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A STUDY OF ETIOLOGY , CLINICAL PROFILE AND OUTCOME OF PLEURAL EFFUSION IN CHILDREN IN A TERTIARY CARE HOSPITAL IN EASTERN INDIA.

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ABSTRACT

Objectives : Pleural effusion, abnormal accumulation of fluid in pleural space, differ significantly in children from adults in relation to etiology, management and outcome. Objectives of this study is to identify common causes of pediatric pleural effusions; to describe the clinical features, radiological finding, laboratory investigation, bacteriologic study and outcome of pleural effusion in children.

Study Design: Prospective Hospital based Observational study.

Materials and methods: Patients with pleural effusion were evaluated by chest X-ray and USG in all cases and CT scan thorax in difficult cases. Pleural fluid samples were analyzed for glucose, protein, lactic dehydrogenase (LDH), adenosine de aminase (ADA), cytology and culture. Intercostal tube drainage was given in empyema cases and decortications was done in one case.

Results: Commonest etiology of pleural effusion was empyema (52% cases), followed by tubercular pleural effusion (26% cases). Most common organism isolated from pleural empyema was Staphylococcus aureus (17.94 % cases) followed by Mycobacterium tuberculosis (7.69%). There is significant correlation among age and etiology (p value 0.015), tuberculosis occurred more in older children and empyema occurred more in younger children. There is no significant correlation among weight and etiology (p value 0.200) , between gender and etiology of pleural effusion (p value >.05) in our study . There is significant correlation of pleural fluid neutrophil count (p value 0.001), lymphocyte count(p value 0.002) with etiology, but no correlation was seen with ADA (p value 0.460), protein (p value 0 .060) , LDH (p value 0 .353) , glucose (p value 0.799) in our study.

Conclusion: Regarding etiology of pleural effusion empyema and tuberculosis are very commonly encountered in clinical practice. Predominant lymphocyte in pleural fluid with high ADA value is suggestive of tubercular etiology whereas neutrophil predominant exudative pleural effusion with high ADA value support the diagnosis of empyema. Staphylococcus aureus is the most common pathogen. Regardless of which treatment is used in pleural effusion, the outcome for children is generally excellent.

KEYWORDS Pleural effusion , children ,etiology, outcome.

INTRODUCTION:

Pleural effusion is the abnormal accumulation of fluid in the pleural space. A pleural effusion indicates an imbalance between pleural fluid formation and removal. It can be caused by a variety of infectious and non-infectious diseases. Causes of pleural effusions in children differ significantly from those in adults. Pleural effusions in children most commonly are infectious (50% to 70% para pneumonic effusion), congestive heart failure is a less frequent cause (5% to 15%) and malignancy is a rare cause (5-10%)1.

Pleural empyema continues to be a serious problem despite recent advances in management. It is reported to occur in up to 28% children hospitalized for community acquired pneumonia2. In developed countries the microbial profile has changed over past five decades3with increasing incidence of penicillin resistant Streptococcus pneumoniae and methicillin resistant Streptococcus4. However the scenario is very different in developing countries5,6 . Understanding of the problem has been hampered by the fact that routine bacterial culture is negative in most cases, presumably because intermittent and unsupervised courses of antibiotics have usually been administered before referral to the tertiary health centre, increasing morbidity and mortality from pleural empyema.

Pleurisy with effusion develops as a complication of primary pulmonary tuberculosis is seen in 2 to 38% of children with pulmonary disease7. Establishing a diagnosis of tuberculosis pleural effusion can also be difficult because the classic findings (lymphocytic exudative pleural effusion, pleural granulomata, and cutaneous sensitivity to purified protein derivative) have low specificity in children.

The present study was done to describe etiology, clinical features and outcome of pleural effusion in children (6 months to 12 years) admitted in the department of Pediatric Medicine, Medical College Hospital, Kolkata and in the department of Chest Medicine, Institute of Post-Graduate Medical Education and Research, Kolkata.

