FACTORS ASSOCIATED WITH DIAGNOSIS OF BACTERIAL PNEUMONIA IN CHILDREN OF NORTHERN THAILAND

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Abstract. The purpose of this study was to determine the association between common clinical features in general practice, and chest radiographic findings among children with suspected bacterial or viral pneumonia. The study was prospective hospital-based carried out in Northern Thailand, from 2000 to 2001. One thousand three hundred ninety-six children under age five years admitted with suspected pneumonia were enrolled in the study. Multinomial logistic regression was used to analyze the radiographic results, clinical outcomes, white blood cell (WBC) counts, percent poly-morphonuclear cells (%PMN), duration of illness before admission, body temperature, age, and gender as variables. Chest radiographs were read by a radiologist following the recommendations of the WHO regarding chest radiographic reading. Chest radiographic findings were classified as normal, viral or bacterial. Fifty-nine children (4.2%) had normal radiographic findings, 1,233 (88.3%) had a viral appearance on chest radiograph, and 104 (7.5%) had a bacterial appearance of chest radiograph. On unadjusted analysis, WBC count, %PMN, body temperature, duration of illness before admission, and gender were strongly associated with outcomes ($p<0.05$). On multivariate analysis, only %PMN, duration of illness before admission, and gender were associated with the findings of the chest radiograph. A PMN results of 40% to 70% [RRR, 5.64; 95% confidence interval (CI), 2.14-14.82], PMN >70% (RRR, 5.11; 95% CI=1.71-15.22), and duration of illness >4 days (RRR, 5.19; 95% CI=1.79-15.06) were positively associated with bacterial radiographic profile. Female (RRR, 0.50; 95% CI=0.29-0.85) was negatively associated with viral radiographic profile. WBC counts in children admitted with suspected pneumonia were not associated with chest radiograph findings, but %PMN and duration of illness before admission were positively associated with a bacterial radiographic result.

INTRODUCTION

Pneumonia is a major cause of death in children globally. Twenty-one percent of deaths in children younger than 5 years of age are caused by pneumonia (Black *et al*, 2003). Early diagnosis and prompt treatment of pneumonias with antibiotics are needed to reduce the mortality rate. However, overuse of antibiotics without proper indications results in increasing antimicrobial resistant strains of bacteria and results in a higher cost of the treatment. In general, clinical practice in many countries, besides evaluating the clinical signs and symptoms of the patient, chest radiographs and complete blood count

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(CBC) specifically the total WBC count and %PMN are obtained to differentiate between bacterial and viral causes of pneumonia. Chest radiography is the most sensitive method for detecting pneumonia. However, interpretation of chest radiography varys by reader and technique; in many situations a radiograph is not available. Therefore, in a setting without a radiograph, WBC count, %PMN, body temperature, duration of illness, age, and gender, may help in making the diagnosis. However, the relationship between radiographic findings and such variables is still unclear. To determine this relationship we analyzed data from a prospective population-based study of hospitalized children with suspected pneumonia in two provinces of northern Thailand from 1 May 2000 to 30 April 2001 (Rerks-Ngarm *et al*, 2004).

MATERIALS AND METHODS

Study population

One thousand three hundred ninety-six children under age 5 with suspected pneumonia were enrolled in the study. The children were admitted to provincial and community hospitals in two provinces, Lampang and Phitsanulok Provinces, northern Thailand. A chest radiograph and CBC were performed on enrollment. The children were enrolled if they were permanently living in the two provinces, admitted with suspected pneumonia diagnosed by a physician, and the parents or guardians agreed to sign a consent form to be enrolled in the study. Exclusion criteria were anyone whose parents or guardian did not sign the consent form.

Interview and physical examination

A history and physical examination were carried out on admission by either a physician or a nurse under supervision of a physician. Heparinized venous blood was obtained for CBC, and a chest radiograph was performed. Duration of illness in days was defined as from the onset of symptoms until admission. Age was the age on admission. Body temperature in centigrade was taken orally, rectally or in the axilla. The axillary temperature was adjusted by adding 0.5ºC to the measured temperature.

A routine CBC was performed by the admitting hospitals. WBC and %PMN were carried out using automated analyzers. If abnormal results were found, a repeat test was carried out using an automated analyzer and/or by blood smear. WBC count was reported as per milliliter (ml).

