

Indicators for surgical intervention in thoracic empyema in children

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ABSTRACT

الأهداف: لتحديد تنبؤ عن التدخل الجراحي من دويلة الصدرية عند الأطفال، والأمراض المرتبطة بها.

الطريقة: تم مراجعة ملفات المرضى اللذين ادخلوا مستشفى النساء والولادة والأطفال بالمدينة المنورة، المملكة العربية السعودية بتشخيص الدويلة الصدوية الصدرية خلال الفترة من يناير 2007م الى يناير 2012م وتضمنت البيانات المستخرجة: البيانات الإجماعية والديموغرافية للأساليب والبيانات السريرية، وطريقة العلاج، ومتابعة البيانات. وفقاً للأساليب العلاجية المقدمة تم تقسيم المرضى إلى مجموعتين، المرضى اللذين تمت معالجتهم بغرز أنبوب صدري (CT) في 51 حالة، و11 حالة تطلبت بضع الصدر (TH) وتمت بعد ذلك مقارنة المجموعتين لتحديد وجود عوامل تنبؤ عن بضع الصدر.

النتائج: من 62 مريضاً، 37 من الإناث و25 من الذكور. كانت المجموعتين متجانسة من ناحية، العمر، جانب الآفة، وجود سعال، أو ضيق التنفس. كان لدى المجموعتين فروق ذات دلالة إحصائية لمدة الشكوى (TH and CT) (13.5 ± 6.5) يوماً مقابل (10 ± 3.6 ، $p=0.005$)، وجود حمى (36.4% و 90.2% ، $p<0.001$)، والتاريخ من التهابات الصدر المتكررة (90.9% مقابل 37.3% ، $p=0.001$)، والنتائج الإشعاعية. ومع ذلك، لم يكن من الواضح أن هذه المتغيرات أثرت على قرار العلاج باستثناء غياب الحمى، الذي كان أقل بكثير في المرضى اللذين عولجوا مع بضع الصدر.

الخلاصة: لم يعثر على أي مؤشر محدد لزيادة المتوقع للتدخل الجراحي كخيار العلاج، باستثناء غياب الحمى، مما قد يعكس إحالة تأخر والاستخدام المطول للمضادات الحيوية والتي لا يمكن تفسيرها دون الحذر كمؤشر للتدخل الجراحي.

Objectives: To determine predictors for surgical intervention of thoracic empyema in children, and its associated morbidity.

Methods: We conducted a retrospective review of medical records of children with empyema thoracis admitted in the Maternity and Children Hospital, Al Madinah Al Munawwarah, Saudi Arabia between January 2007 and January 2012.

The data extracted included: socio-demographic data, clinical data, method of treatment, and follow up data. According to the introduced therapeutic methods, a total of 62 patients were divided into 2 groups; patients treated with chest tube (CT) insertion (51 cases), and 11 cases that required thoracotomy (TH); groups were compared to determine predictors for thoracotomy.

Results: Of 62 patients, 37 were females and 25 were males. In terms of age, side of lesion, presence of cough, or dyspnea, both groups were homogenous. Both groups had significant differences for duration of complaint (TH and CT) (13.5 ± 6.5 days versus 10 ± 3.6 , $p=0.005$), presence of fever (90.2% versus 36.4% , $p<0.001$), history of recurrent chest infections (90.9% versus 37.3% , $p=0.001$), and radiological findings. However, it was not evident that any of these variables influenced treatment decision except absence of fever, which was significantly less in patients treated with thoracotomy.

Conclusion: No specific indicator was found to increase expectancy for surgical intervention as a treatment choice, except the absence of fever, which may reflect the delayed referral and prolonged use of antibiotics and cannot be interpreted truly without caution as an indicator for surgical intervention.

