



A Study on Etiology and Outcome of Persistent Pneumonia in Children in a Tertiary Care Centre in Bhagalpur.

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ABSTRACT Objective: To identify the underlying causes of persistent pneumonia in children. Methods: 82 cases with persistent pneumonia were investigated (biochemical, microbiological, histopathological, immunological and radiological tests) to find out the underlying cause. Results: Out of 82 cases, 24 had Gram negative bacterial infections, 24 had aspiration due to gastroesophageal reflux disease or oil instillation, 16 had pulmonary tuberculosis, 6 had immunodeficiency due to HIV infection, 4 had congenital lung malformation, 4 had cardiac disorders and two had foreign body aspiration as causes of persistent pneumonia. The etiology could not be established in two cases. Conclusion: In the present study, most common underlying cause of persistent pneumonia were persistent infection followed by aspiration and acquired immunodeficiency.

KEYWORDS : Children; Persistent pneumonia; Oil instillation pneumonia; Tuberculosis; HIV infection.

INTRODUCTION

Pneumonia is a major problem in children; the World Health Organization (WHO) estimated that pneumonia occurred in approximately 156 million children (151 million in developing countries and 5 million in developed countries).[1] Pneumonia is the top infectious killer of children under 5 years worldwide, resulting in 935,000 deaths each year.[2] Lower respiratory tract infection (LRTI)/ pneumonia is the most common cause of childhood morbidity and mortality, surpassing the death due to diarrhea in developing countries.[3] Non-resolving pneumonia or persistent pneumonia in children pose a significant challenge to the pediatricians and respiratory physicians. Persistent pneumonia (PP) is defined as the persistence of symptoms and radiographic abnormalities in a child with LRTI for more than a month despite a course of antibiotic therapy for 10 days.[4,5,6] Though many investigators have accepted this definition, some authors still prefer to use a cut-off of longer duration.[7]

Objective of the present study was to identify the causes and the contributing factors of persistent pneumonia in children. Very few studies in medical literature have reported on the etiology and the course of persistent pneumonia in children. Moreover, most studies available in literature have described persistent and recurrent pneumonia as a single entity. [8, 9] Therefore there is a need for clarity on Persistent Pneumonia in children, hence the present study was conducted in order to guide the Pediatricians in our region to prevent and control this disease.

MATERIALS AND METHODS:

This prospective study was conducted in the department of pediatrics, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India. Persistent pneumonia cases (2 months – 13 years) who came to the hospital between March 2015 and February 2017 were included in the present study. Persistent pneumonia was defined as features of lower respiratory tract infection (i.e., cough, tachypnea and fever with or without chest retractions) with radiological evidence of infiltrates or consolidation in the lungs persisting for 30 days or more, despite receiving antibiotics for a minimum period of 10 days. Attempt was made to clearly determine the underlying cause and the microbial agent responsible for the persistent infection in the children

A structured Proforma was used to collect the data. Special attention for history was given to age and sex; duration of symptoms; treatment given, if any; contact with tuberculosis; immunization status; developmental milestones and foreign body aspiration or oil instillation into nostrils. Clinical examination and nutritional assessment were done for all. Weight and height classification was done according to CDC growth charts developed by National Centers for Health Statistics (NCHS) in collaboration with National Centre for Chronic Disease Prevention and Health Promotion (2000).[10] Complete hemogram including hemoglobin, total and differential leukocyte count, absolute eosinophil count, peripheral smear,

erythrocyte sedimentation rate (ESR), blood culture and sensitivity and ELISA for human immunodeficiency virus (HIV) infection were done. Mantoux test was done for tuberculin sensitivity using 1 TU PPD with RT Tween 80 which was administered intradermally and reading was taken after 48-72 hours. Gastric aspirate for young children and sputum for older children were sent for acid fast staining on three consecutive days. Tracheal aspirate was taken for culture from the cases that were admitted in PICU and intubated. Chest roentgenograms posteroanterior view in older children and anteroposterior view in younger children and a lateral view were taken, to document the presence of infiltrates or consolidation. Computed tomogram of thorax with contrast was done whenever necessary. Bronchoscopy and bronchoalveolar lavage (BAL) were done in selected cases. BAL fluid was subjected to microbiological and cytological assessment. Ultrasonography of thorax was performed in suspected cases of pleural effusion and pleural aspirate was obtained and examined for bacteria, adenosine deaminase, AFB stain and cytology. Barium-meal study was performed in suspected cases of gastroesophageal reflux disease. Arterial blood gas analysis was done in selected cases. Chest radiograph and computed tomography images were interpreted by three independent observers. At the end of the study, analysis was done to find out the etiology for persistent pneumonia.

