |
| Biopsy | Desquamative Interstitial Pneumonia | 1 | 10 |
| | Hypersensitivity pneumonitis | 1 | 10 |
| | Idiopathic Pulmonary Hemosiderosis | 1 | 10 |
| | Lymphoid Interstitial Pneumonia | 2 | 20 |
| | Post-infectious (tuberculosis) | 1 | 10 |
| | Focal interstitial pneumonitis | 1 | 10 |
| | Unclassified | 3 | 30 |

Table 2. Diagnostic procedures employed in patients diagnosed with chILD admitted from January 2013 to December 2022

All patients underwent chest radiography, which all showed presence of pulmonary infiltrates. Chest HRCT scan was done in 21 cases. Out of these the presence of ground glass opacities was the most common anomaly seen at 82.61% (n = 19).

Other ancillary tests done in these patients include echocardiography in 47.83% (n = 11) to determine the presence of

pulmonary hypertension and assess its severity, as well as the presence of congenital heart diseases. Only 2 of these patients had normal echocardiographic findings. There was a 17.39% (n = 4) of patients who underwent bronchoscopy. Half of which revealed unremarkable results, while the rest showed findings of nonspecific endobronchitis, tracheomalacia, and distal segment thickening of aryepiglottic folds probably secondary to chronic laryngopharyngeal reflux.

Only two cases (8.70%) had bronchoalveolar lavage. One of which showed nonspecific findings such as inflammatory infiltrates composed of few mononuclear cells, neutrophils, eosinophils, with no atypical or malignant cells noted. There were also 2 patients (8.70%) who had immunodeficiency panel done to determine the presence of a primary or acquired cases immunodeficiency. Both showed normal immunologic profiles.

Out of the cases examined, only 43.48% (n = 10) underwent a lung biopsy, primarily because obtaining parental consent for the procedure was challenging due to its invasive nature. Majority of the histopathologic findings were unclassifiednondiagnostic and with insufficient information. Of those which features are consistent with the classification of chILD, lymphoid interstitial pneumonia was the most 20% = 2). common at (n Other histopathologic features seen in patients who underwent lung biopsy which are consistent with chILD.

All patients received treatment, with steroids being the most common drug given, singly or in combination with hydroxychloroquine and macrolides, as shown in Table 3.

| Table 3 | 3. Therape | utics ı | used in pat | tients c | liag | nosed with |
|---------|------------|---------|-------------|----------|------|------------|
| chILD | admitted | from | January | 2013 | to | December |
| 2022 | | • | | | | |

| | Parameters | Fre- quen cy (n) | Per- cent (%) |
|----------------|---|------------------------|---------------------|
| Thera- | Corticosteroids only | 7 | 30.43 |
| peutics Re- | Hydroxychloroquine only Anti-immunomodulatory Drugs only | - | - |
| ceived | Macrolides only | - | 13.04 |
| | Corticosteroids + HCQ | 3 | 13.04 |
| | Corticosteroids + Macrolides | 3 | 17.39 |
| | Corticosteroids + HCQ + Macrolides | 4 6 | 26.09 |

Outcomes of the patients were identified from outpatient records within 3 months from hospital discharge (Table 4). Improvement was seen in 39.13% of cases, whereas death occurred in 21.74%, due to either infection or respiratory failure. In addition, outcome could not be determined in up to 34.78% of cases due to poor follow up.

Table 4. Clinical outcomes of patients diagnosed withchILD admitted from January 2013 to December 2022

| | Parameters | Fre- quenc y (n) | Percent (%) |
|----------|-------------------------------|------------------------|----------------|
| Out- | Died | 5 | 21.74 |
| comes | Improved activity by 3 months | 9 | 39.13 |
| of | No improvement by 3 months | 1 | 4.35 |
| patients | Lost to follow up | 8 | 34.78 |

DISCUSSION AND CONCLUSION

Childhood interstitial lung disease can occur at any age group ranging from infancy to adolescence. It encompasses a wider range of disorders than in adults but is more commonly seen in infancy and young children. Our study showed a similar trend, with 34.78% of patients diagnosed before 2 years old. Clement et al. linked this to lung growth during alveolar development stages [7]. Fan et al. (2010) supported this, reporting 187 infants under 2 years with diffuse lung disease, half of whom had age-specific disorders.

Although our study showed no significant difference between the genders, it is still notable that there was a slight male predominance in terms of gender distribution, similar to other reports (57-58.1%) [9, 10].