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Empyema thoracis in children is a common condition with increasing incidence world wide.¹⁻³ Low socioeconomic status, use of inappropriate antibiotics, malnutrition, and delay in seeking treatment are risk factors for its development in patients with pneumonia.^{4,5} The management of childhood empyema is still a therapeutic challenge due to lack of evidence-based level A studies, and results from adult studies cannot be used for management decisions in children.⁶ A major difference between empyema in adults and children is that in children, empyema usually affects a previously healthy child, due to which the clinical outcome is usually excellent despite associated morbidity.⁶ Different treatment modalities have been described, including antibiotics, thoracentesis, tube thoracostomy, intrapleural fibrinolytics, open window thoracostomy, video-assisted thoracoscopic surgery (VATS), and thoracotomy. However, to date, there is no consensus on the optimum modality and timing of therapy.⁷⁻¹¹ The approach in most of the cases depends on the stage of the disease and the resources available. Although thoracentesis, antibiotic treatment, and chest tube (CT) drainage are usually sufficient for early stages of the disease, advanced empyema usually needs advanced options like VATS with or without fibrinolysis or thoracotomy. Those who prefer VATS and fibrinolysis report that thoracotomy is associated with high morbidity and prolonged hospital stay; however, other reports have challenged this view.¹² We review our experience in the management of empyema, determining any indicators for surgery preference and its safety in children. Identified predictors could decrease the length of hospital stay of the child, and subsequent family discomfort from a long hospitalization, which usually occurs in empyema thoracis cases.

Methods. We retrospectively retrieved patients' data archived in medical records in the Maternity and Children Hospital, Al Madinah Al Munawwarah, Saudi Arabia between January 2007 and January 2012. We obtained institutional review board permission to retrieve the patients' medical records. Inclusion criteria were children aged less than 12 years old complaining of empyema, which was managed by tube thoracostomy (CT) during the period from January 2007 to January 2012. Children with parapneumonic effusion managed by antibiotics alone or with thoracentesis without chest tube insertion were excluded from the study. Patients managed by thoracoscopy, which was recently introduced in our hospital, and patients managed by thoracotomy as the initial treatment option without prior tube thoracostomy were also excluded from the study.

The diagnosis of empyema was confirmed by pleural fluid analysis that revealed one or more of the following criteria; grossly purulent pleural fluid aspirate, positive gram stain or culture, pleural fluid glucose level less than 40 mg/dl, pleural fluid pH less than 7.00, or pleural fluid lactic dehydrogenase (LDH) more than 1000 IU/l. All patients were managed firstly by chest tube insertion. All chest tubes were inserted in the operating theater under general anesthesia and placed in the fifth or the sixth intercostal space at the mid-axillary line or posterior axillary line. Intrapleural warm saline irrigation through the chest drain was used for some cases, if needed, to enhance adequate drainage. If tube drainage stopped or became minimal with insufficient lung inflation without air leak, or pleural inoculations, confirmed by CT, intrapleural injection of fibrinolytics was used daily for 3 successive days. Thoracotomy was performed for patients with trapped lung with thickened pleura or persistent air leak or destroyed lung parenchyma. This was performed through posterolateral incisions to ensure minimal muscle-sparing. Both study groups were compared according to the following variables: wound infection, chest infection, radiological findings, and mortality rates.

Statistical analysis. Data was collected and analyzed using the Statistical Package for Social Sciences version 13 (SPSS Inc., Chicago, IL, USA). Quantitative data was shown as mean and standard deviation (SD). Qualitative data was expressed as frequency and percentage. Chi-square test was used to measure association between qualitative variables. Student's t-test was used to compare mean and SD of 2 sets of quantitative data distributed normally, while Mann Whitney test was used when this data was not normally distributed. Fisher exact test was used for 2x2 qualitative variables when more than 25% of the cells had an expected count less than 5. Multivariate logistic regression analysis was used to give adjusted odds ratio and 95% confidence interval of the effect of the different predictors for thoracotomy in the studied population. The *p*-value was considered statistically significant when less than 0.05.

Results. A total of 62 medical records of children who met the inclusion criteria were evaluated. Out of those 62, 37 patients were females and 25 were males. Fifty-one patients were treated with CT insertion as a definitive treatment with or without intrapleural fibrinolytics use (thoracostomy, CT group), and 11 patients were treated by thoracotomy as a definitive treatment (TH group). Decortication was carried out in 5 cases, of which 2 required repair of a bronchopleural fistula. Resection was carried out in 6 cases; 2 right upper lobectomies, and one for each right upper and middle,

right lower, left upper, and left lower lobectomies, due to destruction of lung tissue or fibrosis.