RESULTS

The study group consisted of 82 cases. The age ranged from 2 months to 11 years with a mean age of 3.3 years at the time of presentation. Out of 82 cases 54 were males (65.8%) and 28 were females (34.2%) with a male to female ratio of 1.9:1. Most of the cases were underweight with 72 patients (87.8%) falling into less than fifth centile category. Assessment of height/length showed 36 patients (43.9%) below fifth centile while six patients (7.3%) had height/length above 95th centile. History of contact with tuberculosis patient was present in 12(15%). BCG scar was absent in 21.9% of cases. Sixteen cases (19.5%) had positive tuberculin sensitivity by Mantoux test. Gastric aspirate/sputum for acid fast bacilli (AFB) was positive in sixteen out of 82 patients (19.5%). Six patients (7.3%) tested positive for human immunodeficiency virus (HIV). Ten patients had developmental delay. The bacterial growth pattern in the culture of blood, tracheal aspirate, BAL fluid, pleural aspirate and sputum are mentioned in table 1. In two of the six cases with pleural effusion, the pleural aspirate had grown *Hemophilus influenzae* type b on three occasions with the first and the last cultures 18 months apart. Barium meal was performed in twelve out of 82 cases (14.6%) presenting with a history of regurgitation of feeds. It was positive for gastroesophageal reflux (GER) in six cases (7.3%). In two patients gastric volvulus was found as a cause of reflux.

TABLE 1. Culture Positivity in Cases

Organism	Blood N (%)	Tracheal Aspirate N (%)	BAL N (%)	Pleural Aspirate N (%)	Sputum N (%)
<i>Pseudomonas</i>	4 (4.9)	6 (7.3)	2 (2.4)	0 (0)	0 (0)

Acinetobacter	2 (2.4)	2 (2.4)	2 (2.4)	0 (0)	0 (0)
Enterobacter	2 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)
Klebsiella	0 (0)	0 (0)	2 (2.4)	0 (0)	4 (4.9)
Hemophilus influenza. B	0 (0)	0 (0)	0 (0)	2 (2.4)	2 (2.4)
Escherichia coli	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pneumocystis carinii	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mixed flora	0 (0)	8 (9.8)	8 (9.8)	0 (0)	0 (0)
Sterile	74 (90.3)	0 (0)	0 (0)	4 (4.9)	0 (0)
Not done	0 (0)	66(80.5)	68(83.0)	76(92.7)	76(92.7)
Total	82 (100)	82 (100)	82(100)	82 (100)	82(100)

Echocardiography was performed in 24 cases (29.3%) with a clinical suspicion of heart disease. It was found to be abnormal in eight cases (9.8%). The abnormalities found were total anomalous pulmonary venous connection (TAPVC) and Scimitar syndrome in four different cases; and pulmonary artery hypertension was present in four cases.

TABLE 2. CXR and CT findings in cases with persistent pneumonia

Findings Imaging	Consolidation		Collapse		Broncho-pneumonia		Bronchiectasis		Pleural Effusion		Hydropneumo-thorax	
	CXR N(%)	CT N(%)	CXR N(%)	CT N(%)	CXR N(%)	CT N(%)	CXR N(%)	CT N(%)	CXR N(%)	CT N(%)	CXR N(%)	CT N(%)
Right	34 (41.5)	8 (17.4)	22 (26.8)	6 (13.1)	6 (7.3)	0	2 (2.4)	6 (13.1)	2 (2.4)	2 (4.3)	2 (2.4)	2 (4.3)
Left	8 (9.8)	6 (13.1)	8 (9.8)	2 (4.3)	2 (2.4)	0	2 (2.4)	4 (8.7)	4 (4.9)	4 (8.7)	0	0
Bilateral	26 (31.7)	26 (56.6)	0	1 (4.3)	6 (7.3)	0	6 (7.3)	4 (8.7)	0	0	80 (97.6)	44 (95.7)
Absent	14 (17.0)	6 (13.1)	52 (63.4)	36 (78.3)	68 (83.0)	46 (100)	72 (87.8)	32 (69.6)	76 (92.7)	40 (87)	80 (97.6)	44 (95.7)
Total	82 (100)	46 (100)	82 (100)	46 (100)	82 (100)	46 (100)	82 (100)	46 (100)	82 (100)	46 (100)	82 (100)	46 (100)

Candida skin test was done for four cases with suspected cell mediated immunodeficiency, and was negative in all the four cases. CD4+ T cell count was done for two cases with HIV infection and Pneumocystis carinii pneumonia (PCP), which showed CD4 count of 57 cells/microlitre (4%). The underlying causes of PP could be found in 80 cases (97.6%). Table 3 shows the etiological factors in descending order of frequency.

