ORIGINAL

Cost-effectiveness of chest radiographs in children with influenza-like illness and prolonged fever

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Abstract

Introduction: Influenza causes high pressure on healthcare in Emergency Departments, as persistent fever is a common reason for consultation. Pneumonia is the most frequent respiratory complication, and a chest radiograph is usually requested to rule out this condition. Nevertheless, few data are available on the performance of chest radiographs in healthy children with normal lung sounds.

Objectives: To determine the prevalence of bacterial pneumonia in children with influenza-like illness and prolonged fever and to analyze possible clinical predictive factors.

Methods: A cross-sectional, retrospective study was conducted during the 2018 flu season. Healthy children with influenza-like illness and fever lasting 4 days or more who underwent a chest radiograph were included. The following potential risk factors were analyzed: age, duration of fever, and maximum temperature.

Results: Overall, 179 patients with a median age of 3.1 years were included. The median duration of fever was 5 days, and the mean maximum temperature was 39.5ºC. The diagnostic yield of chest radiographs in this study was 19.6%. None of the analyzed predictive factors was found to be associated with pneumonia.

Conclusions: The prevalence of bacterial pneumonia in healthy children with influenza-like illness, prolonged fever, and normal lung sounds is low. None of the factors analyzed proved to be predictive of pneumonia.

RENTABILIDAD DE LA RADIOGRAFÍA DE TÓRAX EN NIÑOS CON SÍNDROME GRIPAL Y FIEBRE PROLONGADA

Resumen

Introducción: *La gripe genera gran carga asistencial en los Servicios de Urgencias, siendo la persistencia de la fiebre motivo de consulta habitual. La complicación más frecuente es la neumonía, por lo que es habitual la indicación de radiografía de tórax (Rx) para descartarla. Sin embargo, hay pocos datos acerca de su rendimiento en niños sanos con auscultación respiratoria normal.*

Objetivos: *Determinar la prevalencia de neumonía bacteriana en niños con síndrome gripal y fiebre prolongada y analizar posibles factores clínicos predictores.*

Métodos: *Estudio transversal, retrospectivo, realizado durante la temporada de gripe de 2018. Se incluyeron niños sanos con síndrome gripal y fiebre ≥ 4 días con Rx. Se analizaron como posibles factores de riesgo: edad, duración de la fiebre y temperatura máxima.*

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Resultados: *Se incluyeron 179 pacientes; edad mediana 3,1 años. La mediana de duración de la fiebre fue de 5 días y la media de la temperatura máxima de 39,5°C. La rentabilidad diagnóstica de la Rx fue del 19,6%. No se hallaron diferencias significativas entre pacientes con neumonía y aquellos sin ella para ninguno de los factores de riesgo analizados.*

Conclusiones: *La prevalencia de neumonía bacteriana en niños sanos con síndrome gripal, fiebre prolongada y auscultación respiratoria normal es baja. Ninguno de los factores analizados resulta útil para predecirla.*

INTRODUCTION

Influenza causes a major care burden on healthcare in pediatric Emergency Departments (ED) during the flu season[1]. Although influenza-like illness is usually self-limiting and has a short course, there is a wide variability in symptom duration according to each case. Persistence of clinical symptoms, especially fever, may point to the presence of a bacterial coinfection, of which pneumonia is one of the most frequent[2] and the main cause of hospital admission[3,4]. A chest radiograph (CXR) is often requested to rule out bacterial coinfections, even in children without clinical signs suggestive of pneumonia on physical examination. Nevertheless, there is no evidence in the literature regarding the yield of CXRs in this latter group of patients.

The aims of this study were to determine the yield of CXRs in healthy patients with influenza-like illness, prolonged fever, and normal lung sounds for the diagnosis of bacterial coinfection and to analyze potential clinical factors that are predictive of pneumonia.

METHODS

A cross-sectional study was conducted in the ED of a tertiary level maternal and child hospital, with an average rate of 105,000 pediatric visits per year.

Patients older than 3 months for whom a CXR wase requested during the 6-week 2018 seasonal flu epidemic (January 1 - February 11) were identified from the hospital electronic medical records and their emergency department reports were reviewed. All healthy patients between 3 months and 18 years of age with influenza-like illness (based on clinical suspicion and/or microbiological confirmation) with a duration of fever of 4 days or longer and normal findings on respiratory auscultation were included. Patients with an abnormal pediatric assessment triangle, hypoxemia (hemoglobin saturation < 93% and FIO_2 21%), receiving antibiotic treatment at the time of consultation, and/or another source of fever requiring antibiotic therapy were excluded.

Definitions:

- Healthy patient: a patient without any of the following underlying conditions: hematology-oncology disease, immunocompromised status, heart disease, chronic pulmonary disease, neuromuscular disease, infantile cerebral palsy, encephalopathy, and/or metabolic disease.
- Influenza-like illness: presence of fever (axillary temperature ≥ 38°C) associated with signs or symptoms of acute respiratory infection (cough, rhinorrhea, headache, odynophagia, myalgia or arthralgia, general malaise, diarrhea, and/or vomiting)[4].
- Normal findings on respiratory auscultation: when good airflow is heard in the lungs bilaterally without adventitious sounds.