Table 1 summarizes the patient demographics of both groups. The mean age was 45.2 months (range from one month to 142 months). There were no statistically significant differences between both groups regarding age, gender, side of lesion, the presence of cough, or the presence of dyspnea after treatment. The presence of fever was significantly higher in the CT group compared with the TH group (90.2% versus 36.4%, $p < 0.001$). The duration of complaint (time from the onset of symptoms to surgical consultation) was significantly higher in the TH group (13.5±6.5 days versus 10±3.6 days) ($p = 0.005$). The history of previous chest infections was significantly higher in the TH group (90.9% versus 37.3%, $p = 0.001$). There was a statistically significant difference between both groups regarding the radiological findings. The presence of pleural effusion was higher in the CT group, but the presence of hydro-pneumothorax was higher in the TH group. Laboratory investigations showed no statistically significant difference between both groups.

There was no statistically significant difference between the 2 groups regarding pleural fluid characteristics (Table 2). Culture of pleural fluid was positive for bacterial growth in 26 cases (41.9%) and negative in 36 cases (58.1%). Infection by a single

organism was recorded in 21 cases, while 5 cases had mixed bacterial infection. The most frequently cultured organism was *Streptococcus pneumoniae*, followed by *Staphylococcus aureus* (8 versus 7 cases).

Intrapleural fibrinolytics were used in 19 patients (37.3%) in the CT group and 2 patients (18.2%) in the TH group (Table 3). In 3 patients (all in the CT group), fibrinolytics were stopped after the first dose because of complications, bleeding in 2 patients and allergy in one patient. In the CT group, intrapleural fibrinolytics led to radiological improvement in 16 out of 19 patients (84.2%), including those patients who stopped it after the first dose. In 3 patients who did not show radiological improvement, open drainage was tried, then they showed gradual improvement as evidenced by complete

Table 2 - Pleural fluid characteristics in 62 medical records of children with empyema thoracis.

| Variables | CT group (n=51) | TH group* (n=11) | Total (n=62) | P-value |
|---------------------|-----------------|------------------|--------------|---------|
| PF positive culture | 23 (45.1) | 3 (27.3) | 26 (41.9) | 0.332 |
| PF pH | 6.9±0.2 | 6.9±0.2 | 6.9±0.2 | 0.627 |
| PF LDH (IU/L) | 4082±5710 | 3174±2306 | 3959±5371 | 0.535* |
| PF glucose (mg/dl) | 28±8 | 28±13 | 28±9 | 0.756* |
| PF protein (gm/dl) | 5.1±1.9 | 6.9±4.8 | 5.3±2.5 | 0.136* |

*Mann-Whitney test, PF - pleural fluid, CT - chest tube, TH - thoracotomy

Table 1 - Demographic data in 62 medical records of children with empyema thoracis.

| Variables | CT group (n=51) | TH group* (n=11) | Total (n=62) | P-value |
|------------------------------|-----------------|------------------|--------------|---------|
| Age (months) | 42.2±32.9 | 59.4±46.8 | 45.2±35.9 | 0.24* |
| Gender: female | 33 (64.7) | 4 (36.4) | 37 (59.7) | 0.101 |
| Right side lesions | 19 (37.3) | 6 (54.5) | 25 (40.3) | 0.29* |
| Duration of complaint (days) | 10±3.6 | 13.5±6.5 | 10.6±4.4 | 0.005 |
| Fever | 46 (90.2) | 4 (36.4) | 50 (80.6) | <0.001 |
| Cough | 46 (90.2) | 9 (81.8) | 55 (88.7) | 0.43 |
| Dyspnea | 36 (70.6) | 10 (90.9) | 46 (74.2) | 0.16 |
| History of chest infection | 19 (37.3) | 10 (90.9) | 29 (46.8) | 0.001 |
| <i>X-ray finding</i> | | | | |
| Effusion | 43 (84.3) | 6 (54.5) | 49 (79.0) | 0.028 |
| Hydro-pneumothorax | 8 (15.7) | 5 (45.5) | 13 (21.0) | |
| <i>CT finding</i> | | | | |
| Free effusion | 32 (62.7) | 0 | 32 (51.6) | <0.001 |
| Encysted effusion | 10 (19.6) | 4 (36.4) | 20(32.3) | |
| Hydro-pneumothorax | 9 (17.6) | 7 (63.6) | 10 (16.1) | |
| Leucocytic count (cells/cmm) | 14.7±3.6 | 14.5±2 | 14.7±3.4 | 0.88 |
| Hemoglobin (gm/dl) | 9.9±1.4 | 10.1±1.4 | 9.9±1.4 | 0.603 |
| LDH (IU/L) | 546±326 | 553±193 | 547±306 | 0.25* |
| Protien (gm/dl) | 6.5±0.4 | 6.3±0.6 | 6.5±0.5 | 0.128 |
| ESR (mm/h) | 95±25 | 110±20 | 98±25 | 0.065 |
| CRP (mg/l) | 90±17 | 92±26 | 90±19 | 0.716 |