Alsharkawy et al. (2021) linked weight loss in chILD patients to systemic inflammation, increased metabolic rate, which promotes a negative nutritional balance, and anorexia, which reduce caloric intake. Deterding et al. reported poor nutritional status in many chILD patients requiring supplementation. In our study, while most had normal weight-for-length/height, 34.78% showed severe wasting, emphasizing the importance of maintaining proper nutrition and aggressive supplementation.

Our study showed that patients with chILD present with various signs and symptoms including, cough, difficulty of breathing, tachypnea, chest retractions, crackles with wheezing on auscultation, and hypoxemia, which were comparable to previous studies [2, 3, 10]. As reported by the American Thoracic Society, tachypnea is the most common sign of chILD, which was noted in 75–93% of patients. Hypoxemia, crackles, and cough were also reported to be common.

Diffuse abnormalities on chest radiographs (CXR) or CT scans are part of chILD diagnostic criteria. CXRs are favored for their low radiation dose, cost, ease, and availability, but their low-contrast resolution often results in nonspecific findings [13]. Guillerman noted hyperinflation as a common CXR abnormality, though in our study, only 34.78% of patients had hyperaerated lungs, with all cases showing nonspecific pulmonary infiltrates. These infiltrates, visible as increased density or "whitening," are common in interstitial lung disease due to pulmonary inflammation and may indicate conditions ranging from infections to malignancies [17]. Patients with interstitial lung disease often show pulmonary inflammation, making lung infiltrates a common finding in chest radiographs, as observed in our study.

High-resolution computed tomography (HRCT) is the preferred imaging for chILD due to its high sensitivity and precision in assessing disease extent. While HRCT findings can be nonspecific, widespread ground-glass opacities (GGO), indicating active disease, were the most common feature in our study (82.61%). A 2019 institutional study linked HRCT findings to survival, with hyperinflation showing the longest mean survival time and mosaic attenuation the shortest (10.3 months) [18]. GGO was prevalent in cases of nonspecific interstitial pneumonia (73.3%), desquamative interstitial pneumonia, and bronchiolitis obliterans

organizing pneumonia, often accompanied by bronchiectasis or hyperinflation.

Hypersensitivity pneumonia (HP) andlymphocytic interstitial pneumonia (LIP) showed GGO on HRCT, while pulmonary interstitial glycogenosis (PIG) presented with consolidation. In our study, GGO with bronchiectasis was observed in DIP, HP, and post-tuberculosis cases, while LIP and idiopathic pulmonary hemosiderosis (IPH) showed GGO with fibrosis and consolidation.

While tissue biopsy is the gold standard for chILD diagnosis, it is challenging in advanced stages due to risks and may yield inconclusive results, especially in areas with honeycombing. Blanco et al. recommended targeting regions with GGO for better results [19]. aligning with our findings of predominant GGO. Diagnostic approaches now favor noninvasive tests and therapeutic trials over routine biopsies. Qureshi et al. suggested steroid therapy for suspected conditions like interstitial pneumonias and fibrosing alveolitis, even without definitive biopsy confirmation [20]. Sankar et al. advised reserving biopsies for cases unresolvable through noninvasive methods or unresponsive to treatment [5].

Bronchioalveolar lavage (BAL) is valuable for cytologic, microbiologic, and molecular analysis [13], while fiberoptic bronchoscopy (FOB) allows airway inspection and biopsies but rarely provides diagnostic insights for chILD [15]. Respiratory involvement, including chILD, poses significant morbidity and mortality risks in primary immunodeficiency [16], though immunologic profiles were normal in two recurrent pneumonia cases from our study. Pulmonary hypertension, linked to chronic hypoxia or connective tissue disorders, was identified in 30.43% of cases (mild) and 4.35% (moderate). Gupta et al. reported cardiovascular involvement in 68% of chILD patients, with pulmonary hypertension being the most common at 50%.

Supportive care for children with chronic lung disease includes oxygen therapy for hypoxemia, proper nutrition, aggressive infection management, and bronchodilators. Most children with ILD also receive immunosuppressive, anti-inflammatory, or antifibrotic drugs for extended periods [7]. Corticosteroids remain the most commonly used drugs, as they may help suppress inflammation in idiopathic ILD. In our institution corticosteroids were the primary treatment, often combined with other therapies.

For steroid-resistant cases, alternative agents like hydroxychloroquine, preferred over chloroquine due to fewer side effects, are used [7]. If symptoms persist, other immunosuppressive drugs such as azathioprine, cyclophosphamide, cyclosporine, or methotrexate may be considered [7], though these were not used in our study. Macrolides like azithromycin and clarithromycin, with immunomodulatory properties [3], were also part of treatment options. with GGO accompanied by fibrosis and consolidation.

