ORIGINAL ARTICLE

ASSOCIATION OF HAEMATOLOGICAL AND RADIOLOGICAL FINDINGS WITH CLINICAL OUTCOME IN HOSPITALIZED CHILDREN 2–36 MONTHS OLD WITH SEVERE LOWER RESPIRATORY TRACT INFECTION

Rehmana Waris, Yasir Bin Nisar*, Naseera Bhatti

Paediatric Medicine, The Children Hospital, Pakistan Institute of Medical Sciences, Islamabad-Pakistan, *Sydney School of Public Health, The University of Sydney, NSW-Australia

Background: Despite reduction in child mortality during last decade, lower respiratory tract infection (LRTI) remained number one killer of under-five. The current study aimed to assess the association of haematological and radiological findings with clinical outcome in hospitalized children 2-36 months old with severe LRTI. **Methods:** In the current cross sectional study, 581 children 2-36 months old with severe LRTI were enrolled and followed at the Children Hospital, Islamabad, between 2011 and 2014. At the time of enrolment, complete history of present illness, anthropometric measurements, blood sample and chest radiograph were obtained. The primary outcome was either early clinical response (within 72 hours) or delayed clinical response (>72 hours). Multivariable logistic regression was performed to examine the association between haematological and radiological findings with clinical outcome, adjusted for potential confounding factors. **Results:** Of 581 enrolled children, 292 (50.3%) children had early, and 289 (49.7%) had delayed clinical response. The multivariable logistic regression showed that leucocytosis (OR 1.79, 95% CI 1.15–2.79), neutrophilia (OR 1.91, 95% CI 1.29–2.84), radiological interstitial pneumonia (OR 2.49, 95%CI 1.70–3.64), and lobar consolidation (OR 6.00, 95%CI 2.41–14.96) were significantly associated with delayed clinical response, after adjusted for potential confounding factors. **Conclusions:** Delayed clinical response was significantly associated with abnormal haematological and radiological findings at the time of admission in children 2-36 months old with severe LRTI. Haematological and radiological findings at the time of presentation are useful for predicting delayed clinical response in children 2-36 months old with severe LRTI.

Keywords: Lower respiratory tract infection, clinical response, radiological findings, haematological findings, Clinical severity score system

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INTRODUCTION

Each year, 7.6 million children died in the first 5 years of their life.[1] Of 7.6 million deaths of children younger than 5 years, 4.879 million (64%) children died of infectious causes.[1] Among infectious disorders, respiratory tract infection, diarrhoea, and malaria were the leading causes of death worldwide of all deaths in children younger than 5 years.[1] Despite large reductions in child mortality between 2000 and 2010, lower respiratory tract infection remained number one killer of children younger than 5 years, caused 1.396 million deaths per annum.[1] Respiratory tract infections and acute diarrhoea are the most frequent childhood illnesses and causes of attendance at health facilities in low- and middle-income countries. Lower respiratory tract infection (LRTI) or pneumonia and severe diarrhoea are the most common reasons of hospital admission in children in low-and middle-income countries.[2] Incidence of, and mortality from, LRTI varies by age and region. The burden of disease is mainly in younger age groups; 81% of deaths from LRTI happen in children younger than 2 years.[2]

The diagnosis of LRTI is suggested by the presence of non-specific clinical features, such as cough, fever, and fast breathing, with or without auscultatory findings. Clinical setting where radiological studies are available, the disease is confirmed by chest radiography.[3] At the same time, the current clinical practice is still frequently based on the peripheral leukocyte count in evaluating patients presenting with respiratory symptoms. However, often, a finding of leucocytosis prompts a physician to obtain a chest radiograph, while a normal leukocyte count supports a less extensive investigation, often omitting chest radiography, and even starting inappropriate treatment.[4]

Most of the radiological studies in LRTI have focused on epidemiologic, diagnostic and etiological perspectives. The evaluation of clinical outcome measures (time to improvement of symptoms) has been infrequently taken into account in comparison with underlying type of radiological abnormalities.[5–7] Moreover, little is known about the link between key radiological attributes to clinical improvement in children with LRTI in resource constrained settings.[5,8] The current study aimed to assess the role of haematological and radiological findings at the time of admission on the clinical response in hospitalized children 2–36 months of age with severe LRTI.