*Mann-Whitney Test, LDH - lactic dehydrogenase, ESR - erythrocyte sedimentation rate, CRP - C - reactive protein, CT - chest tube, TH - thoracotomy

Table 3 - Patients' outcomes in 62 medical records of children with empyema thoracis.

| Variables | CT group (n=51) | TH group* (n=11) | Total (n=62) | P-value |
|---------------------------------------|-----------------|------------------|--------------|---------|
| Usage of fibrinolytics | 19 (37.3) | 2 (18.2) | 21 (33.9) | 0.305 |
| Pre-intervention hospital stay (days) | 1.3±1.9 | 5.9±5.5 | 2.1±3.3 | 0.005* |
| Total length of stay (days) | 15.8±8.6 | 21.3±11 | 16.8±9.2 | 0.128* |
| Chest tube duration (days) | 15.5±8.4 | 21.1±10.9 | 16.5±9.1 | 0.114* |
| Morbidity | | | | |
| Wound complications | 3 (5.9) | 1 (9.1) | 4 (6.5) | 0.552 |
| Scoliosis | 1 (2.0) | 1 (9.1) | 2 (3.2) | 0.326 |
| Mortality | 1 (2.0) | 0 | 1 (1.6) | 1.000 |

* Mann-Whitney test, CT - chest tube, TH - thoracotomy

lung inflation. Intrapleural fibrinolytics did not show any radiological improvement in 2 patients who used it in the TH group, and they developed persistent air leak requiring open thoracotomy. Patients in the TH group stayed longer in the hospital before starting the definitive treatment (5.9±5.5 days versus 1.3±1.9 days). The total duration of hospital stay, and the duration of chest tube placement was longer in the TH group, although there was no statistical difference (21.3±11 versus 15.8±8.6 days, and 21.1±10.9 versus 15.5±8.4 days) (Table 2). Wound complications occurred in 3 cases from the CT group as chronic inflammation at the site of chest tube, which healed by the secondary intention after chest tube removal. One patient from the TH group had a superficial dehiscence in the thoracotomy wound requiring secondary sutures. Mild scoliosis occurred in 2 patients (one in each group) followed by a significant improvement after 6 months of treatment. Mortality was recorded in only one patient; a one-month-old boy in the CT group. He died from severe septicemia on the second day of hospitalization after inserting the chest tube, which drained approximately 300 cc of pure pus. On follow up after 6 months, all patients had no hospital admissions related to empyema, and radiological examinations revealed no recurrence of empyema in all cases in addition to sufficient lung inflation.

Although, univariate statistics showed a statistically significant difference between both groups in relation to the duration of complaint, the presence of fever, the history of recurrent chest infections, and the radiological findings, multivariate logistic regression confirmed solely the impact of fever, which was significantly less in the patients treated with thoracotomy (Table 4).

Discussion. Empyema is a dynamic process that progresses through 3 fairly distinct stages, as classified by the American Thoracic Society. Stage 1, the early exudative phase, involves a collection of thin reactive fluid and few cells in the pleural space. Stage 2, the

Table 4 - Predictors of thoracotomy in 62 medical records of children with empyema thoracis.

| Variables | OR | (95% CI) | P-value |
|--|--------|-------------------|---------|
| Duration of complaint | 1.091 | (0.918 - 1.296) | 0.322 |
| Fever | 0.086 | (0.009 - 0.779) | 0.029 |
| History of chest infection | 17.228 | (0.609 - 487.082) | 0.095 |
| X-ray finding | 9.393 | (0.737 - 119.735) | 0.085 |
| Computed tomography finding (hydro-pneumothorax) | 1.109 | (0.431 - 2.852) | 0.830 |

