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ORIGINAL ARTICLE

From Observation to Intervention: A Critical Analysis of Treatment Timelines in Pediatric Empyema

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ABSTRACT

Background: Empyema thoracis is a significant cause of morbidity and mortality in children, especially in resource-poor countries where it tends to present late. The impact of the timing of treatment on outcomes is considerable, although there is little information from resource-poor countries.

Objective: The objective of this study is to evaluate the treatment timelines from the onset of symptoms to definitive care in pediatric patients with empyema, and the factors associated with delayed care.

Methods: A cross-sectional study was conducted at the Department of Pediatric Surgery, Liaquat University of Medical & Health Sciences, Jamshoro/Hyderabad, Pakistan, between August 2018 and July 2022. A total of 470 patients aged 5 months to 14 years, diagnosed with empyema thorax, were included in this study. The treatment period was classified into early (≤7 days), intermediate (8-14 days), and delayed (>14 days).

Results: Mean age was 4.8±3.2 years, with a male preponderance (64.9%). Median time from onset of symptoms to intervention was 14 days (IQR: 9-21 days). Early, intermediate, and delayed interventions occurred in 21.9%, 38.1%, and 40% of patients, respectively. Delayed interventions were associated with higher complication rates (52.1% vs 11.7%, p<0.001), longer hospital stay (24.3±8.6 vs 10.2±3.4 days, p<0.001), and higher rate of thoracotomy (43.6% vs 5.8%, p<0.001). In multivariate analysis, independent predictors for delayed intervention were treatment in peripheral centers (aOR: 4.21), rural residents (aOR: 3.42), distance of travel >100km (aOR: 2.87), and lower socioeconomic status (aOR: 2.56).

Conclusion: The timing of treatment has a significant influence on the outcome of empyema cases in children. Moreover, if treatment is delayed, several complications arise, such as invasive procedures. Early detection and referral programs play a critical role in improving treatment outcomes, especially in resource-limited settings.

Keywords: Pediatric empyema, treatment timeline, delayed intervention, resource-limited setting, treatment outcomes.

INTRODUCTION

Empyema thorax is the collection of pus in the pleural space, a complication of pneumonia and a major current health problem in children around the world today[1].Although the prevalence varies greatly according to the region, resource-poor regions of developing countries are also still affected by this condition[2,3]. In Pakistan and other developing countries with poor healthcare resources, pediatric empyema is a major source of morbidity, prolonged hospitalization, and high expenditure of healthcare in these countries[4,5].

The natural history of empyema is predictable, with the disease passing through three well-recognized stages of the pathologic process: the exudative stage (Stage I), characterized by the presence of a thin, fluid pleural exudate; the fibrinopurulent stage (Stage II), during which fibrin deposition leads to locules; and the organizing stage (Stage III), during which the overlying peel becomes thick and fibrotic and entraps the lung[6]. This has special implications regarding the time-sensitive nature of treatment of empyema, wherein any delay means inevitable progression to more advanced stages that may often require more elaborate surgical procedures[7,8].

The treatment of pediatric empyema has come a long way in the past few years and is still a topic of much debate concerning the best management approach and the timing of the procedure [9,10]. The treatment options range widely from a conservative approach with antibiotics and simple chest tube drainage to more complicated ones such as fibrinolysis, VATS, and open thoracotomy with decortication[11,12,13]. Nevertheless, the most important factor that determines the success of the management in most cases does not depend on the method of management used, but on the timing of this approach[14,15].

Video-assisted thoracoscopic surgery has recently been accepted as the most preferred surgical approach, exhibiting success rates of 90-96% with an average postoperative hospital stay of 6-7 days[11,16]. In the case of loculated empyemas, intrapleural fibrinolytic therapy has been shown to be successful, with success rates between 67-95%[17,18]. Conventional tube thoracostomy remains a highly successful treatment in 78-85% of cases when done early in the disease process[4,19]. Nevertheless, in cases of delayed presentation, open thoracotomy with decortication often becomes an inevitable option[7,8].

Children from developing nations such as Pakistan have the typical presentation towards the end stages of their disease, after having received multiple courses of empirical antibiotics administered by their primary healthcare institutions[3,5]. According to local statistics, at least 90% of patients who needed decortication were referred after more than three weeks from the onset of symptoms[8]. Furthermore, delays in diagnosis are also contributed to by the lack of accessibility of radiology facilities in the rural area[5,20]. Moreover, the aforementioned systemic delays have serious clinical implications, whereby patients who present with advanced empyema would need more invasive approaches to surgery and intravenous antibiotics[4,7,21].