MATERIAL AND METHODS

The current prospective cross-sectional study was conducted at the Children Hospital, Pakistan Institute of Medical Sciences, Islamabad Pakistan. All children with LRTI admitted to the Children Hospital were screened for enrolment based on the clinical score system[9], and followed up till they were improved and discharged from the hospital. The severity of illness was categorized according to clinical score system, as follows[9]: (i) Respiratory rate: 0 points, <30 breaths/min; 1 point, 31–45 breaths/min; 2 points, 46–60 breaths/min; 3 points, >60 breaths/min. (ii) Wheezing: 0 points, none; 1 point, terminal expiratory or heard only with a stethoscope; 2 points, entire expiration or audible on expiration without a stethoscope; 3 points, inspiration and expiration without a stethoscope. (iii) Retractions: 0 points, none; 1 point, intercostal only; 2 points, tracheosternal; 3 points, severe with nasal flaring. (iv) General condition: 0 points, normal; 3 points, irritable, lethargic, poor feeding. Based on clinical severity score, the disease severity can be divided into the following ranks: 0–4.9 points, mild; 5–8.9 points, moderate; and 9–12 points, severe disease.[9] Children age 2–36 months with LRTI and who had clinical severity score between 9 and 12 (severe illness) were enrolled in the current study. Children with LRTI and who also had congenital heart disease, cerebral palsy, chromosomal defects such as Down's syndrome, Edward's syndrome, spinal muscular atrophy or storage disorder were not enrolled in the current study. The data collection was conducted between October 2011 and March 2014.

Informed verbal consent was obtained from parents/caregivers of children. Before the commencement of the study, ethics approval was obtained from the Hospital Ethics Committee, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

Clinical severity score was assessed for each child. Respiratory rate was counted twice for 1 minute each within 5 minutes when the child was quiet, feeding or asleep. We used the average value of the two readings. If the difference between the two readings was ≥5 breaths per minute, we took a third reading. The average of the two readings with a difference of <5 breaths per minute was selected. Both audible and auscultatory wheeze and the general condition of each child were assessed. Based on these findings, clinical severity score for each child was calculated. All these children were given inhaled salbutamol and reassessed after up to three cycles of bronchodilator therapy, repeated (if necessary) at 20 minute interval[10] and often a shot of steroids. Clinical severity score was again calculated and a child whose score was decreased from severe disease (clinical severity score of 9–12) to moderate disease (clinical severity score of 5–8.99) was discharged on oral antibiotics and salbutamol. All those children, whose clinical severity score remained between 9 and 12, were admitted in the wards of the Children Hospital and were enrolled in the current study.

At the time of enrolment, information regarding the demographic features and complete history of current illness were asked and reported. Actual temperature was measured at the time of enrolment and anthropometry measurements using the standard technique were collected from each of the enrolled child. Children <2 years of age were weighed with minimum clothing on a digital baby scale, with a 16 kg capacity and a sensitivity of 10 grams and their lengths were measured in decubitus dorsal on a flat surface with an anthropometric rule scaled in centimetres up to a maximum of 1 millimetre. Children aged ≥2 years were weighed with a minimum of clothing on an adult scale accurate to 100 grams. Height was measured with children standing upright against a vertical rule with a metric scale, reading up to 150 centimetres, marked off in centimetres and fixed to the wall.[11] The nutritional status of the enrolled children was assessed by means of z-scores for weight/age, stature/age and weight/stature, taking as reference standard the percentile curves published by the NCHS (National Centre for Health Statistics). Nutritional status was classified in accordance with World Health Organization criteria as stunting (<-2 height-for-age z-score), wasting (<-2 weight-for-height z-score) and underweight (<-2 weight for-age z-score).[12]