Chest radiograph

Chest radiographs were taken by technicians at the admitting hospitals. A postero-anterior view was obtained using a green sensitive bucky and an 8”x10” or 10”x12” film size was used. The films were read without clinical data provided by a radiologist at Chiang Mai University (in northern Thailand) following World Health Organization (WHO) criteria, including primary endpoint (lobar or alveolar infiltrate > 2.5 cm diameter), pleural infiltration, and other infiltration. Primary endpoint and pleural infiltration were classified as having a bacterial cause, other infiltrations as having a viral cause, a combination of both as having bacterial cause, and no infiltration as normal radiographs (Cherian *et al*, 2005). The radiologist completed a WHO radiography interpretation training course prior to the study.

Statistical methods

Statistical analysis was performed using Stata Release 8.0 (Stata Corporation, 2000). Categorical variables were compared using a Pearson chi-square test. Continuous variables, including WBC counts (cells/ml), %PMN, body temperature (ºC), duration of illness (days), and age (months) were divided into 3 groups using cut-off levels of

25 and 75 percentile. Clinical consideration for each variable was also taken into account. The diagnoses were defined as normal, viral, and bacterial chest radiographs. Simple and multivariate multinomial logistic regression analyses were performed to determine the predictors of radiographic profiles. All covariates were transformed to indicator variables. On multivariate regression analysis, covariates included in the regression model were WBC count, %PMN, body temperature, duration of illness, age, and gender. All covariates were kept in the final model, even though none of these variables were significantly different, because we wanted to estimate the degree of association between them and the outcome. All statistical tests were 2-sided. Statistical significantce was defined as $p < 0.05$.

Ethical clearance

This study was reviewed and approved by the ethics committee of the Ministry of Public Health, Thailand.

RESULTS

Patients

One thousand three hundred ninety-six children with suspected pneumonia met the inclusion criteria for enrollment. Of these, 56.7% were boys. The ages ranged from neonate (zero months) to 59.9 months (mean 23.8 months); 27.1% were <13 months old, 50.1% were 13 to 36 months old, and 22.8% were 37 to 59 months old. The duration of illness prior to admission ranged from the day of admission to 36 days before admission (median 2 days). Twenty-six percent had a duration of illness before admission shorter than 2 days, 52.7% had illness from 2 to 4 days, and 21.3% had an illness longer than 4 days. Their body temperature ranged from 35.9 to 42.3ºC (mean 38.5ºC). Thirty-three point five percent had a temperature <38ºC, 39.5% had a temperature 38 to 39ºC, and 27.0% had a temperature >39ºC. The WBC count ranged from 1,400/ml to 90,000/ml (mean 13,292/ml). The % PMN ranged from 6% to 96% (mean 54.1%).

Chest radiography

Fifty-nine subjects (4.2%) had a normal chest radiograph, 1,233 subjects (88.3%) a chest radiograph consistent with a viral infection and 104 cases (7.5%) had a chest radiograph consistent with bacterial infection.

Comparative clinical and chest radiographic profiles

The demographic and clinical characteristics of the patients by chest radiographic profiles are shown in Table 1. The WBC count and %PMN were significantly greater in patients with a chest radiograph consistent with bacterial infection. Almost half (44.2%) of patients having a WBC count >16,000/ml had a chest radiograph consistent with bacterial infection. About one-third of patient (34.6%) having %PMN >70% had a chest radiograph consistent with bacterial infection. Boys had more abnormal chest radiographs than girls (59.3% of boys *vs* 40.7% of girls). A chest radiograph consistent with viral infection was more common in boys than girls (57.9% of boys *vs* 42.1% of girls). The distribution of abnormal chest radiographs did not differ by age group. Duration of illness prior to admission was significantly longer in patients with a chest radiograph consistent with bacterial infection.

The duration of illness before admission was >4 days in 32.7% in those with a chest radiograph consistent with bacterial infection, 20.8% in those with a chest radiograph consistent with viral infection and 11.9% in those with a normal radiograph. Body temperature in patients with a chest radiograph consistent with bacterial infection was significantly higher than the other two groups. The proportion of patients with a body temperature >39ºC was 42.3% in

Table 1
Baseline characteristics.