Although some studies conducted in developed countries have investigated the treatment outcomes of empyema, very few have analyzed the treatment timelines and their effects on outcomes in resource-limited environments[4,5,8]. The purpose of the current study is to fill the existing knowledge gap by thoroughly examining the treatment timelines in pediatric patients with empyema at a large tertiary care referral center in Pakistan.

METHODOLOGY

This hospital-based cross-sectional analytical study was conducted from August 2018 to July 2022 at the Department of Pediatric Surgery, Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro/Hyderabad, Pakistan. LUMHS is a major tertiary care teaching hospital serving as the primary referral center for Sindh province, receiving patients from both urban and remote rural areas.

Children aged 5 months to 14 years, with clinically and radiologically confirmed empyema thorax, were considered for

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participation. The criteria for diagnosis included clinical presentation, typical radiographic features, and pleural fluid characteristics suggestive of empyema (presence of frank pus, pH < 7.2, glucose < 60 mg/dL, LDH concentration > 1000 IU/L, or positive bacterial culture). Exclusion criteria included tubercular empyema, post-traumatic empyema, associated chronic pulmonary disease, immunodeficiency conditions, and incomplete medical records. By consecutive sampling, 470 patients satisfying all criteria were recruited.

Staging of Empyema was done according to classifications: Stage I (Exudative) - with thin, easily flowing fluid; Stage II (Fibrinopurulent) - with fibrin deposition and fluid loculations; and Stage III (Organizational) - with thick fibrous peel, requiring decortication. The treatment course was divided into early intervention (≤7 days), intermediate intervention (8-14 days), and late intervention (>14 days) after onset of symptoms.

Data collection was done using a structured proforma that recorded demographic information, clinical features, stages of disease, treatment approaches, and outcomes. Nutritional status was determined by WHO growth standards. Statistical analysis was done using SPSS version 26.0. Comparison between categorical variables was done using the chi-square test, while comparisons between continuous variables were done by independent t-tests. Logistic regression was used to determine independent predictors of delayed treatment. Significance level was set at $p<0.05$. Informed consent was sought from parents or guardians of all children involved in the study.

RESULTS

A total of 523 children with empyema thorax were initially screened, and 470 children were enrolled after the exclusion of 53 patients who had tuberculous empyema (28 patients), trauma-induced empyema (8 patients), immunodeficiency diseases (6 patients), chronic pulmonary diseases (5 patients), and inadequate records (6 patients).

The average age was 4.8±3.2 years with a median of 4.0 years (IQR: 2.5-7.5 years). The majority of the patients (53.4%) were aged 1-5 years. Males comprised the majority, accounting for 305 (64.9%) of the patients, giving a male to female ratio of 1.85:1. Rural residence was noted in 320 (68.1%) patients, of whom 212 (45.1%) had to travel over 100 kilometers to access the tertiary care center. Lower socioeconomic class was found in 338 (71.9%) patients. Severe malnutrition was recorded in 89 (18.9%) patients. It is pertinent to note that only 164 (34.9%) patients had received pneumococcal conjugate vaccine. Parental education levels were low; 187 (39.8%) parents had no formal education, and 142 (30.2%) had primary education only (Table 1).

The clinical presentation was uniform in the group: all 470 patients (100%) had fever, 458 (97.4%) had cough, 412 (87.7%) had respiratory distress, and 287 (61.1%) had chest pain. The documentation of prior healthcare contact was available in 91.7% of cases, with 367 (78.1%) having received antibiotics. The staging of disease showed that 87 (18.5%) were in Stage I, 228 (48.5%) in Stage II, and 155 (33.0%) were in Stage III. The right side was involved in 56.8%, left side in 39.4%, and bilaterally in 3.8% of cases.

The median time from onset of symptoms to definitive management was 14 days (IQR: 9-21). Using intervention timing, 103 patients (21.9%) underwent early intervention (≤7 days), 179 patients (38.1%) underwent intermediate intervention (8-14 days), while 188 patients (40.0%) underwent delayed intervention (>14 days).