On follow up 54 cases (65.9%) showed improvement after appropriate treatment out of which sixteen (20%) had pulmonary tuberculosis; ten (12.2%) had Gram negative infections; four (4.9%) had GERD; four (4.9%) had HIV with tuberculosis; two (2.4%) had congenital heart disease; two (2.4%) had bronchial foreign body; two (2.4%) had H. influenzae type b pneumonia with empyema; and twelve (14.6%) had lipoid pneumonia. Fourteen cases (17.1%) remained unchanged during the period of the present study including six (7.3%) with bronchiectasis; two (2.4%) with hypoplasia of right lung and Scimitar syndrome; two (2.4%) with HIV and PCP who was started on HAART; two (2.4%) lipoid pneumonia and bronchiectasis; and two (2.4%) with unknown etiology. The latter two had been planned for open lung biopsy. Twelve cases (14.6%) expired including two (2.4%) with GERD; two (2.4%) with pulmonary tuberculosis; two (2.4%) with TAPVC; two (2.4%) with Gram negative septicemia; and four (4.9%) with lipoid pneumonia.

TABLE 3. Etiologic factors in cases with persistent pneumonia

	Number of cases	Percentage
Gram negative bacteria	24	29.3
Aspiration	24	29.3
Tuberculosis	16	19.2
Immunodeficiency	6	7.3
Cardiac disorder	4	4.9
Congenital malformation	4	4.9
Foreign body	2	2.4
Unknown	2	2.4
Total	82	100.0

DISCUSSION

In the present study most common cause for persistent pneumonia was Gram negative infection and aspiration secondary to either

Eighteen cases (22.0%) had undergone ultrasound of the thorax. Consolidation alone was reported in six cases (7.3%); collapse alone in two (2.4%); both consolidation and collapse in two cases (2.4%); pleural effusion alone in six cases (7.3%) and consolidation with pleural effusion in two cases (2.4%). The findings in the chest roentgenogram and the computed tomography (CT) of the thorax have been mentioned in table 2. The hilar adenopathy was present in the chest radiographs of eight cases (9.8%) including one with calcified hilar nodes whereas in CT-thorax, mediastinal nodes, were found in two additional patients. Congenital malformations were found in four cases (8.6%), including hypoplasia of right lung in two and congenital cystic adenomatoid malformation (CCAM) of right lung in another two cases.

Immunological studies were done for eight cases (9.8%). Serum immunoglobulin and complement levels were done for two cases with persistent Hemophilus influenzae pneumonia, which were found to be normal.

gastroesophageal reflux disease (GERD) or oil instillation. Tuberculosis was the next most common cause. This was followed by immunodeficiency due to HIV infection; congenital malformation of the lung including hypoplasia of right lung and congenital cystic adenomatoid malformation (CCAM); and cardiovascular disorders including total anomalous pulmonary venous connection (TAPVC) and Scimitar syndrome. Two cases had retained bronchial foreign body as a cause of persistent pneumonia. Most of the reports in literature describe the etiology of recurrent pneumonia.[11,12] Some of the authors have also discussed both recurrent and persistent pneumonia together. [8,9] Eigen et al could identify a definite etiology in only 20 out of 81(25%) children evaluated for recurrent / persistent pneumonia. Eight of these 20 had significant neuromuscular dysfunction leading to recurrent aspirations.[8] However, the data for recurrent and persistent pneumonias are not clearly spelt out separately. Lodha et al were able to identify the underlying illness in 16 out of 19 (84 %) cases in contrast to 97% of cases in the present study. The most frequent underlying causes in their study were posttubercular bronchiectasis and asthma.[6]

The studies mentioned above were retrospective in nature and were based on the case records of children with persistent/recurrent pneumonia. Persistent pneumonia usually results from deficiencies in the local pulmonary or systemic host defenses or from underlying disorders that modify the lung defenses.[12] The underlying factors associated with persistent pneumonia can be broadly classified into following categories: [7, 13](a)Resistant or highly virulent organisms; atypical organisms.(b) Inadequate antibiotic therapy.(c) Congenital malformations of the upper or the lower respiratory tract, thoracic cage, vessels and cardiovascular system.(d) Recurrent aspirations. (e)Defects in the clearance of airway secretions especially cystic fibrosis and other ciliary dyskinesias. (f)Disorders of systemic or local immunity.

In a study conducted on 238 children with recurrent or persistent pneumonia, oropharyngeal in coordination with aspiration syndrome was the commonest underlying cause (48%). The other important causes were immune disorders (10%), congenital heart disease (9%), and pulmonary abnormalities (8%). No underlying cause could be determined in about 8% of the children.[11] However, one recent Italian case-control study found that wheezing, atopy/allergy, asthma,

and chronic rhinosinusitis were the main factors associated with recurrent pneumonia.[14]

CONCLUSION

In our study the most common cause for persistent pneumonia was Gram negative bacterial infection and other causes were aspiration due to gastroesophageal reflux disease or oil instillation followed by tuberculosis. Persistent pneumonia continues to be a major challenge for the clinicians. The results of our study would help pediatricians in our region to prevent and control the frequent underlying causes of persistent pneumonia in children.

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