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Study of Simple Predictors to Differentiate Acute Respiratory Tract Infections From Acute Asthma in Children Aged 6 Months to 5 Years

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ABSTRACT
In our study, 171 children in the age group of 6 months to 5 years with respiratory symptoms were included. The accuracy of presence of chest in drawing in the prediction of pneumonia is 90.7%, the accuracy of persistence of tachypnea following bronchodilator therapy in predicting pneumonia is 80% and that of presence of fever in predicting pneumonia is 75%.The combined presence of chest in drawing and persistent tachypnea in a child had an accuracy of 88.29% in clinically predicting pneumonia. The presence of fever along with persistent tachypnea was 80% accurate in the prediction of pneumonia. The presence of all the 3 symptoms i.e, fever along with chest indrawing and persistent tachypnea in a child had an excellent specificity of 9 5.4% and a highly significant accuracy of 90.7% in the clinical prediction of pneumonia. Reduction in tachypnea following the administration of a bronchodilator had a good negative predictive value of 83.6% in the prediction of presence of pulmonary infiltrates on the chest X-ray. After exclusion of asthmatics, the specificity of chest in drawing in the prediction of pulmonary infiltrates increased from 90-91.6%, specificity of tachypnea increased from 85.5-86.8% and the specificity of fever increased from 72.4-80%. The combined presence of fever, persistent tachypnea and chest in drawing showed an excellent specificity of 97.2% and a high positive predictive value of 97.4% in clinically diagnosing pneumonia.

INTRODUCTION

Acute respiratory infections constitute one of the leading causes of morbidity and mortality in children under the age of five in developing nations. An estimated 3.9 million children globally die from ARI each year, with most of them belonging to developing countries. Pneumonia is the inflammation and consolidation of lung tissue due to an infectious agent. This could be a result of infection by several microorganisms, including bacteria, fungus, viruses and parasites. Pneumonia can be particularly severe in developing nations[1,2]. Depending on the child's age and the etiological factor causing pneumonia, the symptoms can differ.

Some Typical Signs and Symptoms Include:

- Fever.
- Chills.
- Cough.
- Rapid breathing.
- Wheezing or grunting while breathing.
- Breathing difficulty causing retractions.
- Vomiting.
- Chest pain.
- Abdominal pain.
- Poor feeding or loss of appetite (in older children).
- Cyanosis in extreme cases.

In case of bacterial pneumonia, the patient typically gets sick very rapidly and exhibits sudden onset of high grade fever and unusually rapid breathing. Symptoms typically arise more gradually and are less severe when pneumonia is of viral etiology. Wheezing may occur more frequently in viral pneumonia. Bacterial infections constitute the primary cause of pneumonia in developing countries like India where infant mortality rates are high[3-5]. In Viral pneumonia, Viruses enter the respiratory system through the mobile respiratory droplets that are inhaled through the mouth and nose. Once within the lungs, the virus invades the cells lining the airways and alveoli. This invasion usually results in cell death, either by direct virus induced cytotoxicity or through a process of cell self-destruction referred to as apoptosis[6]. The response of the immune system to the infection results in further lung damage. White blood cells, primarily lymphocytes, activate chemical cytokines which result in fluid leakage into the alveoli. This cell destruction and fluid-filled alveoli interrupt the normal diffusion of oxygen into the blood across the alveolar capillary membrane. In addition to damaging the lungs, several viruses have an effect on different organs and therefore disrupt many body functions. Viruses may also make the body more vulnerable to other infections., bacterial pneumonia usually complicates viral pneumonia[7-9]. Viral pneumonia is often caused due to infection by respiratory syncytial virus (RSV), adenovirus and metapneumovirus. Herpes simplex virus rarely causes pneumonia except in newborns. Those with a compromised immune system are at an increased risk of pneumonia caused by Cytomegalovirus (CMV). In Bacterial pneumonia, Bacteria normally enter the lung through the inhalation of aerosolized droplets, but they can also spread through the bloodstream from an infection in other areas of the body. Numerous bacteria can easily enter the alveoli since they inhabit the upper respiratory tract's nasal, oral and sinus cavities. Once inside, these microbes may enter the alveoli and the gaps between cells through connecting pores. The immune system attracts neutrophils as an immunological consequence of this invasion[10-12]. The organisms are engulfed and destroyed by neutrophils, which also release cytokines, resulting in the stimulation of the immune system. This causes the fever, chills and fatigue that are typically seen in bacterial and fungal pneumonia. The alveoli are filled with bacteria, neutrophils and fluid exudating from the surrounding capillaries which impairs oxygenation[13-16]. Hence the current study aims to find the clinical predictors which can be used to differentiate between bronchial asthma and pneumonia in children between the ages of 6 months and 5 years. Accurate assessment of these clinical signs and symptoms can guide the clinicians in treatment of asthma by rapid administration of bronchodilator and also can prevent the unnecessary usage of antibiotics.

MATERIALS AND METHODS

Type of Study: Descriptive study.

Place of Study: Department of Pediatrics, Fathima Institute of Medical Sciences, Kadapa, A.P.