Obtaining tissue biopsy а is considered as gold standard for diagnosis of chILD, however, the process in performing this in children is difficult especially when they present in advanced clinical stages and considered high risk for general are anesthesia. Additionally, biopsy may not always render conclusive results. According to the study of Blanco et al., several factors were with obtaining inconclusive associated histology. Biopsies performed in advanced stages of the disease were less informative. Furthermore, specimens obtained from regions exhibiting substantial honeycombing on HRCT produced unsatisfactory results, possibly attributed to the presence of reduced tissue and an abundance of enlarged air spaces with thick fibrotic walls. Consequently, regions displaying ground glass opacities were preferred as the biopsy site [19]. This could be a sensible approach, given that the majority of HRCT findings in our study indicated the presence of GGO. The trend nowadays is moving towards a systematic approach to the diagnosis, which includes noninvasive tests and response to therapy, rather than subjecting every patient to biopsy. The study of Qureshi et. al looked into the usefulness of lung biopsy in the management of ILD. According to this study, conditions like interstitial pneumonia, diffuse interstitial pneumonia, interstitial pulmonary fibrosis, fibrosing alveolitis,

bronchiolitis obliterans, organizing hypersensitivity pneumonia, sarcoidosis. pneumonitis, or eosinophilic pneumonia may necessitate steroid treatment when patients exhibit symptoms. In cases where one of these conditions is suspected clinically without a definitive tissue diagnosis, it may be prudent consider a therapeutic trial. This to recommendation grounded in is the observation that even after lung biopsy procedures were conducted, the administration of steroids remained the most prevalent form of therapy in their series [20]. According to Sankar et. al, lung biopsy could be reserved for those children in whom the diagnosis is inconclusive after exhausting noninvasive diagnostic modalities and having poor response to treatment [5].

Bronchioalveolar lavage (BAL) is useful if providing specimens for cytologic, microbiologic, and molecular examinations [13].

Fiberoptic bronchoscopy (FOB) allows physicians to inspect and perform biopsy of the airways, BAL and transbronchial biopsy. However. it rarely gives diagnostic information on chILD [15]. Respiratory involvement, especially chILD, causes a significant risk of morbidity and mortality among patients with primary immunodeficiency [16]. Two patients included in our study who presented with recurrent pneumonia underwent immunologic studies. Both cases showed normal immunologic profiles.

This retrospective study concludes that chILD occurs most commonly in infants less than 2 years old. Although there is no statistically significant gender difference in its prevalence, this study still noted a slight male predominance. Majority of cases had normal nutritional status; however a number of cases were severely wasted. This emphasizes the importance of nutritional supplement as an integral part of the management of chILD. Signs and symptoms of chILD are nonspecific as any other chronic lung disease, hence, there must be a high index of suspicion when considering such diagnosis. As with previous studies, findings on chest xray and HRCT can give clues to the diagnosis, such as ground glass infiltrates. Additional ancillary tests like echocardiography, BAL, bronchoscopy, and immunodeficiency panel may be used to assess complications and risk factors. Several studies have shown improvement of symptoms with use of corticosteroids. Our study noted similar findings.

LIMITATIONS OF THE STUDY AND Recommendations

This study examined a limited cohort of 23 cases over a 10-year period. For future research, we suggest expanding the review period to encompass a larger study population. In this investigation, we explored the correlation between patients' gender, signs and symptoms, chest radiograph and HRCT findings, as well as the medications they

received, with their outcomes three months post-discharge. We propose that future research should also consider examining the association between 2D echocardiography findings and biopsy results with patient outcomes. It is important to note that this study exclusively focused on patients with chILD who were admitted to our institution and subsequently discharged, with follow-up in the outpatient department. Patients referred to and seen in the outpatient department without admission were not included. To enhance the comprehensiveness of demographic data within our institution, we recommend incorporating these patients into future studies.

ACKNOWLEDGEMENT

The primary investigator extends heartfelt thanks to those instrumental in making this study a reality. Dr. Jenni Rose Dimacali's invaluable supervision and guidance were a privilege to experience. Gratitude to Dr. Maria Luz Del Rosario for patient review and continuous support. The motivation and encouragement received propelled the investigator to complete the study. Special appreciation to the Education, Training, and Research Department and the Institutional Research-Ethics Committee for consistently guiding and inspiring him to produce this significant study. Without their approval and trust, this study would not have advanced. Sincere gratitude to the Medical

Records and Outpatient Department staff and Pediatric Pulmonology fellows, especially Dr. Joie Aseamie Flores, for dedicating their time to assist during data collection. Family and friends played a crucial role in providing support and motivation throughout. The investigator acknowledges the divine blessings that sustained the study to its successful completion.

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