	Chest radiography pattern in percent			Total	*p*-value
	Normal (*n*=59)	Viral (*n*=1,233)	Bacterial (*n*=104)	(*N*=1,396)	
Demographics					
Gender					0.016
Boy	40.7	57.9	51.1	56.7	
Age (months)					0.285
<13	25.4	27.2	26.9	27.1	
13-36	44.1	50.9	44.2	50.1	
37-59	30.5	21.9	28.9	22.8	
Clinical data					
Duration of illness[a] (days)					0.017
0-1	28.8	26.4	19.2	26.0	
2-4	59.3	52.8	48.1	52.7	
>4	11.9	20.8	32.7	21.3	
Body temperature (ºC)					0.009
<38	33.9	34.1	26.0	33.5	
38-39	42.4	40.0	31.7	39.5	
>39	23.7	25.9	42.3	27.0	
WBC count					0.000
<9,001	33.9	27.3	22.1	27.2	
9,001-16,000	42.4	48.7	33.7	47.3	
>16,000	23.7	24.1	44.2	25.6	
%PMN[b]					0.000
<40	30.5	24.7	8.7	23.7	
40-70	42.4	54.5	56.7	54.2	
>70	27.1	20.8	34.6	22.1	

[a]Duration of illness before admission
[b]Polymorphonuclear cell

those with a chest radiograph consistent with bacterial infection compared to 25.9% in those with a chest radiograph consistent with a viral infection and 23.7% in those with a normal radiograph.

Table 2 shows the unadjusted and adjusted relative risk ratios (RRRs) obtained from multinomial logistic regression analysis stratified by chest radiography patterns. For unadjusted analysis, all covariates except age, were associated with specific radiography patterns. For those with a chest radiograph consistent with bacterial infection, WBC count>16,000/ml (crude RRR, 2.86; 95% CI=1.23-6.66), PMN 40% to 70% (crude RRR, 4.72; 95% CI=1.87-11.93), PMN >70% (crude RRR, 4.50; 95% CI=1.67-12.15), body temperature >39ºC (crude RRR, 2.33; 95% CI= 1.01-5.36), and duration of illness before admission >4 days had the strongest unadjusted association. For those with a chest radiograph consistent with viral infection, female (crude RRR, 0.50; 95% CI=0.29-0.85) had the strongest unadjusted association. After adjusted analysis, only %PMN, duration of illness before admission, and gender were significantly associated with chest radiography patterns. For children with a chest

Table 2
Crude and Adjusted Relative Risk Ratios (RRRs) obtained from multinomial logistic regression analysis (*N*=1,396).

	Crude						Adjusted					
	Viral (*n*=1,233)			Bacterial (*n*=104)			Viral (*n*=1,233)			Bacterial (*n*=104)		
	RRR[a]	95%CI[b]	*p*-value	RRR[a]	95%CI[b]	*p*-value	RRR[a]	95%CI[b]	*p*-value	RRR[a]	95%CI[b]	*p*-value
Demographics												
Gender												
Boy	reference			reference			reference			reference		
Girl	0.50	0.29-0.85	0.010	0.66	0.35-1.26	0.207	0.50	0.29-0.85	0.011	0.64	0.33-1.24	0.187
Age (months)												
<13	1.49	0.74-3.01	0.268	1.12	0.48-2.64	0.796	1.40	0.65-3.02	0.391	1.31	0.51-3.34	0.577
13-36	1.61	0.87-2.99	0.131	1.06	0.50-2.26	0.877	1.55	0.82-2.94	0.178	1.10	0.50-2.42	0.812
37-59	reference			reference			reference			reference		
Clinical data												
Duration of illness (days)												
0-1	reference			reference			reference			reference		
2-4	0.97	0.54-1.76	0.920	1.21	0.56-2.64	0.625	1.01	0.55-1.86	0.985	1.42	0.64-3.16	0.385
>4	1.91	0.78-4.67	0.158	4.13	1.46-11.67	0.007	1.97	0.79-4.92	0.147	5.19	1.79-15.06	0.002
Body temperature (ºC)												
<38	reference			reference			reference			reference		
38-39	0.94	0.51-1.71	0.832	0.98	0.45-2.13	0.955	0.93	0.50-1.72	0.817	0.89	0.40-1.95	0.763
>39	1.08	0.54-2.18	0.824	2.33	1.01-5.36	0.047	1.06	0.52-2.16	0.880	1.74	0.74-4.10	0.207
WBC count												
<9,001	reference			reference			reference			reference		
9,001-16,000	1.43	0.78-2.61	0.246	1.22	0.55-2.68	0.625	1.32	0.71-2.46	0.387	1.01	0.45-2.29	0.979
>16,000	1.26	0.63-2.54	0.514	2.86	1.23-6.66	0.015	1.16	0.55-2.43	0.696	2.14	0.87-5.27	0.096
%PMN												
<40	reference			reference			reference			reference		
40-70	1.59	0.86-2.96	0.142	4.72	1.87-11.93	0.001	1.83	0.95-3.52	0.071	5.64	2.14-14.82	0.000
>70	0.95	0.48-1.90	0.887	4.50	1.67-12.15	0.003	1.16	0.53-2.52	0.713	5.11	1.71-15.22	0.003