A blood sample was obtained for full blood count and sent to the Pathology Department for analysis. Chest radiograph was performed on each enrolled child and a senior radiologist studied all the radiographs without knowing the clinical symptoms. The three mutually exclusive radiographic categories were defined as follows: (a) unequivocal focal or segmental consolidation with or without pleural effusion; (b) interstitial pneumonia with diffuse broncho-vascular markings with or without hilar lymphadenopathy; and (c) normal chest radiographs. All children were then managed according to the hospital's standard protocols. Briefly, all the enrolled children were kept nil by mouth and intravenous rehydration was given. Oxygen inhalation was given via nasal prongs. Inhaled salbutamol was given at 6–8 hourly intervals. All the enrolled children were given first line injectable antibiotics - Ampicillin and Amikacin at 8–12 hourly intervals. All children were followed up at 12 hourly intervals till the time of discharge. At each follow up clinical severity score was performed and noted. Discharge from hospital with oral medication, if required, was decided when clinical severity scores was reduced to <9 (moderate to mild disease).

Based on complete blood picture at the time of enrolment, a child was classified to have leucocytosis if

the total leukocyte count was >17500/mm^3, neutrophilia if absolute neutrophil count was >8500/mm^3, and lymphocytosis if absolute lymphocyte count was >13500/mm^3. The anaemic condition of each child was classified based on the World Health Organization guidelines, as no anaemia if serum haemoglobin concentration was ≥11 g/dl, mild anaemia if serum haemoglobin concentration was 10–10.9 g/dl, moderate anaemia if serum haemoglobin concentration was 7–9.9 g/dl and severe anaemia if serum haemoglobin concentration was <7 mg/dl[13].

The outcome measure was clinical response to the standard management of children 2-36 months of age with severe LRTI. The clinical response was based on clinical severity score. A child had early clinical response if his/her clinical severity score was <9 (moderate or mild disease) within 72 hours after the initiation of treatment, while a child had delayed clinical response if his/her clinical score remained between 9 and 12 after 72 hours of treatment. Children with early clinical response were discharged on oral medication, while children with delayed clinical response were further managed with second line antibiotics.

Using a standard formula for single proportion[14], and assuming 10% prevalence of children age 2-36 months with severe LRTI admitted at the Children Hospital (based on annual hospital admission data), absolute precision of 2.5%, and with 95% confidence level, the required sample size was 555 children age 2–36 months with severe LRTI admitted at the Children Hospital.

Data was entered using Microsoft Excel and analysis was conducted using STATA 13.1 (Stata-Corp, College Station, TX, USA) softwares. Descriptive analysis was performed to calculate the frequencies and percentages for categorical variables and mean (±Standard deviation) with median (interquartile range) for continuous variables. To assess the association of haematological and radiological findings with clinical outcome, logistic regression analysis was done, first univariate and later multivariable analysis was performed to evaluate independent effect of haematological and radiological findings on clinical outcome. Three separate logistic regression models were constructed by using a backward elimination process. In the first logistic regression model, radiological findings were assessed for clinical outcome and the model was adjusted for potential confounding factors including child's age, sex, and nutritional status, duration of illness, actual temperature and respiratory rate at the time of admission. In the second logistic regression model, haematological findings were assessed for clinical outcome and the model was adjusted for potential confounding factors. In the third logistic regression model, both haematological and radiological findings were assessed together for clinical outcome and the model was adjusted for potential confounding factors. The results were presented as odds ratio (OR), 95% confidence interval (95% CI) and p-value. The significant level was considered at 5%.

RESULTS

In total 11,713 children presenting with respiratory tract infections at the Children Hospital during the study period. Of these, 888 (7.6%) children were diagnosed to have LRTI and were admitted. Out of 888 admitted children with LRTI, 581 (65.4%) children had severe LRTI and were enrolled in the current study. Of 581 enrolled children, 292 (50.3%) children had early clinical response and 289 (49.7%) had delayed clinical response (Figure-1).

Table-1 presents the comparison of baseline characteristics of children 2–36 months old with severe LRTI between early and delayed clinical improvement. No statistically significant difference was observed in terms of age, age categories, gender, history of fever, cough, difficult breathing, fits, presence of wheeze, lethargic on examination, weight for height z-score and respiratory rate at the time of admission between children who had early clinical response and those who showed delayed clinical response. The statistically significant differences were observed regarding history of poor feeding, vomiting, mean duration of current illness, actual temperature at the time of admission, mean weight for z-score, height for age z-score, proportion of children with underweight and stunting between children who had early clinical response and those who had delayed clinical response.