Data on the following variables were collected: age, sex, characteristics of fever, indication for and results of diagnostic influenza test, CXR results according to the attending pediatrician and radiologist, antibiotic prescription, and outcome.

Patients were seen interchangeably by pediatrics residents, family and community medicine residents, and assistant pediatricians. Patients initially evaluated by either first-year pediatrics residents or family and community medicine residents were subsequently evaluated together with the assistant pediatrician. The indication of a diagnostic influenza test (influenza A/B virus - RNA in nasopharyngeal aspirate) depended on the attending physician and was recommended in cases in which a positive result avoided the need for other complementary examinations. During the study period, CXRs performed in the ED were systematically reviewed by a radiologist between 24 and 72 hours after they were taken. For this study, CXRs reported by the radiologist as showing infiltrates compatible with bacterial coinfection (lobar infiltrates, alveolar infiltrates, pleuropneumonia, pleural effusion, etc.) were defined as abnormal.

The collected data were stored and processed in a Microsoft Access® relational database. Quantitative and categorical variables were tabulated. Data analysis was performed using the statistical program SPSS® v25.0 for Windows. Results of descriptive analysis are shown as counts (percentages) for categorical variables and median (interquartile range [IQR]) or mean (standard deviation [SD]) for quantitative variables. The Kolmogorov-Smirnov test was used to assess data distribution and the student's t and Mann-Whitney U tests for comparison of quantitative data. 95% confidence intervals for proportions were calculated using the Wilson method. A P value less than 0.05 was considered significant. The clinical variables analyzed as possible risk factors for an abnormal CXR were age, duration of fever, and maximum temperature.

The study was approved by the Research Ethics Committee of the Sant Joan de Déu Foundation (PIC-166-18). Informed consent was waived because of the epidemiological nature of the study and because an anonymized database was used.
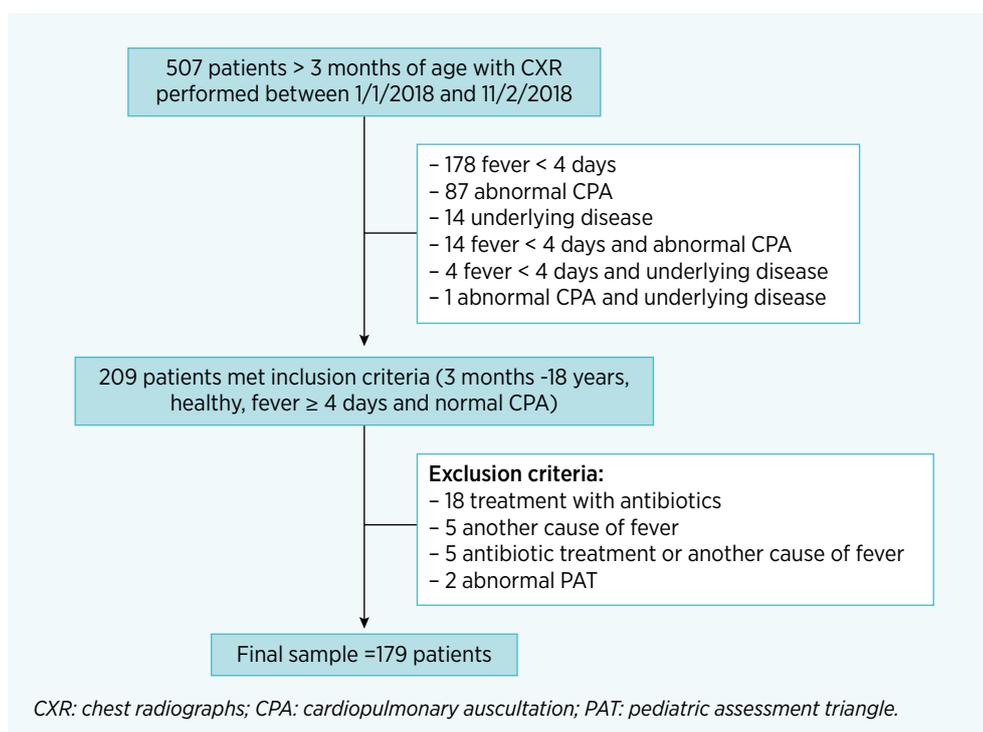
507 patients > 3 months of age with CXR performed between 1/1/2018 and 11/2/2018

– 178 fever < 4 days
– 87 abnormal CPA
– 14 underlying disease
– 14 fever < 4 days and abnormal CPA
– 4 fever < 4 days and underlying disease
– 1 abnormal CPA and underlying disease

209 patients met inclusion criteria (3 months -18 years, healthy, fever ≥ 4 days and normal CPA)

Exclusion criteria:
– 18 treatment with antibiotics
– 5 another cause of fever
– 5 antibiotic treatment or another cause of fever
– 2 abnormal PAT

Final sample =179 patients

CXR: chest radiographs; CPA: cardiopulmonary auscultation; PAT: pediatric assessment triangle.

FIGURE 1. Flowchart.