Time of intervention showed significant correlation with the stage of disease ($p<0.001$); 56.3% of patients undergoing early intervention had Stage I disease, while 59.6% of patients undergoing delayed intervention had progressed to Stage III. The treatment needs differed significantly among the groups ($p<0.001$); drainage alone was adequate in 60.2% of patients undergoing early intervention, compared to 19.1% of patients undergoing delayed intervention; thoracotomy was needed in 5.8% versus 43.6%, respectively (Table 2).

Table 1: Demographic and Clinical Characteristics of Study Population (N=470)

Characteristic	n (%) or Mean ± SD
Age	
Mean age (years)	4.8 ± 3.2
Median age (years)	4.0 (IQR: 2.5-7.5)
Age Distribution	
< 1 year	42 (8.9%)
1-5 years	251 (53.4%)
6-10 years	128 (27.2%)
11-14 years	49 (10.4%)
Gender	
Male	305 (64.9%)
Female	165 (35.1%)
Male to Female ratio	1.85:1
Residence	
Rural	320 (68.1%)
Urban	150 (31.9%)
Distance to Tertiary Center	
< 50 km	142 (30.2%)
50-100 km	116 (24.7%)
> 100 km	212 (45.1%)
Socioeconomic Status	
Lower	338 (71.9%)
Middle	108 (23.0%)
Upper	24 (5.1%)
Nutritional Status	
Normal	224 (47.7%)
Mild-moderate malnutrition	157 (33.4%)
Severe malnutrition	89 (18.9%)
Vaccination Status	
Pneumococcal conjugate vaccine received	164 (34.9%)
Not vaccinated/unknown	306 (65.1%)
Parental Education	
No formal education	187 (39.8%)
Primary education only	142 (30.2%)
Secondary education	89 (18.9%)
Higher education	52 (11.1%)
Clinical Presentation	
Fever	470 (100%)
Cough	458 (97.4%)
Respiratory distress	412 (87.7%)
Chest pain	287 (61.1%)
Decreased breath sounds	452 (96.2%)
Tachypnea	398 (84.7%)
Healthcare History	
Previous healthcare contact	431 (91.7%)
Previous antibiotic therapy	367 (78.1%)
Prior hospitalization	198 (42.1%)
Disease Stage at Presentation	
Stage I (Exudative)	87 (18.5%)
Stage II (Fibrinopurulent)	228 (48.5%)
Stage III (Organizational)	155 (33.0%)
Laterality	
Right-sided	267 (56.8%)
Left-sided	185 (39.4%)
Bilateral	18 (3.8%)
Intervention Timeline	
Median time to intervention (days)	14 (IQR: 9-21)
Early intervention (≤7 days)	103 (21.9%)
Intermediate intervention (8-14 days)	179 (38.1%)
Delayed intervention (>14 days)	188 (40.0%)

Hospital stay was markedly shorter in the early intervention group (10.2±3.4 days) compared to the delayed intervention group (24.3±8.6 days, $p<0.001$). ICU admission was necessary in 7.8% of early intervention cases versus 30.9% of delayed cases ($p<0.001$). Complication rates were substantially higher with delayed intervention (52.1% vs 11.7%, $p<0.001$). Treatment success rates were 98.1% for early intervention compared to 82.4% for delayed intervention ($p<0.001$). Mortality was 0% in the

early intervention group, 1.7% in the intermediate group, and 4.3% in the delayed intervention group (p=0.024).

Multivariate logistic regression analysis identified independent predictors of delayed intervention (Table 3).

Treatment at peripheral healthcare facilities emerged as the strongest predictor (aOR: 4.21, 95% CI: 2.45-7.24, p<0.001), followed by rural residence (aOR: 3.42, 95% CI: 2.12-5.52, p<0.001), low parental education (aOR: 2.94, 95% CI: 1.78-4.86, p<0.001), distance exceeding 100 kilometers (aOR: 2.87, 95% CI: 1.89-4.36, p<0.001), lower socioeconomic status (aOR: 2.56, 95% CI: 1.58-4.15, p<0.001), and severe malnutrition (aOR: 2.18, 95% CI: 1.32-3.60, p=0.002). Vaccination status showed a trend toward association but did not achieve statistical significance (aOR: 1.54, 95% CI: 0.98-2.42, p=0.062).