Table-2 presents the comparison of haematological and radiological findings and duration of clinical improvement in children 2–36 months old with severe LRTI between those who had early clinical response and those who had delayed clinical response. No statistically significant differences were seen in mean leukocyte count, mean absolute neutrophil count, mean absolute lymphocyte count, mean serum haemoglobin concentration, proportion of children with lymphocytosis, and anaemia between children who had early clinical response than those who had delayed clinical response. The statistically significant differences were seen in terms of proportion of children with leucocytosis, neutrophilia, abnormal radiological findings, mean duration of improvement in temperature, respiratory rate, and feeding status, and the mean duration of hospital stay between children

who had early response and those who had delayed response.

Table-3 shows the univariate and multivariate logistic regression analyses of haematological and radiological findings with clinical improvement in children 2–36 months old with severe LRTI. The model 1 showed that children who had radiological interstitial pneumonia (OR 2.69, 95% CI 1.84–3.91), and those who had lobar consolidation (OR 6.03, 95% CI 2.43–14.96) at admission had higher odds of delayed response compared to children with normal chest radiography after adjusted for age, gender, nutritional status, duration of illness, actual temperature and respiratory rate at the time of admission. The model 2 showed that children who had leucocytosis (OR 1.79, 95% CI 1.15–2.79), and neutrophilia (OR 1.91, 95% CI 1.29–2.84), had higher odds of delayed response than children who did not have these haematological findings at the time of admission after adjusted for age, gender, nutritional status, duration of illness, actual temperature and respiratory rate at the time of admission.

The final model (model 3), which assessed the haematological and radiological findings together, showed that children who had radiological interstitial pneumonia (OR 2.49, 95% CI 1.70–3.64), and those who had lobar consolidation (OR 6.00, 95% CI 2.41–14.96), had higher odds of delayed response compared to children with normal chest radiography after adjusted for age, gender, nutritional status, duration of illness, actual temperature and respiratory rate at the time of admission. Further, no statistically significant association for haematological findings with clinical improvement was observed in the final model.