OR - odds ratio, CI - confidence interval

fibropurulent phase, involves large quantities of white cells and fibrin deposition with the formation of loculations. Stage 3, the organizing phase, involves the formation of a thick fibrinous peel encasing the lung and limiting its mobility. The most common presentation of empyema in our patients was cough, which occurred in 88.7% of the cases, followed by fever (80.6%) and dyspnea (74.2%). This finding agrees with a study that reported cough as the most common symptom (87%) followed by fever (85%).¹³ On the contrary, fever was the most common symptom in 98%, cough in 94%, and dyspnea in 44% in another patients sample.¹⁴

The mean duration of complaint in this study was 10.6 days, which makes no difference from 11.4 days reported in earlier study.¹³ In this study, we aimed to determine any predictors for the need for thoracotomy, which if identified could avoid delays in surgical referral and decision-making. Based on the factors studied and statistical analysis, we did not identify any significant predictors for thoracotomy except for the absence of fever ($p<0.029$), which may reflect the delay in surgical referral as it was evident that length of hospital stay for the TH group before starting the definitive treatment was significantly longer compared with the CT group ($p=0.005$). In the TH group, fever presented in only 4 cases (36.4%). On the contrary, fever was prominent in all cases that underwent open thoracotomy.¹² In adult studies, delayed referral and gram-negative organisms

were the main predictors for thoracotomy.¹⁵ In the same context, prolonged delay to surgery, persistent fever, and thickening of pleura on CT scan were predictors for thoracotomy.¹⁶ In our study, we did not identify any plausible indicators. Furthermore, pleural fluid analysis did not differ significantly between both groups, more patients in the CT group had positive pleural fluid culture compared with the TH group (45.1% versus 27.3%), which denotes the long duration of antibiotic therapy.

The mean total of hospital stay in the TH group was 21.3 days, which is comparable to 20.9 days in 191 patients treated by thoracotomy following failure of tube thoracotomy in a previous study.¹⁷ Shorter durations have been previously reported as 15 and 9.5 days;^{18,19} however, the median hospital stay was 5 days in open thoracotomy patients.¹²

The aim of treatment of empyema is to drain the infected fluid and restore lung expansion as much as possible to normal lung function.²⁰ Chest tube drainage and intravenous antibiotic therapy might be adequate for stage 1, but in stage 2 or 3 this option's efficacy is debatable. There may be clinical improvement with pleural space drainage and antibiotic therapy, but re-expansion of the trapped lung is less likely to occur, and surgical intervention may be needed in a significant number of cases in these later stages.^{10,21} Of the 62 children included in this study, only 11 cases (17.7%) were managed by open thoracotomy, while 51 responded well to tube thoracostomy. Similarly, thoracotomy was used as a definitive treatment in 12 out of 70 patients (17.14%),²² whereas 37.1% of patients treated by thoracotomy, and 17.1% of those treated by VAST required thoracotomy finally.²³ In the CT group, the mean total hospital stay was 15.8 days, which was similar to 15.4,¹⁹ 13.2,²⁴ and 14.1²⁵ days reported in previous studies. However, longer durations of hospital stay were reported as 21.7,²⁶ and 24.2²⁷ days, and shorter durations were also reported at 6.5²⁸ and 6²⁹ days. Mortality from empyema in children was very low, especially in patients treated operatively. In this study, only one case from the CT group died, and no mortality was recorded in the TH group. This agrees with the 3.3% aggregate mortality rate in patients managed by conservative therapy or tube thoracotomy compared to no mortality in patients managed by thoracoscopy or thoracotomy reported by others.³⁰ Regarding morbidity, we had 2 wound infections in the CT group in comparison with one in the TH group. In addition to that, scoliosis developed in one patient in each group.

Study limitations. As a retrospective study, there are some limitations such as a deficiency in information; for example, radiological. If available, more specific results might have been obtained. Also, we did not compare video-assisted thoracoscopy, as only a small number of patients have been managed by this modality in our hospital, and our experience is limited.

In conclusion, thoracotomy, when indicated, is a safe and more effective therapeutic modality for managing children with empyema. Although there were no specific predictors for increasing the chance of using thoracotomy as a treatment of choice over other therapeutic modalities in the management of empyema in children, the absence of fever was a remarkable feature for those patients undergoing thoracotomy. However, we cannot interpret that as a clinical marker for thoracotomy indication without caution.

Further research is required to build the evidence for managing empyema in children rather than generalizing adult patients' evidence-based practice into other developmental stages.

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Ethical Consent

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.