Objectives of this study were as follows:

1. To identify common causes of pediatric pleural effusions.
2. To describe the clinical features, radiological finding, and laboratory investigation parameters in pediatric pleural effusion.

3. To describe bacteriologic study of pleural fluid in different age groups in children.
4. To evaluate the outcome of pleural effusion.

MATERIALS AND METHODS:

Study population: Admitted children between ages 6 months to 12 years, with clinical and radiological impression of pleural effusion.

Study period: January 2011 to December 2013.

Exclusion Criteria:

a) Any patient with history of chest trauma.
b) Patient with history of Cardiothoracic surgery.

Study design: Prospective Hospital based Observational study.

Study technique: Patients having respiratory symptoms and clinical impression of pleural effusion were evaluated by posterior-anterior and lateral decubitus chest X-ray. When the distance between outer border of the lung and inner border of the chest was more than 10 mm in lateral decubitus view, a diagnostic thoracentesis was performed. Pleural fluid samples were sent for analysis of glucose, protein, lactic dehydrogenase (LDH), adenosine de aminase (ADA), cytology and culture. Ultrasonography of thorax was done in every patient to note amount of pleural effusion and any septation . For therapeutic aspiration 2% lignocaine was used as local anesthesia. A new chest X-ray was done to detect post thoracentesis complications and to assess the possibility of residual pleural effusion.

In difficult cases guidance either by ultrasonography or CT scan thorax was taken. Transudate and exudates were differentiated according to Light's criteria. Clinical outcome was assessed based on the need for invasive procedures like simple aspiration to more invasive procedure like intercostal tube drainage and decortication.

After initial management all the patients were followed up on OPD monthly for 6 months. Repeat Chest X-Ray was done after four to six weeks.

Data were obtained and recorded on Excel data sheet and analyzed by using standard statistical software SPSS version 18.

RESULTS :

There was 28 (56%) male patients and 22 (44%) female patients in our study with a male to female ratio of 1.27:1. Mean age was 6.361 years (+ 3.61 SD). Commonest age group in both male (46.42% cases) and female (50% cases) was 1.1-5 years. Most common symptom was shortness of breath (96%), followed by fever(90%), cough (66%), chest pain(32 %) in our study (Table-1).

Table 1 . Distribution of study population according to symptoms.

Symptoms	Number	Percentage(%)
Fever	45	90
Cough	33	66
Shortness of breath	48	96
Weight loss	19	38
Chest pain	16	32
Swelling body	4	8
Swelling in legs	5	10
Swelling in face	4	8
Swelling in cervical region	3	6
Palpitation	2	4
Decreased urinary output	4	8

On clinical examination, all patients had diminished breath sound, 58% had tachypnoea, 56% had dull percussion in right side of chest, 48% had tachycardia, 44% had dull percussion in left side of chest, 16% had dull percussion on both sides of chest, 12% had bronchial breath sound, 10% had anemia, 10% had edema, 8% had ascites, 6% had lymphadenopathy and 4% had hepatosplenomegaly in our study.

Chest X Ray showed right sided pleural effusion in 56% cases, left sided effusion in 44% cases, bilateral effusion in 16% cases. Associated parenchymal disease was seen in 12% cases and mediastinal lymphadenopathy was seen in 2% case in our study. Ultrasonography showed fluid with internal echo in 38% cases, echogenic and septeded effusion in 14% cases.

In this study commonest associated risk factor was malnutrition(24% cases) and other risk factors were contact history of tuberculosis (14% cases), rheumatic heart disease (4% cases) and steroid resistant nephrotic syndrome (2% cases). Empyema cases were not associated with any risk factor. In our study most cases of childhood empyema were observed in the month of September (23.07%) followed by month of June (19.23%).