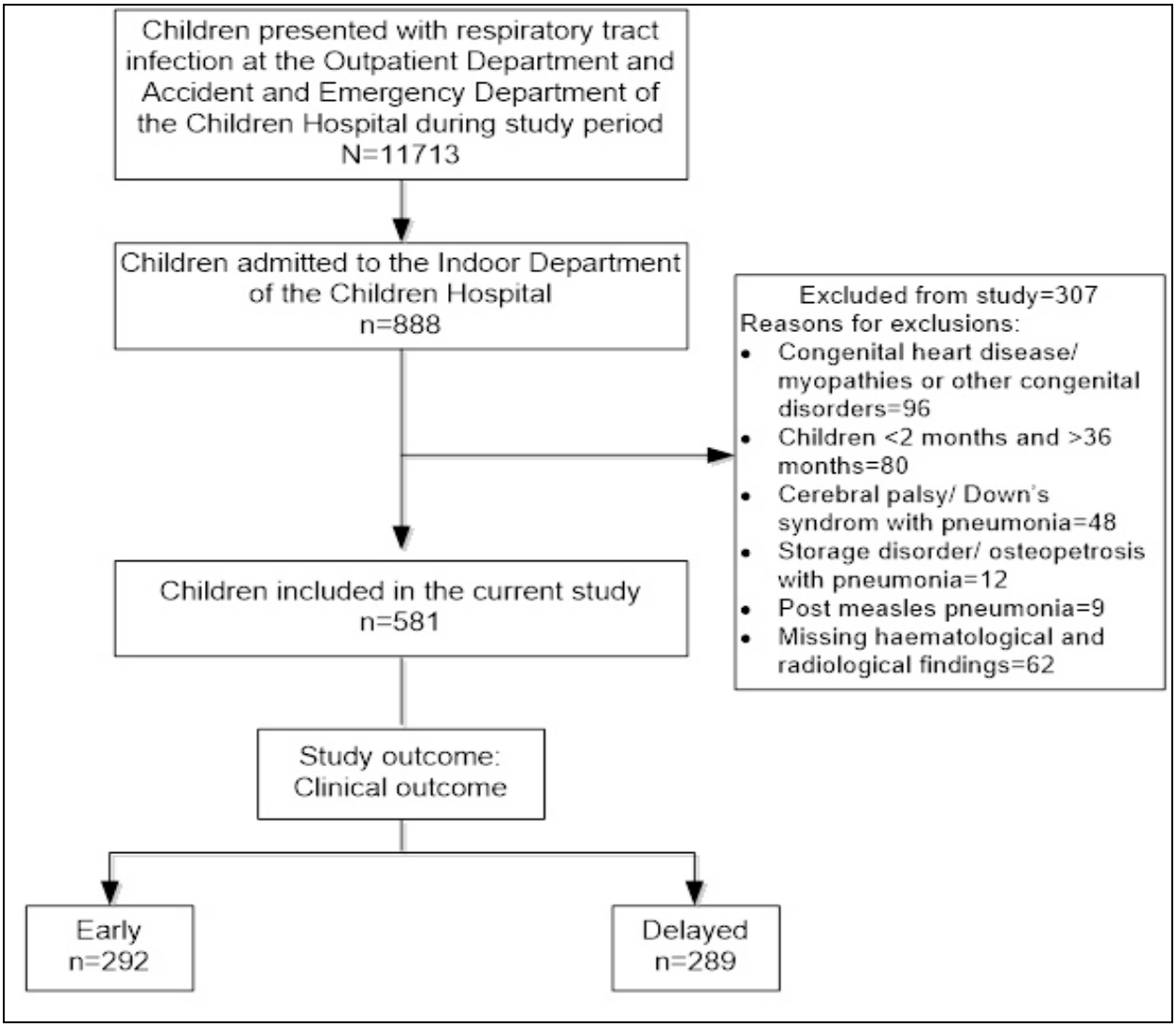

Figure-1: Sampling profile of the study

Table-1: Comparison of baseline characteristics of children age 2-36 months with severe LRTI between early and delayed clinical response (n=581)

Variable	Clinical outcome		*p*
	Early response n=292 (%)	Delayed response n=289 (%)	
Demographic features			
Age (in months)			0.077
Mean (SD)	8.14 (8.36)	6.96 (7.78)	
Median (IQR)	5.0 (3.0, 10.0)	4.0 (2.0, 8.0)	
Age categories			0.086
2 to 6 months	181 (62.0)	204 (70.6)	
7 to 12 months	64 (21.9)	47 (16.3)	
13 to 36 months	47 (16.1)	38 (13.1)	
Gender			0.680
Male	177 (60.6)	180 (62.3)	
Female	115 (39.4)	109 (37.7)	
History			
Fever			0.230
No	30 (10.3)	39 (13.5)	
Yes	262 (89.7)	250 (86.5)	
Cough			0.682
No	12 (4.1)	10 (3.5)	
Yes	280 (95.9)	279 (96.5)	
Difficult breathing			0.557
No	14 (4.8)	11 (3.8)	
Yes	278 (95.2)	278 (96.2)	
Poor feeding			0.029
No	131 (44.9)	104 (36.0)	
Yes	161 (55.1)	185 (64.0)	
Vomiting			0.008
No	240 (82.2)	211 (73.0)	
Yes	52 (17.8)	78 (27.0)	
Fits			
No	269 (92.1)	259 (89.6)	
Yes	23 (7.9)	30 (10.4)	
Duration of illness (in days)			0.033
Mean (SD)	4.10 (2.88)	4.72 (4.03)	
Median (IQR)	3.0 (2.0, 5.0)	3.0 (2.0, 7.0)	
On examination			
Wheezing			0.402
No	69 (23.6)	77 (26.6)	
Yes	223 (76.4)	212 (73.4)	
Lethargy			0.260
No	287 (98.3)	287 (99.3)	
Yes	5 (1.7)	2 (0.7)	
Respiratory rate (breaths/min)			0.125
Mean (SD)	62.3 (9.16)	63.4 (9.06)	
Median (IQR)	62.0 (56.0, 68.0)	64.0 (60.0, 68.0)	
Actual temperature (in ^{o}F)			0.032
Mean (SD)	98.4 (8.30)	99.5 (1.36)	
Median (IQR)	99.0 (98.0, 100.0)	100.0 (98.0, 100.0)	
Weight for age Z-score (WAZ)			0.001
Mean (SD)	-1.19 (1.61)	-1.69 (1.69)	
Median (IQR)	-1.23 (-2.23, -0.19)	-1.86 (-2.75, -0.81)	
Height for age Z-score (HAZ)			0.001
Mean (SD)	-1.23 (1.93)	-1.82 (2.04)	
Median (IQR)	-1.33 (-2.69, -0.03)	-2.09 (-3.31, -0.38)	
Weight for height Z-score (WHZ)			0.367
Mean (SD)	-1.07 (1.67)	-1.31 (1.93)	
Median (IQR)	-1.09 (-2.31, -0.26)	-1.13 (-2.83, 0.05)	
Nutritional status			
Underweight (WAZ <-2)			0.045
No	202 (69.2)	177 (61.2)	
Yes	90 (30.8)	112 (38.8)	
Stunting (HAZ <-2)			0.007
No	203 (69.5)	170 (58.8)	
Yes	89 (30.5)	119 (41.2)	
Wasting (WHZ <-2)			0.345
No	261 (89.4)	251 (86.9)	
Yes	31 (10.6)	38 (13.1)	