Treatment modalities employed included chest tube drainage alone (37.4%), thoracotomy with decortication (21.3%), chest tube with fibrinolytics (19.6%), VATS (15.7%), and conservative management (6.0%). VATS achieved the highest success rate (93.2%) with the shortest mean hospital stay (12.4±4.2 days). Thoracotomy demonstrated a 96.0% success rate but required the longest hospitalization (22.6±7.8 days) and had the highest complication rate (58.0%), reflecting the advanced disease stage in patients requiring this intervention. Conservative therapy had the lowest success rate (60.7%), with 64.3% requiring subsequent re-intervention (Table 4).

Positive pleural fluid cultures were obtained in 186 (39.6%) cases, with Staphylococcus aureus (36.6%) and Streptococcus pneumoniae (28.0%) being the predominant organisms isolated (Figure 1). Overall treatment success was achieved in 89.6% of cases, the total complication rate was 33.6%, and mortality occurred in 11 patients (2.3%).

Table 2: Clinical Outcomes Stratified by Intervention Timeline

Variable	Early Intervention (≤7 days) n=103	Intermediate Intervention (8-14 days) n=179	Delayed Intervention (>14 days) n=188	p-value
Disease Stage				<0.001
Stage I	58 (56.3%)	24 (13.4%)	5 (2.7%)	
Stage II	39 (37.9%)	119 (66.5%)	71 (37.8%)	
Stage III	6 (5.8%)	36 (20.1%)	112 (59.6%)	
Treatment Modality				<0.001
Conservative management	12 (11.7%)	14 (7.8%)	2 (1.1%)	
Chest tube drainage alone	62 (60.2%)	78 (43.6%)	36 (19.1%)	
Chest tube + fibrinolytics	18 (17.5%)	42 (23.5%)	32 (17.0%)	
VATS	5 (4.9%)	32 (17.9%)	36 (19.1%)	
Thoracotomy with decortication	6 (5.8%)	13 (7.3%)	82 (43.6%)	
Hospital Stay (days)	10.2 ± 3.4	16.8 ± 5.2	24.3 ± 8.6	<0.001
ICU Admission	8 (7.8%)	32 (17.9%)	58 (30.9%)	<0.001
ICU Stay (days)	2.4 ± 1.2	3.8 ± 1.8	5.6 ± 2.9	<0.001
Complications				<0.001
Any complication	12 (11.7%)	46 (25.7%)	98 (52.1%)	
Persistent air leak	3 (2.9%)	12 (6.7%)	28 (14.9%)	
Re-expansion pulmonary edema	1 (1.0%)	4 (2.2%)	12 (6.4%)	
Wound infection	2 (1.9%)	8 (4.5%)	22 (11.7%)	
Bronchopleural fistula	0 (0%)	3 (1.7%)	14 (7.4%)	
Sepsis	2 (1.9%)	8 (4.5%)	18 (9.6%)	
Residual pleural thickening	4 (3.9%)	14 (7.8%)	32 (17.0%)	
Re-intervention Required	4 (3.9%)	18 (10.1%)	42 (22.3%)	<0.001
Treatment Success	101 (98.1%)	165 (92.2%)	155 (82.4%)	<0.001
Mortality	0 (0%)	3 (1.7%)	8 (4.3%)	0.024

Table 3: Predictors of Delayed Intervention (>14 days) - Multivariate Logistic Regression Analysis

Predictor Variable	Delayed Intervention n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Prior Treatment at Peripheral Healthcare Facility				
No	28/94 (29.8%)	Reference	Reference	
Yes	160/376 (42.6%)	5.12 (2.98-8.79)	4.21 (2.45-7.24)	<0.001
Residence				
Urban	42/150 (28.0%)	Reference	Reference	
Rural	146/320 (45.6%)	4.18 (2.68-6.52)	3.42 (2.12-5.52)	<0.001
Parental Education				
Secondary or higher	38/141 (26.9%)	Reference	Reference	
No formal/Primary only	150/329 (45.6%)	3.52 (2.24-5.53)	2.94 (1.78-4.86)	<0.001
Distance to Tertiary Center				
≤100 km	72/258 (27.9%)	Reference	Reference	
>100 km	116/212 (54.7%)	3.24 (2.18-4.82)	2.87 (1.89-4.36)	<0.001
Socioeconomic Status				
Middle/Upper	36/132 (27.3%)	Reference	Reference	
Lower	152/338 (45.0%)	3.12 (1.98-4.91)	2.56 (1.58-4.15)	<0.001
Nutritional Status				
Normal/Mild-moderate malnutrition	138/381 (36.2%)	Reference	Reference	
Severe malnutrition	50/89 (56.2%)	2.86 (1.78-4.59)	2.18 (1.32-3.60)	0.002
Pneumococcal Vaccination Status				
Vaccinated	56/164 (34.1%)	Reference	Reference	
Not vaccinated/Unknown	132/306 (43.1%)	1.72 (1.14-2.59)	1.54 (0.98-2.42)	0.062
Age Group				
>5 years	68/177 (38.4%)	Reference	Reference	
≤5 years	120/293 (40.9%)	1.24 (0.84-1.83)	1.18 (0.76-1.84)	0.456
Gender				
Female	62/165 (37.6%)	Reference	Reference	
Male	126/305 (41.3%)	1.12 (0.76-1.65)	1.08 (0.71-1.64)	0.724