[a]Relative Risk Ratio using normal chest radiographic profile as the comparison group (n=59)
[b]Confidence interval
[c]Polymorphonuclear cell
[d]Adjusted for all variables, including gender, age, duration of illness, body temperature, WBC count, and %PMN

radiograph consistent with bacterial infection, PMN 40% to 70% (adjusted RRR, 5.64, 95% CI=2.14-14.82), PMN >70% (adjusted RRR, 5.11, 95% CI=1.71-15.22), and duration of illness before admission >4 days had the strongest adjusted associations. For those with a chest radiograph consistent with viral infection, female (adjusted RRR, 0.50, 95% CI=0.29-0.85) had the strongest adjusted association.

DISCUSSION

In this study, after controlling for other factors, WBC count was not related to chest radiography patterns, but %PMN and duration of illness before admission were strongly associated with a chest radiograph consistent with bacteria infection. Gender was significantly associated with a chest radiograph consistent with viral infection. The %PMN greater than or equal to 40% and a duration of illness before admission longer than 4 days were positively associated with a chest radiograph consistent with bacterial infection, while female sex was negatively associated with a chest radiograph consistent with viral infection.

The finding of the lack of association between the WBC count and the findings on chest radiography in consistent with a previous study (Virkki *et al*, 2002). The samples were drawn from patients treated at the Department of Pediatrics, Turku University Hospital, Findland. Viral and bacterial pneumonias were differentiated by a combination of radiographic and laboratory findings. The WBC count was not significantly associated with a specific diagnosis of or viral infection.

In one study the WBC count was associated with chest radiographic findings. (Melbye *et al*, 1988). However, this study was done in patients > 15 years old, in Norway; The details of the statistical results were not shown, therefore, this may reflect an unadjusted association. The results from the present study also showed an unadjusted association between WBC count >16,000/ml and bacterial chest radiographic consistent with bacterial infection (p=0.015). Vieira *et al* (2003) studied lower respiratory tract infection due to respiratory viruses in the neonatal period on admission to the neonatal intensive care unit and compared them with the clinical, laboratory and radiological evaluations of the patient. They found a correlation between viral infection and low initial and subsequent white blood cell counts.

The WBC counts seem to depend on the day of illness, as seen in a study investigating the effect of duration of illness on WBC count and total neutrophil counts in untreated children with clinical and radiographic findings consistent with bacterial pneumonia (Triga *et al*, 1998). In children with presumed bacterial pneumonia the number of the WBC count was greater during the first 2 days of illness. Thereafter, the WBC count declined, reaching the lowest levels on the fourth day.

Previous studies regarding PMN and pneumonia were similar to the present study. Ponka and Sarna (1993) studied the hospital records of patients with viral, mycoplasma and bacteremic pneumococcal pneumonia regarding the diagnosis and its association with the information obtained on admission from patient history, physical examination, simple laboratory tests and chest radiography. They found the neutrophil band count was one of the best discriminating variables. Another study in children found the absolute number of neutrophils was significantly higher in pneumococcal pneumonia than in viral pneumonia (Korppi *et al*, 1997).

One reason for the longer duration of illness in patients with chest radiographs consistent with bacterial infection is the in-

fection may be a super-imposed infection on an underlying viral infection, such as that found in measles patients. Loukides *et al* (1999) found 26% of adult measles patients had bacterial pneumonia on admission, during hospitalization or after discharge.

Males had a greater percentage of viral (and probably bacterial) pneumonia cases in this study which is consistent with a previous study (Jensen-Fangel *et al*, 2004) which found in young children, boys were hospitalized with pneumonia more often than girls, however, the reverse applied in patients 15-25 years old. The authors hypothesized gender plays a role in susceptibility to respiratory infections in early childhood.

In conclusion, after adjusting for other factors, we found no association between WBC counts and chest radiographs findings in hospitalized children with suspected pneumonia. %PMN and duration of illness prior to admission were strongly associated with a chest radiograph consistent with bacterial pneumonia. These findings along with other clinical data may be applied to elucidate the etiology of infection in cases of pneumonia, especially in developing countries or resource limited settings.

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