HAZ: Height for age Z-score. IQR: Interquartile range. LRTI: Lower respiratory tract infection. SD: Standard deviation. WAZ: Weight for age Z-score. WHZ: Weight for height Z-score

Table-2: Comparison of haematological and radiological findings, and duration of clinical improvement of children age 2–36 months with severe LRTI between early and delayed clinical response (n=581)

Variable	Clinical outcome		*p*
	Early response n (%)	Delayed response n (%)	
Radiological findings			<0.0001
Normal	211 (72.3)	141 (48.8)	
Interstitial pneumonia	74 (25.3)	123 (42.6)	
Lobar consolidation	7 (2.4)	25 (8.6)	
Haematological findings			
Total leukocyte count (/mm^3)			0.085
Mean (SD)	12936 (7772)	14374 (11935)	
Median (Interquartile range)	11600 (8600, 15350)	123000 (8700, 17200)	
Absolute neutrophil count (/mm^3)			0.161
Mean (SD)	6223 (4735)	11691 (6635)	
Median (IQR)	4929 (3139, 7800)	6026 (3584, 9541)	
Absolute lymphocyte count (/mm^3)			0.146
Mean (SD)	6076 (9340)	5219 (3560)	
Median (Interquartile range)	4794 (3456, 6844)	4290 (2952, 6604)	
Haemoglobin (g/dl)			0.767
Mean (SD)	10.4 (2.32)	10.3 (1.72)	
Median (Interquartile range)	10.3 (9.4, 11.2)	10.3 (9.3, 11.4)	
Haematological classification			
Leucocytosis			0.005
No	251 (86.0)	222 (76.8)	
Yes	41 (14.0)	67 (23.2)	
Neutrophilia			0.004
No	230 (78.8)	197 (68.2)	
Yes	62 (21.2)	92 (31.8)	
Lymphocytosis			0.632
No	280 (96.9)	278 (96.2)	
Yes	9 (3.1)	11 (3.8)	
Anaemia			0.105
No	92 (31.5)	97 (33.6)	
Mild	82 (28.1)	74 (25.6)	
Moderate	116 (39.7)	108 (37.4)	
Severe	2 (0.7)	10 (3.5)	
Duration of clinical improvement (in days)			
Actual temperature			<0.0001
Mean (SD)	1.06 (1.22)	2.60 (2.59)	
Median (Interquartile range)	1.00 (0.01, 2.6)	2.00 (0.01, 4.0)	
Respiratory rate (breaths/min)			<0.0001
Mean (SD)	59.2 (0.53)	63.9 (1.02)	
Median (Interquartile range)	56.0 (35, 68.0)	64.0 (60, 69)	
Feeding status			<0.0001
Mean (SD)	2.03 (0.95)	4.16 (2.22)	
Median (Interquartile range)	2.00 (2.0, 2.0)	4.00 (3.0, 5.0)	
Duration of hospitalization (in days)			<0.0001
Mean (SD)	2.37 (1.01)	6.16 (4.04)	
Median (Interquartile range)	2.00 (2.0, 3.0)	5.00 (4.0, 7.0)	