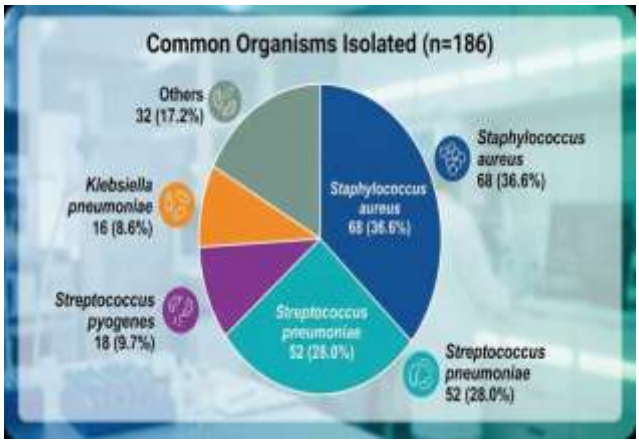
OR = Odds Ratio; CI = Confidence Interval Adjusted for all variables in the model

Table 4: Treatment Modalities, Success Rates, and Overall Outcomes

Treatment Modality	n (%)	Success Rate n (%)	Hospital Stay (days) Mean ± SD	Complication Rate n (%)	Re-intervention Required n (%)	Mortality n (%)
Conservative management (antibiotics alone)	28 (6.0%)	17 (60.7%)	14.2 ± 6.8	8 (28.6%)	18 (64.3%)	1 (3.6%)
Chest tube drainage alone	176 (37.4%)	152 (86.4%)	13.8 ± 5.4	42 (23.9%)	24 (13.6%)	2 (1.1%)
Chest tube + fibrinolytics	92 (19.6%)	78 (84.8%)	15.6 ± 5.8	28 (30.4%)	14 (15.2%)	2 (2.2%)
VATS	74 (15.7%)	69 (93.2%)	12.4 ± 4.2	12 (16.2%)	5 (6.8%)	1 (1.4%)
Thoracotomy with decortication	100 (21.3%)	96 (96.0%)	22.6 ± 7.8	58 (58.0%)	4 (4.0%)	5 (5.0%)
Overall Outcomes	N=470					
Treatment success		421 (89.6%)				
Total complications				158 (33.6%)		
Total re-interventions					64 (13.6%)	
Overall mortality						11 (2.3%)
Mean hospital stay			16.4 ± 7.2			
ICU admission		98 (20.9%)				

VATS = Video-Assisted Thoracoscopic Surgery

Figure 1: Common Organisms Isolated



DISCUSSION

This study of 470 pediatric patients with empyema shows that there are marked delays in treatment in our resource-limited setting, with a median of 14 days from onset of symptoms until treatment is initiated, with 40% of patients awaiting treatment for longer then 14 days. We have shown here that there is a direct correlation between treatment delay and poor outcomes of treatment for empyema.

"The median time to intervention of 14 days in the current study is significantly longer than that seen in developed countries, where intervention for 7-10 days for most children is the rule[9,11]. In Western systems of healthcare, it is found that 60-70% of patients with empyema are referred for intervention in the first week[11,22], which is vastly different from the finding in the current study of 21.9%, but is consistent with other developing countries, where Kumar et al found that the average stay in the hospital is 15.35 days[4], or with the finding of Singh et al that 90% of children requiring decortication were referred more than three weeks after onset of their symptoms[8]."