Study Population: Children in the age group of 6 months to 5 years admitted in Fathima Institute of Medical Sciences, Kadapa, A.P.

Inclusion Criteria: Children aged 6 months to 5 years who presented withrespiratory symptoms and whose parents or guardians have given consent for participation in the study.

Exclusion Criteria:

- Severe malnutrition.
- Foreign body inhalation.
- Unstable vitals.
- Children without consent from their parents or guardians.

Study Duration: 18 months.

Sample Size: 171.

Diagnostics: Before viewing the chest X-ray, a clinical diagnosis of pneumonia was made if even after three

nebulizations, the respiratory rate did not fall below the threshold for the respective age. The radiological diagnosis of pneumonia verified by two radiologists was taken as the gold standard. Agreement of two pediatric radiologists upon the evaluation of pulmonary infiltrates was necessary for evaluation of the disease in our study. According to WHO standards and definitions used for epidemiological studies, the radiologists only took into consideration three radiological patterns for evaluation: (1) normal, (2) the presence of pulmonary infiltrates (reduced pulmonary view), or (3) pulmonary hyperinflation without pulmonary infiltrate. They were not provided any clinical information of the subjects. Wheezing, the absence of pulmonary infiltrates on chest X-ray and quick improvement (reduction of respiratory rate below cutoff limit for each age) after bronchodilator medication were used to diagnose the presence of bronchospasm. If there was a reduction in respiratory rate along with the presence of pulmonary infiltrates on an X-ray, it was concluded that the subject had both bronchospasm and pneumonia concurrently.

RESULTS AND DISCUSSIONS

Table 1: Symptoms and History Analysis

Symptoms+History	No. of children (n)	Percentage (%)
Fever	66	47.2
Cough+cold	140	100
Fast breathing	140	100
Chest indrawing	55	39.2
Decreased feed intake	84	60
Lethargy	31	22.1
Running nose	34	24.2
Vomiting	28	20
Audible wheeze	21	15
Cyanosis	0	0
Family H/O allergy/asthma	32	22.8
Previous H/O nebulisations	43	30.7
Previous H/O respiratory Distress	140	100
One episode	90	64.2
More than two episodes	50	35.7

Table 2: Signs Elicited in the Children

Signs	No. of children (n)	Percentage (%)
Temperature >37.4°C	66	47.14
Under nutrition	84	60
Wheeze	112	80
Crepitating	129	92.14

140 children who had a previous similar episode of cough and fast breathing were subjected to bronchodilator challenge. The response in terms of reduction of tachypnea was then evaluated.

Table 3: Association Between Persistence of Tachypnoea After Bronchodilator Challenge and Pneumonia

Tachypnoea	X ray infiltrate		
	Yes	No	Total
Yes	35	13	48
No	15	77	92
Total	50	90	140

Sensitivity: 70%, Specificity: 85.5%, PPV: 72.9%, NPV : 83.6%.

Among 50 children who had radiological infiltrates 35 children had persistent tachypnoea after trial bronchodilator. In 15 children tachypnoea disappeared (Sensitivity: 70%). Out of 90 children who had no infiltrates on chest x ray 77 children showed resolution of tachypnoea after the administration of bronchodilator. But 13 children continued to have persistent tachypnoea despite normal chest x ray (Specificity: 85.5 %). Out of 48 children with persistent tachypnoea, 35 children had infiltrates on chest x ray. (PPV=72.9 %). Out of 92 children whose tachypnoea resolved following bronchodilator, 77 children had normal x ray. (NPV=83.6%). $p<0.05$. Overall accuracy of persistant tachypnoea after bronchodilator in predicting pneumonia is 80%.

Fever: Evaluating the importance of fever as a predictor in clinically diagnosing pneumonia against the gold standard of radiological infiltrate, 42 out of 66 children who had fever showed infiltrates on chest x ray. 11 children who did not have fever had infiltrate (Sensitivity: 79.2%). Out of 87 children who had normal x ray 63 did not have fever (Specificity: 72.4%). $p<0.05$. Overall accuracy of fever in predicting pneumonia is 75%. Chest indrawing and Pneumonia: Sensitivity : 92 % Specificity: 90%, PPV: 83.6%, NPV: 95.2%. 46 children who presented with chest indrawing showed x ray infiltrate (Sensitivity: 92%). Out of 90 children with normal chest x ray, 81 children had no chest indrawing (Specificity : 90%). Amongst 55 children who had chest indrawing, 46 had x ray infiltrates (PPV : 83.6%). Of the 85 children who did not have chest indrawing, 81 had a normal chest x ray (NPV : 95.2%). $p<0.05$. The overall accuracy of chest indrawing in predicting pneumonia is 90.7%.

Association Between Fever and Persistence of Tachypnoea and Pneumonia: 38 out of 49 children who had fever at presentation and showed no response of tachypnea to bronchodilator had infiltrates on chest x ray (PPV: 77.5%) while 17 children who had neither fever nor persistant tachypnoea following bronchodilator had infiltrate on chest x ray. On the other hand 11 out of 49 children who had both fever and persistant tachypnoea after bronchodilator showed no infiltrate. 74/85 children who were afebrile and in whom tachypnoea disappeared after bronchodilator had normal chest x ray. (Specificity: 87.05%). $p<0.05$. Accuracy of combined presence of both fever and persistent tachypnea in predicting pneumonia is 80%.