Diagnostic aspiration was done in all cases (98%) except one case of heart failure where USG showed minimal bilateral pleural effusion. Pleural fluid analysis showed neutrophil predominance in 52% cases, lymphocyte predominance in 28% patients. ADA value >40 units was seen in 72% cases. Raised ADA value > 40 units was observed among tubercular and empyema cases. ADA value < 40 units was observed among heart failure and nephrotic syndrome patients. Low glucose level <40mg/dl was seen in 64% of cases. Exudative pleural effusion was seen in 42 cases (84%) and transudative pleural effusion was seen in 5 patients(10%) .

Commonest etiology of pleural effusion was empyema (52%), followed by tubercular pleural effusion (26%), dengue haemorrhagic fever (8%), heart failure (6%) and nephrotic syndrome (4%). (Table-2)

Table-2. Etiology of Pleural Effusion

Etiology	Number		Percentage (%)
	Male	Female	
Empyema	14	12	52
Tuberculosis	7	6	26
Nephrotic syndrome	2	0	4
Heart Failure	1	2	6
Aplastic Anemia	1	0	2
Dengue Haemorrhagic Fever	3	1	8
Ewing Sarcoma	1	0	2

Pleural fluid culture was done in suspected empyema and tuberculosis patients. Most common organism isolated from pleural fluid was Staphylococcus aureus in 17.94 % cases, followed by Mycobacterium tuberculosis in 7.69%, Klebsiella and Acinatobactor in 5.1% each. Growth of organism was seen in 14 (48.27%) of total 29 empyema cases. Growth of Mycobacterium tuberculosis was seen in 3 (23.7%) among 13 cases of tubercular pleural effusion. Staphyloccus aureus was predominantly isolated from pleural fluid in 5.1-10 years age group. Acinatobactor was isolated in 2 cases of empyema in the age group of 1.1-5 years. Mycobacterium tuberculosis was isolated from two cases of empyema in the age group of 10.1-12 years (Table 3).

Table 3. Types of organism isolated in relation to age group and sex

Pathogens	Age Groups								Total
	0.6-1 yrs		1.1-5 yrs		5.1-10 yrs		10.1-12 yrs		
Staphylococcus aureus	Male	Female	Male	Female	Male	Female	Male	Female	
	0	1	2	0	3	1	0	0	7
Klebsiella pneumonia	0	0	1	0	0	1	0	0	2
Acinatobactor	0	0	1	1	0	0	0	0	2
Mycobacterium tuberculosis	0	0		0	1	0	1	1	3

Therapeutic aspiration was done in 11 cases (22%). Intercostal tube drainage was given in 19 cases (38%). Intercostal tube drainage was given in patients when pleural fluid showed neutrophil predominant cell, growth of organism seen in pleural fluid, LDH was >1000 u/l and patients had moderate to severe respiratory distress. Intercostal tube drainage was given two times in 4 (8%) cases. Decortication was done in one case in our study.

Commonest complication in our study was surgical emphysema seen in 10% cases, followed by pyopneumothorax and hydropneumothorax in 8% each. Bronchopleural fistula was seen in one patient where decortication was done. Pleural thickening was seen in 2 cases (4%). Average hospital stay in our study was 14.9 days and was more in case of empyema (20.07 days) .

There is significant correlation among age and etiology (p value 0.015) of effusion in our study. Tuberculosis occurred more in older children and empyema occurred more in younger children. No significant correlation was found between weight and etiology of effusion (p value 0.200) and between gender and etiology of pleural effusion (p value >.05) in this study.

There is significant correlation of pleural fluid neutrophil count (p value 0.001), lymphocyte count (p value 0.002) with etiology; but no significant correlation was seen with ADA (p value 0 .460), protein (p value 0 .060), LDH (p value .353) and glucose value (p value 0.799) with etiology in our study (Table 4).

