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Clinical and laboratory profile of pleural effusion in children- experience of a tertiary care centre

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Abstract
Background and Objectives: Pleural effusion is an abnormality that results from collection of fluid in the pleural space. The etiological mechanisms of pleural effusion is considerably different in children and adults. Clinical presentations are variable and dependent on the underlying disease process, size, and site of effusion. The most important investigation to identify the cause of effusion is analyzing the pleural fluid cytologically and biochemically. This also helps to classify an effusion into exudate or transudate which is indicative of the underlying pathophysiological process involved. Knowledge of the clinical profile of effusion in children would help in adoption of an optimal diagnostic & therapeutic approach. Based on this background, we studied clinico-radiological and etiological pattern of pleural effusion at our hospital.
Methodology: We conducted a prospective observational study over 1 year from January 2017 to December 2017 at department of Pediatrics, ANMMCH, Gaya, Bihar which is a tertiary care level teaching hospital. Children of >1 year to <15 years with unilateral or bilateral pleural effusion diagnosed on the basis of clinical features and/or imaging studies were included in our study.
Results: Over the study period, we enrolled 42 children in our study. Mean age of presentation was 6.3±3.8 years. Mean weight on admission was 18.1± 5.2 kg. Male (23): female (19) ratio was 1.21:1. The most common symptom was breathing difficulty (83.3%), followed by loss of appetite (76.2%), fever (69%), cough (59.5%) and weight loss (40.5%). Right sided effusion (n = 18, 42.9%) was more common than left side (n= 11, 26.2%), while the effusion was bilateral in 13 (30.9%) children. Majority of the children had exudative pleural effusion as compared to transudative pleural effusion (54.8% vs 45.2%). The three most common causes of pediatric pleural effusion (nearly 50%) were parapneumonic, tubercular and nephrotic syndrome. Pleural biopsy was needed in only in 2 (4.8%) children and we were able to diagnose more than 95% children with simple biochemical, molecular and cytological examination.
Conclusion: Pleural effusion was commoner in young school going children. Parapneumonic effusion, tubercular effusion and effusion due to nephrotic syndrome were the most common causes. Breathing difficulty was the most common presenting feature. Majority of children had exudative effusion. In most cases, underlying aetiology could be identified by simple biochemical, cytological and molecular studies.

Keywords: empyema, exudate, parapneumonic, pleural effusion, pleural fluid, transudate

Introduction

Pleural effusion is an abnormality that results from collection of fluid in the pleural space due to imbalance in hydrostatic and oncotic pressure, increased capillary permeability and impaired lymphatic drainage. In simpler words, pleural fluid accumulates when too much fluid either enters or too little fluid exits, out of plural space. This condition may result from a primary phenomenon or secondary to a variety of disorders such as infections. This accumulated fluid can be originated from excessive filtration or defective absorption [1] caused by different infectious agents such as *Streptococcus pneumoniae*, which is the most common, or non-infectious factors like lymphoma or congestive heart failure. The etiological mechanisms of pleural effusion is considerably different in children and adults in that effusion in children is secondary to infections, while the most common cause in adults has been documented to be congestive heart failure and malignancies [2].

Pleural effusion in children is most commonly seen in males and younger children [3]. The incidence and distribution of pleural effusion is increasing in most industrial countries according to the population studies [4]. Clinical presentations are variable and dependent on the underlying disease process, size, and site of the effusion [5]. Clinical presentation of this disorder is myriad and ranges from being asymptomatic in mild effusion to a range of complications such as respiratory failure due to massive fluid accumulation, septicemia, bronchopleural fistula, pneumothorax and pleural thickening. Common symptoms include persistent fever, cough, anorexia, malaise, tachypnea, dyspnea, chest pain, abdominal pain, abdominal distension and vomiting. However, in physical examinations a pleural rub may be the only initial manifestation during the early stage of pleurisy. In case of massive effusion, chest expansion on the affected side gets impaired, mediastinum may get shifted and trachea and cardiac apex may get displaced to the contralateral side.

The most important investigation to identify the cause of pleural effusion is analyzing the pleural fluid cytologically and biochemically. This helps to classify an effusion into exudate or transudate which is indicative of underlying pathophysiological process involved. Such a distinction also allows appropriate investigations to be instigated enabling

better patient management [6]. Light *et al* has established criteria that allows with a high degree of accuracy to differentiate transudates from exudates [7]. Imaging studies such as chest radiography, ultrasonography and computed tomography are beneficial in reaching a more accurate assessment. Treatment of the underlying etiology and providing supportive care are sufficient to heal effusion in almost all cases which ranges from antibiotic therapy, chest tube drainage and using fibrinolytics. Selection of the best management approach results in a favorable outcome and significantly reduces morbidity and mortality. Prognosis is influenced by the underlying disorder as well as the treatment approach.