Association Between Fever and Pneumonia: Sensitivity of fever in predicting pneumonia is 77.5%. On excluding the population of children in whom the

cause of tachypnea was likely to be asthma the specificity of fever in predicting pneumonia had a significant increase from 72.4-80%. p<0.05.

Association Between Chest Indrawing and Pneumonia: 42/48 children, who had infiltration on chest x ray presented with chest indrawing. 33/36 who with a normal chest x ray had no chest indrawing. Specificity has increased from 90-91.6% after excluding probable asthmatics.(p<0.05).

Table 4: Sensitivity and Specificity

Association of pneumonia with the following	Sensitivity (%)		Specificity (%)	
	n1= 140	n2= 84	n1= 140	n2= 84
Persistent tachypnoea	70	71.7	85.5	86.8
Fever	80	77.5	72.4	80
Chest indrawing	92	87	90 91.6	
Fever+Persistent tachypnoea	69.09	79.5	87.05	90
Chest indrawing+ Persistent tachypnoea	80	80.4	91.1	94.7
Fever + Chest indrawing +Persistent tachypnoea	83.01	80.8	95.4	97.2

n1: Entire study population n2:excluding likely asthmatics

92 children who had resolution of tachypnea after administration of bronchodilator were advised follow up after two days, only 41 children came for follow up (44.5%). Of these 41 children 36 were normal while 5 children had another acute attack. They were treated with bronchodilator. 3 children who initially had fever with chest indrawing deteriorated further and hence were admitted.

In the current study, 140 children of age group of 6 months to 5 years who presented with acute cough and signs of respiratory distress with a previous history of similar episode were considered for analysis. These children underwent a trial of nebulisations under careful monitoring. The response of tachypnoea to nebulisations was then assessed. Good response to nebulisations was seen in 92/140 children. They had a resolution of tachypnea. 77 of them had a normal chest radiograph (NPV: 83.6%). Fever which was defined as a rise in temperature of >37.4°C, had a specificity of 72.4% in the prediction of pneumonia in our study. Chest indrawing had an excellent specificity of 90%. However the presence of all the three features i.e. fever along with chest indrawing and persistent tachypnoea has a very high specificity of 95.4% in the clinical prediction of pneumonia[17,18]. 56 children amongst the 120 had a history of more than two similar episodes and/or family H/O asthma and/or previous H/O nebulisations. In children who had a significant history, acute presentation with cough and features of respiratory distress could point towards asthma being the probable etiology. Excluding these 56 children the same analysis was done in the remaining 84 children. As expected, there was an increase in the specificities of fever, chest indrawing and persistent tachypnoea either alone or in combination after exclusion of asthmatics from the entire study population indicating that the clinical picture could have been due to pneumonia. In pneumonia (presence of infiltrates on cx ray) was diagnosed only in 53/140 children (37.8%) which signifies the necessity of considering asthma as the reason for respiratory distress[19]. There are similar studies which also found the prevalence of pneumonia being low in children presenting with cough and tachypnea. Study conducted by A.V Castro *et al* in Brazil found that radiologically confirmed pneumonia was found in only 15.8% of the children who presented with complaints of rapid breathing and cough. Also in another study conducted in New Delhi by H.P.S. Sachdev[20,21] x ray infiltrates were seen only in 10% children with similar complaints. in similar children. Presence of fever at the onset, has a good specificity in the clinical prediction of pneumonia. In our study, the presence of chest indrawing and pneumonia have a significant association, with a very high specificity of 90%. This does not match with the findings of study conducted in Brazil by A.V. Castro[22] where the feature of chest indrawing had a poor correlation with pneumonia. The presence of fever in combination persistent tachypnea and chest indrawing has a significant association with the radiologically confirmed pneumonia with a highest specificity of 95.4%. On excluding 56 subjects who either had previous H/O nebulisations and/or family H/O asthma and/or more than two episodes suggestive of asthma, the specificity of fever, chest indrawing and persistent tachypnoea either alone or in combination increased in the prediction and diagnosis of pneumonia. This is in accordance with the observations of the study conducted by H.P.S Sachdev 1994 which concluded that the most reliable predictors of asthma were two or more earlier similar episodes (sensitivity 84%, specificity84%) followed by temperature <37.6°C (sensitivity 73% and specificity 84%). Absence of fever and an audible wheeze with a family history of asthma had excellent specificities (98-100%). The combined presence of fever, persistent tachypnea and chest indrawing showed an specificity of 97.2% and a positive predictive value of 97.4% in clinically diagnosing pneumonia.

CONCLUSION

It is concluded that these combination of persistent tachypnea, presence of fever, chest indrawing as a clinical predictors can differentiate acute respiratory tract infections from acute asthma in children aged 6 months to 5 years.

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