Table 4. ANOVA Analysis, pleural fluid study and etiology of effusion

	Sum of Squares	df	Mean square	F	Sig
Pl Fuild cell	361645.069	6	60274.178	1.033	.417
Between Groups	2508791.011	43	58343.977		
Within groups	2870436.080	49			
Total					
Protein	22.524	6	3.754	4.653	.06
Between Groups	33.885	42	.807		
Within Groups	56.408	48			
Total					
LYMPHOCYTE	41169.693	6	6861.616	12.723	.002
Between Group	22650.882	42	539.307		
Within Groups	63820.575	48			
Total					
Neutrophil	50847.037	6	8474.506	17.731	.001
Between Groups	20074.054	42	477.954		
Within Groups	70921.091	48			
Total					
LDH	3.235E8	6	5.391E7	1.148	.353
Between Groups	1.878E9	40	4.694E7		
Within Groups	2.201E9	46			
Total					
ADA	4929.955	6	821.659	.965	.460
Between Groups	36602.365	43	851.218		
Within Groups	41532.320	49			
Total					
Glucose	11.345	6	1.891	.507	.799
Between Groups	160.275	43	3.727		
Within Groups	171.620	49			
Total					

DISCUSSION:

In our study male patients (56%) outnumbered the females (44%) with a male to female ratio of 1.27:1. K.M. Eastham, et al 8 in their study also observed that male child were more susceptible than female. In this study maximum children were in 1.1- 5 years age group (46%) followed by 5.1-10 years age group (30%). Similar results have been observed in other international9 and Indian10 studies also.

Commonest presenting symptoms was shortness of breath (96%), followed by fever (90%) and cough (66 %). This is also in accordance with a study in United Kingdom11. Commonest associated risk factors were malnutrition and contact history of tuberculosis, which was seen in 24% and 14% cases respectively. One children with steroid resistant nephrotic syndrome (2%) had history of long term immunosuppressive drugs intake. However one study9 showed that most of the children had no predisposing risk factors to infection. Commonest sign was diminished breath sound (100%), followed by tachypnoea (58%) and dull percussion over right side of chest. Ori Efrati et al1 observed that specific sign indicating pleural effusion are much more difficult to elicit in the infant or young children. In infants breath sounds from one lung often are transmitted throughout the chest, making unilateral findings difficult to appreciate. Merino JM et al12 also observed that the findings of tubercular pleural effusion on physical examinations can mimic bacterial pneumonia with dullness to percussion, diminished breath sound and pyrexia.

In this study most of the cases (53.83 %) of empyema was presented during the hot and humid months (May to August) of the year. This also seen by Barenwal AK et al 2 in their study. In the tropical zone, excessive sweating and moist skin favors growth of cutaneous flora, leading to high incidence of Staphylococcal pyoderma. Another study 13 also observed that hematogenous spread from these lesions may lead to pneumonia and parapneumonic empyema.

Commonest etiology of pleural effusion in our study was empyema (52%) followed by tubercular pleural effusion (26%), dengue haemorrhagic fever (8%), heart failure(6%), nephrotic syndrome (4%). Ewing sarcoma and aplastic anemia was diagnosed in one patient each. This is consistent with studies of K.M Eastham, et al 8 and Ori Efrati, et al 1. They showed that pleural effusion in children was most commonly infectious (50 to 70% parapneumonic effusion); congestive heart failure (5 to 15%) and malignancy (5 to 10%) are less frequent causes.

One study10 from India showed that incidence of tuberculous effusion is more than parapneumonic effusion. In western countries parapneumonic effusion has higher incidence and is increasing. But in the said study patients below 3 years were not included. In our study significant correlation was found between age and etiology (p value 0.015) of effusion. Tuberculosis occurred more in older children and empyema occurred more in younger children. Kim HJ et al 14 also observed that tuberculous pleural effusion commonly occur in adolescents and is uncommon in the preschool aged child .

Most common organism isolated from pleural fluid was Staphylococcus aureus (17.94%) followed by Mycobacterium tuberculosis (7.69%), Klebsiella and Acinatobactor (5.1% each). Growth of organism was seen in 14 (48.27%) of total 29 empyema cases in our study. In an another series15 Staphylococcus aureus was most common organism followed by Streptococcus pneumonia and Klebsiella. Frank tubercular empyema is rare, occurring in only about 2% cases of tuberculous pleurisy as noted in a study 16.