Although the mechanics of accumulation of pleural fluid is the same in both adults and children, evaluation differs in terms of aetiology, symptomatology, character of fluid, diagnostic technique, treatment as well as prognosis. Knowledge of the clinical profile of PE in children would help in adoption of regionally optimized diagnosis & therapeutic approach. Based on this background, we intended to study the clinico-radiological and etiological diagnosis of PE at our tertiary care teaching hospital.

Aim and Objectives

Aim: To study the pattern of pleural effusion in children presenting to a tertiary care teaching hospital.

Objectives

1. To study the clinical and diagnostic features of PE in children.
2. To study the aetiology of PE in children.
3. To classify pleural fluid into transudative and exudative type and compare the various laboratory parameters in them.

Methodology

Study setting: Deptt of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar.

Study design: Prospective observational study.

Study duration: 1 year from January 2017 to December 2017.

Inclusion criteria: Children of >1 year to <15 years with unilateral or bilateral pleural effusion diagnosed on the basis of clinical features and imaging studies (chest X ray and/or USG and/or CT chest).

Exclusion criteria: Children with a history of significant chest trauma preceding occurrence of pleural effusion, children with bleeding disorder and children whose parents refused consent were excluded.

Study technique: After obtaining written informed consent from either parent, we enrolled children in our study. Structured proforma was used to collect information regarding the presenting complaints, detailed history and general and systemic examination. Routine investigations like complete blood count (CBC), ESR, Serum LDH, urea, creatinine, SGOT, SGPT was done in all cases. Blood culture was done in children whose PE was considered to be infective in origin. Pleural fluid cytology, biochemistry, microbiology and CBNAAT (Cartridge Based Nucleic Acid Amplification Test) test was done to confirm the diagnosis in selected cases. Under all aseptic precautions ultrasonography guided pleural fluid aspiration was done with a 20 c.c. syringe, care was taken to protect neurovascular bundle and for any complication that could occur. Sputum examination for AFB staining by Ziel Nelson technique, Gram staining and Culture & sensitivity of pleural fluid was done as per clinical condition. Chest X-ray PA view was done in all children. Chest sonography and/or CT chest was done if warranted. Other specific investigation like pleural biopsy (by Abrahms needle) or fiberoptic bronchoscopy was done if required as per nature of specific diseases.

Statistically analysis: Data so collected was tabulated and entered into Microsoft Excel worksheet. Statistical analysis was done by SPSS version 20 (IBM SPSS Statistics Inc.) Windows software program. Variables were represented as percentages, proportion, mean and standard deviation as appropriate. Chi-square test or Fisher exact test was used for qualitative data as applicable. Student's t-test was used for continuous data. Level of significance was set at $P < 0.05$.

Observations and Result

Over the study period, we enrolled 42 children in our study. Mean age of presentation was 6.3±3.8 years. Mean weight on admission was 18.1± 5.2 kg. Male (23): female (19) ratio was 1.21:1. Table 1 depicts the common demographic parameters of the children studied.

Table 1: Demographic parameters of the study participants

	Number	Percentage
1-5 years	12	28.6%
5-10 years	19	45.2%
>10 years	11	26.2%
Male gender	23	54.8%
Female gender	19	45.2%
Rural area resident	32	76.2%
Urban area resident	10	23.8%
Total	42	100%

Breathing difficulty (83.3%), loss of appetite (76.2%), fever (69%) and cough (59.5%) were the commonest presenting features of children with PE in our study. Chest pain was more common a feature in parapneumonic effusion and empyema, whereas weight loss was commonly associated with tubercular effusion. Mean total leukocyte count was 15,128 cells/cu mm. Highest mean TLC counts was seen in empyema (21,532 cells/cu mm), followed by parapneumonic effusion (16,926cells/cu mm) and tubercular effusion (12,187cells/cu mm). Mean ESR was 36.8 mm/hour which was highest in tubercular effusion (mean= 84.6mm/hr) followed by empyema (42.3mm/hr) and parapneumonic effusion (37.2mm/hr). Table 2 shows the important clinical and laboratory parameters of study participants.