RESULTS

During the study period, a CXR was performed in the ED in 507 patients older than 3 months; 209 met the inclusion criteria. Thirty patients met one or more of the exclusion criteria, resulting in a final sample was 179 patients (Figure 1). The median age of the patients was 3.1 years (IQR, 1.6-4.8 years) and 95 (53.1%) were male. The median duration of fever was 5 days (IQR, 4-6 days) and the mean maximum temperature was 39.3ºC (SD 0.6ºC). A diagnostic influenza test was performed in 21 (11.7%) patients; 15 (71.4%) were positive.

In 58 (32.4%) patients the pediatrician considered the CXR suggestive of bacterial coinfection and prescribed antibiotics. On the other hand, the radiologist reported 35 CXRs as abnormal (diagnostic yield, 19.6%; 95%CI 14.4-26%). The interobserver agreement between pediatricians and radiologists in interpreting the CXRs was 83.3%; when compared to the reports of the radiologist, the pediatrician overdiagnosed pneumonia in 26 patients and underdiagnosed three. Two patients (1.1%) were admitted to hospital.

No significant differences were found between patients with abnormal CXRs and those with normal CXRs for any of the potential risk factors analyzed (Table 1). Among the patients who underwent a diagnostic influenza test, two of those who tested positive had an abnormal CXR (1/15; 6.7%) vs. one who tested negative (1/6; 16.7%) *(p= 0.5).*

DISCUSSION

To our knowledge, this is the first study to specifically analyze the prevalence of bacterial pneumonia in children with influenza-like illness, prolonged fever, and absence of clinical signs of the disease. Two studies analyzing the prev-alence of occult pneumonia in febrile pediatric patients show lower percentages than those found in our study, accounting for 5.3% and 11%, respectively[5,6]. These differences may be due to sample selection, since, although both studies included febrile children with normal lung sounds and absence of signs of respiratory distress, they did not define the duration of fever or require the presence of respiratory symptoms.

The clinical variables analyzed as potential risk factors did not show to be useful to predict pneumonia in our study. These results are similar to those found in the study by Shah et al.[6] in which age, maximum temperature, and duration of cough were not associated with pneumonia. Nevertheless, the authors did find a correlation with duration of fever, showing a prevalence of pneumonia of 15% in patients with fever for 24 hours or longer and 7% in those with a shorter duration of fever. Likewise, Murphy et al.[5] found a significant association in patients with fever lasting longer than 3 and 5 days. It should be noted that only patients who had fever for 4 days or longer were included in our study, which may explain why duration of fever did not prove to be helpful. Given the limited use of clinical factors, attempts have been made to identify other factors to aid in the diagnosis of pneumonia. An elevated leukocyte count has been associated with an increased risk of occult pneumonia in patients with fever without a focus, and CXR is recommended in cases with a leukocyte count of 20,000/mm^3 or greater[5-7]. On the other hand, several studies in children have evaluated the usefulness of new biomarkers to differentiate between viral and bacterial infection and to optimize its management with inconclusive results[8]. In the specific case of influenza-like illness, a study in adults suggests the usefulness of serum procalcitonin measurement as a discriminatory test for possible bacterial complications[9]. Blood tests would not be justified in most of our patients, as they are healthy, stable children with influenza-like illness as the source of fever. In

TABLE 1. Analysis of risk factors for an abnormal chest radiograph (n=179).

Variables	Normal CXR (n= 144)	Abnormal CXR (n= 35)	p
Age	3.1 years	3.2 years	0,955
Duration of fever	5 days	5 days	0,989
Maximum temperature	39.4ºC	39.5ºC	0,411

Variables are expressed as median. CXR: chest radiograph. For comparison the Mann-Whitney U test for independent samples was used.

addition, it would lead to a significantly longer length of stay in the emergency department at a time when pressure on care is already high. The use of rapid biomarker tests that allow the result to be available in a few minutes from a capillary blood sample could be a valid option[10,11]. Better selection of these patients would not only lead to a decrease in radiation exposure but also to a reduction of unnecessary antibiotic prescriptions due to errors in the interpretation of CXRs[12,13].

Among the limitations of this study are those inherent to its retrospective design; some information may have been lost, which could have influenced the sample selection. Secondly, the indication for CXR was at the discretion of the attending physician, and patients with the same clinical characteristics who did not undergo CXR were not analyzed, which may have led to an overestimation of the prevalence of pneumonia. Thirdly, due to the lack of a routine diagnostic influenza test in the entire sample we could not analyze whether a positive result was associated with an increased risk of bacterial pneumonia. Finally, the CXRs were read by different pediatricians and radiologists, which may have led to certain variability due to subjective interpretation.

Although pneumonia was diagnosed in one out of five patients in our study, we consider CXRs should not be systematically performed in healthy children with influenza-like illness and prolonged fever as the only symptom. Careful selection of patients at increased risk is important in order to avoid radiation and antibiotic overprescription, the latter of which may be the result of misinterpretation of the CXR. Given the lack of useful clinical factors to identify cases at an increased risk and as blood analysis is an invasive method, we believe point-of-care biomarker testing for a better selection of these patients should be analyzed.

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