The positive correlation between delayed intervention and high disease stage is consistent with the pathophysiology of empyema development, which traverses phases of exudation, fibrinopurulence, and organization[6,23]. This is indicative of the pathophysiology that with progressively delayed interventions, fewer therapeutic alternatives become available. The large difference in the frequency of thoracotomy between the early intervention group, where it occurred in 5.8%, and the delayed intervention group, where it occurred in 43.6%, is a compelling demonstration of this phenomenon. VATS data from Bender et al. shows a success rate of 96.4% with mean postoperative stays of 6.3 days[11].

Our total complication rate of 33.6% is higher than the 9.9-11.6% rates found in recent VATS series from developed nations[13,24], likely related to the later presentation of disease in our patient population. Our mortality rate of 2.3% is lower than that of some resource-constrained nations[19,25] but higher than the less-than-1% rates found in developed nations[9,26]. Of great significance, however, is the finding that mortality in the early intervention group was 0%, as opposed to 4.3% in the delayed group.

Our results for chest tube drainage procedure were consistent with Ghritlaharey et al., who achieved 84.78% success with tube thoracostomy, as well as Goyal et al., with 78.6% success rates[19,25]. Success rates of fibrinolytic therapy were in line with the literature of 67-95%[17,18]. Shankar et al. showed that fibrinolytic therapy is non-inferior to VATS, whereas superiority of thoracotomy with Decortications over other techniques for multiloculated empyema was shown by Balci et al. in their study[18,27].

VATS procedure achieved excellent results with consistency of its application as a preferred surgical procedure for such patients[11,12,13].

Antecedent care at peripheral health facilities was found to be significantly associated with delayed care as a predictor (aOR: 4.21), with 91.7% of children having received previous care and 78.1% of children having received previous antibiotics before seeking care, indicating several missed opportunities for earlier diagnosis and proper referral[3,5,20]. Being from a rural area (aOR: 3.42) and distances of more than 100 kilometers (aOR: 2.87) indicate established urban-rural health disparities in accessing specialist care[4,5]. Lower SES (aOR: 2.56) is a predictor as it is a result of delayed health-seeking behavior due to limited funds. Severe malnutrition (aOR: 2.18) is both an independent risk factor for severe infection as well as a surrogate for socio-economic risk factors[4,28]. Poor parental literacy (aOR: 2.94) interferes with health literacy and the capability to perceive potential danger signs requiring urgent medical care[5,29].

The substantial rise in thoracotomy demands in the delayed treatment group aptly accentuates that prompt treatment helps retain various therapeutic possibilities. Numerous clinical studies have validated that prompt thoracoscopy[12,14,24,30] or urgent open surgery[15,31] is superior to conservative treatment for a considerable length of time. Primary features of health system strengthening would basically encompass training sessions for grass root health care givers about empyema detection and referral systems, improvement in diagnostic facilities with ultrasound availability in district hospitals[20,32], universal referral systems with predefined initial criteria for prompt referral, and sound antibiotic utilization practices[9,20]. These would accompany intensified pneumococcal vaccination efforts since only 34.9% of our patients had been immunized with pneumococcal vaccine, which could make a substantial difference in the number of incident cases of empyema[33,34].

Study limitations include being cross-sectional, showing association but not causation. Data from one center could be limited by generalization. Data on timeline could be prone to information bias as it is dependent on recall. A positive culture of Pleural fluid of 39.6% is attributed to the high prevalence of previous antibiotic use in our context[9,20].

CONCLUSION

This research reveals that timing is a strongly defining factor for patient outcomes in pediatric empyema. Delaying treatment past the 14th day of onset of symptoms significantly increases the risk of possible complications, hospital stay, need for surgery, and death.

These factors of prior management of admitted children at peripheral facilities, rural residence, distance, low socioeconomic conditions, severe malnutrition, and low parental educational levels are predicators of delayed presentation that could be altered by the following interventions in the health delivery system: improvement of diagnostic services at peripheral health facilities, improvement of the referral system, training of primary health care staff, and extension of pneumococcal vaccine.

Early intervention in pediatric empyema saves lives, prevents complications, and decreases the length of stay in the hospital. Delay in treatment should continue to remain one of the concerns for improving pediatric respiratory outcomes in resource-constrained environments.

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