Right sided effusion (n = 18, 42.9%) was more common than left side (n= 11, 26.2%), while the effusion was bilateral in 13 (30.9%) children. Most of children had uncomplicated or free fluid type of effusion (n=35, 83.3%) while 7 children (16.7%) had septated effusion. Septations were most common in empyema (n= 3, 60%) followed by parapneumonic (n=2, 28.6%) and tubercular (n=1, 14.3 %) and (malignancy (n=1, 14.3%). History of contact with a

known case of tuberculosis was positive in 3 children out of total 7 patients of tubercular pleural effusion. However 2 children with non-tubercular causes of PE also gave a history of contact with tuberculosis patient, but active tuberculosis was ruled out in all of them by relevant investigations. Sputum for AFB was positive in 2 children, whereas CBNAAT was positive in 3 children. Rifampicin resistance was not detected in any child with tubercular PE. Montaux test was positive (>10mm) in 3 out of 7 children with tubercular PE. 2 children out of 7 cases with tubercular PE hadn't received B.C.G vaccine. Pleural fluid bacterial culture was positive only in 5 (11.9%) out of 42 such children. The organisms isolated were *Streptococcus* (n=3), *Acenatobacter* (n=1) *Staphylococcus* (n=2), and *Klebsiella* (n=1).

Table 2: Symptomatology and laboratory parameters of the study participants.

	Number or Mean	Percentage or SD
Symptomatology:-		
Fever	29	69%
Cough	25	59.5%
Breathing difficulty	35	83.3%
Loss of appetite	32	76.2%
Weight loss	17	40.5%
Chest pain	13	30.9%
Laboratory Parameters:-		
TLC in blood (per cu mm)	15128	4896
ESR (mm/hr)	36.8	14.9
Pleural fluid TLC (per cu mm)	532	217
Pleural fluid Protein (g/dl)	1.9	0.7
Pleural fluid glucose (mg/dl)	69.8	27.6
Pleural fluid LDH (IU/L)	163.2	51.3
Pleural fluid ADA (IU/L)	15.2	6.9

Majority of the children had exudative pleural effusion as compared to transudative pleural effusion (54.8% vs 45.2%). We used clinical scenario and Light's criteria [7] to distinguish between exudative and transudative pleural effusion. The three most common causes of pediatric pleural effusion in our study as shown below in table 3 were parapneumonic, tubercular and nephrotic syndrome. Together these 3 accounted for nearly half of all cases of PE. Surprisingly, we also had 1 case of PE due to malignancy which is not common in pediatric age group. We couldn't confirm the cause of exudative PE in 1 child. Among the causes of transudative PE, nephrotic syndrome, congestive heart failure (1 case of congenital heart disease and 3 cases of acquired heart disease) and dengue fever were the commoner ones.

Table 3: Etiologic profile of pleural effusion in children

	Condition/Disease	Number	Percentage
Transudative effusion (n=19)	Nephrotic syndrome	7	16.7%
	Dengue fever	2	4.8%
	Congestive heart failure	4	9.5%
	Chronic kidney disease	2	4.8%
	Chronic liver disease	4	9.5%
Exudative effusion (n=23)	Parapneumonic	7	16.7%
	Empyema	5	11.9%
	Tuberculosis	7	16.7%
	Pancreatitis	2	4.8%
	Malignancy	1	2.4%
	Unconfirmed cause	1	2.4%
Total		42	100%

We also studied important laboratory parameters in different types of pleural effusion as shown below in table 4. Mean pleural fluid protein was significantly higher in all cases of exudative tubercular effusion as compared to children with transudative effusion ($p<0.001$). However, the same wasn't true for pleural fluid glucose. Whereas, pleural fluid glucose was significantly lower in empyema and parapneumonic effusion as compared to children with transudative effusion ($p<0.001$), it was almost comparable when compared between tubercular effusion and transudative effusion. Pleural fluid ADA was significantly higher in children with tubercular effusion and empyema as compared to other children ($p<0.001$). However, ADA levels were comparable among children with other causes of exudative pleural effusion and transudative pleural effusion ($p >0.05$). Pleural fluid LDH was significantly higher in exudative PE as compared to transudative PE ($p<0.001$)