Table-3: Association of haematological and radiological findings with clinical outcome in children 2-36 months of age with severe LRTI using unadjusted and adjusted logistic regression analyses (n=581)

	Unadjusted		Adjusted model 1		Adjusted model 2		Adjusted model 3	
Variable	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Radiological findings								
Normal	1.00 (reference)		1.00 (reference)				1.00 (reference)	
Interstitial pneumonia	2.49 (1.74, 3.56)	<0.0001	2.69 (1.84, 3.91)	<0.0001			2.48 (1.70, 3.64)	<0.0001
Lobar consolidation	5.34 (2.25, 12.69)	<0.0001	6.03 (2.43, 14.96)	<0.0001			6.00 (2.41, 14.96)	<0.0001
Haematological findings								
Leucocytosis								
No	1.00 (reference)				1.00 (reference)		1.00 (reference)	
Yes	1.85 (1.20, 2.84)	0.005			1.79 (1.15, 2.79)	0.010	1.46 (0.80, 2.67)	0.220
Neutrophilia								
No	1.00 (reference)				1.00 (reference)		1.00 (reference)	
Yes	1.73 (1.19, 2.52)	0.004			1.91 (1.29, 2.84)	0.001	1.51 (0.91, 2.50)	0.112
Lymphocytosis								
No	1.00 (reference)				1.00 (reference)		1.00 (reference)	
Yes	1.24 (0.51, 3.05)	0.633			1.16 (0.46, 2.90)	0.754	0.64 (0.23, 1.81)	0.400
Anaemia								
No	1.00 (reference)				1.00 (reference)		1.00 (reference)	
Mild	0.86 (0.56, 1.31)	0.472			0.90 (0.58, 1.39)	0.632	1.01 (0.64, 1.60)	0.955
Moderate	0.88 (0.60, 1.30)	0.529			0.86 (0.58, 1.29)	0.477	0.89 (0.58, 1.35)	0.576
Severe	4.74 (1.01, 22.23)	0.048			3.81 (0.80, 18.22)	0.094	4.10 (0.81, 20.64)	0.087

Model-1 assessed radiological findings with clinical response using logistic regression analysis and adjusted for age, gender, and nutritional status, duration of illness, and actual temperature and respiratory rate at the time of presentation. Model-2 assessed haematological findings with clinical response using logistic regression analysis and adjusted for age, gender, and nutritional status, duration of illness, and actual temperature and respiratory rate at the time of presentation. Model-3 assessed radiological and haematological findings together with clinical response using logistic regression analysis and adjusted for age, gender, and nutritional status, duration of illness, and actual temperature and respiratory rate at the time of presentation. CI: Confidence interval. OR: Odds ratio.

DISCUSSION

In the current study we investigated the role of haematological and radiological findings on the clinical response in children 2–36 months of age with severe LRTI. We found that children with haematological findings at the time of admission, leucocytosis and neutrophilia, had 1.8 and 1.9 times higher odds of delayed response than children who did not have leucocytosis and neutrophilia, respectively, after adjusted for other potential confounding factors. Children who had radiological findings, interstitial pneumonia and lobar consolidation, had 2.7 and 6.0 times higher odds of delayed response than children who had normal chest radiography, respectively, after adjusted for potential confounding factors. Further, the final model which assessed haematological findings and radiological findings together and was adjusted for other potential confounding factors showed that children who had radiological interstitial pneumonia and lobar consolidation, had 2.5 and 6.0 times higher odds of delayed response compared to children with normal chest radiography. These findings of the current study are important for paediatricians working in this region, where radiographic facilities are available, to make decision at the time of admission regarding the management of children with severe LRTI based on chest radiography. Further, the findings of the current study will also help paediatricians to choose alternative antibiotics based on the findings of chest radiographs to predict delayed response in children 2–36 months old with severe LRTI.