In this study significant correlation was found between pleural fluid neutrophil count (p value 0.001) and etiology of empyema. Pleural fluid culture was positive in 48.27% patients which is slightly less than other studies2,6. They showed that yield on culture is significantly lower which varied from 48 to 82%. It could be due to prior use of antibiotics and late referral. Alternatively it may suggest that continual presence of bacteria is not necessary to sustain the ongoing inflammatory response after the initial bacterial invasion.

In this study therapeutic aspiration was done in 11 cases (22%) and intercostal tube drainage was given in 19 cases (38%). Chest drain was removed if there was less than 1-2 ml/kg fluid accumulation per 24 hours. A chest X ray was done following drain removal. Another follow up chest X ray was done at 4 to 6 weeks to ensure that resolution is occurring. This X ray will not be normal in most cases despite complete clinical recovery of the child as radiological recovery lags behind clinical recovery and some residual thickening is present even as late as 6 months after discharge.

In this study no death was seen among the fifty patients. Case fatality rates of 3 to 6% have been reported in some recent series, with the highest rate occurring among infants younger than 1 year of age. Pleural thickening was seen in only one case similar to the finding by Ori Efrati, et al 1 in their study.

Regardless of which treatment is used in empyema, the outcome for children is generally excellent. All Children with empyema needed antibiotic therapy in high doses via the intravenous route in the early stages of the disease. In our study intravenous antibiotic was given for at least 3- 4 weeks. But R.E. Strachan et al,17 showed that once a child has been afebrile for 24 hours then consideration can be given to changing from intravenous to oral antibiotic, which may vary from 7 days to 6 weeks.

In our study tubercular pleural effusion was seen in 26% cases. Mean age of the tubercular pleural effusion patient was 9.0500 years with p value of 0.015. There was significant correlation between pleural fluid lymphocyte count (p value 0.002) and etiology of effusion. Raised ADA value > 40 units/l along with lymphocyte predominant cell was observed in the pleural fluid. In their studies Merino JM, et al 12 showed that ADA levels were above 40 U/L in 90% of cases of tubercular pleural effusion. All the tubercular patients in our study responded well with treatment with no complication. Pleural thickening usually resolved in months with no sequelae reflected in lung function testing.

In this study four patients were diagnosed as dengue hemorrhagic fever with right sided pleural effusion which improved with supportive management. Setiawan MW et al 18 stated that pleural effusions are common with dengue hemorrhagic fever and are usually exudates but can be transudates. The effusions are usually bilateral but sometimes are right sided only, rarely left sided and are small in most instances.

In our study two cases (4%) were diagnosed as nephrotic syndrome, three cases (6%) were diagnosed as heart failure. Pleural fluid showed transudative effusion and responded well without any therapeutic aspiration. In this study one patient was diagnosed as malignant pleural effusion in a case of Ewing's sarcoma. Pleural fluid was haemorrhagic, lymphocyte predominant and exudative in nature. Therapeutic aspiration was done two times along with chemotherapy.

Average hospital stay in our study was 14.9 days. Hospital stay was more in case of Ewing's sarcoma (25 days) and empyema (20.07 days) patients.

SUMMARY AND CONCLUSION:

Pleural effusion, which occour less frequently in children than in adults, can be caused by a variety of infectious and non infectious causes. Microscopic, bacteriologic, biochemical and etiologic analysis are helpful to classify the pleural effusion. Regarding etiology of pleural effusion empyema and tuberculosis are very commonly encountered in clinical practice. Predominant lymphocyte in pleural fluid with high ADA value is suggestive of tubercular etiology whereas neutrophil predominant exudative pleural effusion with high ADA value support the diagnosis of empyema. Staphylococcus aureus is the most common pathogen. An ultrasound should be performed on all children with pleural effusion as it is the safe technique to differentiate pleural fluid and consolidation, estimate effusion size and demonstrate the presence of fibrinous septations and guide chest drain placement. Regardless of which treatment is used in pleural effusion, the outcome for children is generally excellent.

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