Table 4: Important laboratory parameters in different types of pleural effusions

Disease/Condition	Pleural fluid Protein (g/dl)	Pleural fluid Glucose (mg/dl)	Pleural fluid LDH (Units/liter)	Pleural fluid ADA (IU/liter)
Tubercular effusion (n=7)	3.61 ± 1.07	63.5 ± 8.4	367.2 ± 103.9	56.1 ± 15.3
Parapneumonic effusion (n=7)	3.93 ± 1.23	51.4 ± 7.2	441.3 ± 124.7	21.3 ± 8.4
Empyema thoracis (n=5)	4.41 ± 1.29	37.3 ± 10.9	1032.8 ± 251.3	33.9 ± 11.4
Pancreatitis (n=2)	3.36 ± 0.98	65.4 ± 6.9	212.6 ± 87.4	17.9 ± 5.2
Malignancy (n=1)	3.97	58.9	2289	11.9
Chronic liver disease (n-=4)	0.87 ± 0.34	64.8 ± 8.7	74.3 ± 13.7	6.1 ± 1.4
Chronic kidney disease (n=2)	1.09 ± 0.47	71.3 ± 9.3	69.7 ± 15.9	5.4 ± 1.3

Discussion

Many of the previous studies have reported that pediatric pleural effusion is most commonly seen in males and younger children. In the present study, mean age of presentation was 6.3 ± 3.8 years and males were predominantly involved with male: female ratio of 1.21:1. Male predominance was also reported by Hasan *et al* [8] in their comprehensive study at a tertiary care centre. Whereas Hassan *et al* [8] reported a lower mean age (65% children were less than 5 years of age) as compared to our findings, Memon *et al* [9] in their study reported the median age of presentation as 5-8 years which is comparable to our study. The most common symptom in our study is breathing difficulty (83.3%), followed by loss of appetite (76.2%), fever (69%), cough (59.5%) and weight loss (40.5%). Theses finding are compatible with the study done by Porcel and Vives [10]. Afsharpaiman *et al* [11] also observed that more than half of all cases with pleural effusion had breathing difficulty in their study. Breathlessness is an important symptom which compels the patient to report to health facility. Majority of PE was unilateral (69.1%) while 30.9% had bilateral pleural effusion. Right sided effusion

(42.9%) was more common than left side (26.2%) in our study. This is quite comparable to the study done by Reddy *et al*. [12] in southern India where out of 135 patients of pleural effusion, 89 were right-sided, 37 left-sided, and 9 were bilateral effusions. Most of the children had uncomplicated or free fluid type of effusion (83.3%) while 16.7% had septated effusion. Septations were most common in empyema (3 out of 5 or 60%) followed by parapneumonic (2 out of 7, 28.6%). Septations were also reported to be more common in empyema cases by Devota *et al*. [13] Septations probably are related to inadequate treatment or starting treatment at late stage of disease process.

In the present study, exudative PE was more common than transudative PE (54.8% vs 45.2%). Most of researchers have reported similar higher incidence of exudative PE. In their study, Saliya MP *et al* [14] reported 82.35% of children to have exudative type of PE which is considerably higher than our study. This can be due to non-inclusion of children with nephrotic syndrome and CHF in their study which contribute significantly to transudative PE. On comparing different types of pleural effusion, we found that parapneumonic effusion and tubercular effusion were the commonest cause of exudative PE. Maher *et al* [15] have reported similar high incidence of parapneumonic and tubercular PE. While we needed pleural biopsy only in 2 (4.8%) children and were able to diagnose more than 95% children with simple biochemical, molecular and cytological examination, lately there are studies with considerably high rates of pleural biopsy [16] for diagnosing the cause of PE. Our study suggest that thoracoscopy /pleural biopsy is not required in most of the cases of exudative pleural effusion in children, its use should be limited to selected cases of undiagnosed or recurrent pleural effusion.

Conclusion

Pleural effusion is commoner in young school going children. Parapneumonic effusion, tubercular effusion and effusion due to nephrotic syndrome are the most common causes in children. Majority of the effusion were exudative in origin as compared to transudates. Septations were commoner in empyema and these patients might require longer course of treatment. Breathing difficulty is the most predominant presenting feature of children with PE. In majority of such children, the underlying aetiology can be identified by simple biochemical, cytological and molecular studies.

Limitation

First limitation is that the present study was a single centre study and so our findings may not be reflective of the general population. Second limitation is the relatively small sample size. Third limitation is short duration (1 year) of our study. As some children were already on conservative management before enrolment in the present study, effect of previous treatment could have affected our diagnostic workup and differential diagnosis.

Conflict of interest: None

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