Our results are consistent with other studies. Bharti and colleagues conducted a study in India between 1997 and 1998 to evaluate the role of chest radiograph in predicting outcome of acute severe pneumonia in children <5 years of age. In their study, 83 hospitalized children with severe pneumonia were enrolled. Of 83, 43 (51.8%) had lobar consolidation, 26 (31.3%) had interstitial abnormalities, and 14 (16.9%) had normal chest radiograph. The authors found that length of hospital stay was significantly longer in children who had abnormal chest radiographs compared to those who had normal chest radiograph.[15] Clark *et al* reviewed 711 children with pneumonia in 13 hospitals in United Kingdom. Of 711, 141 (19.8%) had lobar consolidation, 65 (9.1%) had effusion and 435 (61.2%) had patchy findings on chest radiograph. The investigators found that children with effusion and lobar consolidation on chest radiograph had longer duration to use antibiotics and stayed for longer duration at the hospital.[16] Salih and co-workers in Sudan evaluated the role of chest radiograph for the diagnosis of pneumonia in 1–59 months old children. Of 156 children enrolled, 47 (30.1%) had alveolar pneumonia (lobar consolidation) and 36 (23.1%) had non- alveolar pneumonia (infiltrate/ interstitial) on chest radiograph. Remaining 73 (46.8%) children had normal chest radiographs. Further, investigators found that 29 (34.9%) children had severe radiological pneumonia (presence of both signs on chest radiograph) and those children had significantly longer duration of stay at the hospital.[17] In Taiwan, Lin *et al* found that children up to 18 years of age who had lobar consolidation had significantly longer duration of stay at the hospital due to persistent fever.[18]

Many bacteria and viruses and their combinations can cause the LRTIs in children. However, there is a lack of rapid and commercially available laboratory tests for many pathogens which may explain why the aetiology is rarely established in clinical practice and why antibiotic treatment is empirical in most cases.[19] Most children with bacterial LRTI have a typical illness with high temperature, leucocytosis and lobar or segmental consolidation on the chest radiograph.[15,20–22] Nevertheless, it is reported previously that about 30% of patients might have an atypical illness, demonstrating the clinical variability of bacteraemic LRTI.[23] In the current study the mean leukocyte count was 13,651/mm^3. The percentage of children who had delayed clinical response had significantly higher leucocytosis (23.2%) compared to children with early clinical response (14%). A study by Furer *et al* in Israel reported that 30% of children with bacterial pneumonia had leucocytosis. They, similar to the current study findings, also found no association between leucocytosis and longer hospital stay. However, unlike our study, they defined leucocytosis at a lower levels of leukocytes (>10,000/mm^3) than our classification.[4]

The current study has much strength. First, it was conducted in one of the largest, tertiary care hospital, which has a large catchment area in this region of the country. Second, the study has an appropriate sample size to assess the effect of haematological and radiological findings. Last, all models were adjusted for the potential confounding factors which effect clinical response, such as age, nutritional status, actual temperature and respiratory rates at the time of admission. However, there is a need to conduct further multicentre study with appropriate sample size, to evaluate the role of haematological and radiological findings on the clinical response in children with severe LRTI. The information about some other potential confounding factors such as environmental and genetic factors was not collected in the current study, which was the major limitation of the current study.

CONCLUSIONS

To conclude, we found that the children 2–36 months of age with severe LRTI who had leucocytosis, neutrophilia, and radiological findings at the time of admission had significantly higher odds of delayed clinical response compared to their counterparts without these risk factors. Hence, it is pertinent to examine the haematological and radiological findings at the time of admission to predict the clinical outcome in children 2–36 months of age with severe LRTI.

AUTHOR'S CONTRIBUTION

YBN conceptualized and designed the study, carried out the data analyses, drafted the initial manuscript, and revised the manuscript. RW conceptualized and designed the study, collected data, reviewed the analyses and, provided necessary feedback, and reviewed and revised the manuscript critically. NB conceptualized and designed the study, collected data, and critically reviewed the manuscript. YBN, RW and NB addressed reviewers' comments. All authors agreed to be accountable for all aspects of the work and approved the final manuscript as submitted.

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Address for Correspondence:

Dr. Yasir Bin Nisar, Room 128C, Edward Ford Building, Sydney School of Public Health, The University of Sydney-Australia

Email: yasi8204@uni.sydney.edu.au