Doi: 10.32677/IJCH.2017.v04.i01.011

Original Article

Outcome predictors of severe and very severe pneumonia in children between 2 and 59 months of age admitted in a tertiary care hospital

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Received – 08 October 2016 Initial Review – 23 October 2016 Published Online – 14 December 2016

ABSTRACT

Objective: The objective of this study was to determine the factors associated with outcome (morbidity and mortality) in children aged 2-59 months with severe and very severe pneumonia. **Materials and Methods:** This is a hospital-based, prospective, observational study conducted in the pediatric department of a tertiary care hospital. Totally 300 children of either sex between 2 and 59 months of age with the WHO-defined severe pneumonia and very severe pneumonia were enrolled in the study. Associations of outcomes and various clinical symptoms were assessed using Chi-square test first and then through logistic regression models. **Results:** In our study, 86 (28.7%) children stayed in hospital more than 5 days, 113 (37.7%) needed change in antibiotics, 24 (8%) developed complications (5% effusion and 3% pneumothorax), and 31 (10.3%) expired. Multivariate analysis showed that younger age at presentation, household pollution (cooking fuel other than liquefied petroleum gas), and children who did not receive exclusive breastfeeding were prone to develop more severe pneumonia. Head nodding and cyanosis were independent factors significantly associated with mortality on multiple logistic regression. Radiologically proven pneumonia cases required change in antibiotics more frequently and stayed for longer duration in hospital as compared to clinical pneumonia cases. **Conclusions:** Children with signs of severe respiratory distress such as head nodding, cyanosis and altered sensorium, anemia, decreased or increased total leukocyte count, and hypoxemia have greater risk of mortality. Children with risk factors including overcrowding, indoor air pollution, lack of exclusive breastfeeding and proper immunization, and abnormal chest radiograph are less likely to respond to the first-line antibiotics; therefore, they may be treated aggressively with the second-line antibiotics from the beginning so that their hospital stay may be reduced.

Key words: *Outcome, Mortality, Pneumonia, Predictors*

Pneumonia is a leading cause of morbidity and mortality in under-five children. According to the recent WHO estimate, pneumonia is responsible for 15% of deaths in the under-fives, killing 9,20,136 children in 2015. Nearly 23% of the total under-fives' death and 20-30% of under-fives' admissions in India are due to pneumonia. According to hospital-based studies, case fatality rate (CFR) was reported to vary between 8.7% and 47% [1-4]. Both community as well as hospital-based studies have highlighted a variety of factors contributing to mortality in childhood pneumonia [3-8]. With socioeconomic progress and improvement in health awareness and referral services, an increasing proportion of pneumonia deaths will occur in hospitals [9].

It is presumed that positive chest X-ray findings are mainly due to the bacterial pneumonia which needs to be treated with antibiotics; hence, we planned to evaluate the risk factors associated with outcome in radiologically proven pneumonia and to compare it with that of the WHO-defined severe and very severe pneumonia. There are only a few studies on other relevant outcomes including the need for change of antibiotics, prolonged hospital stay (i.e., more than 5 days), and need for mechanical ventilation. These factors need to be evaluated so that we can predict the outcome early during illness and can take interventions accordingly. We planned this study to identify these factors and other relevant outcomes so that we can modify the course of illness.

MATERIALS AND METHODS

This is a hospital-based study over a period of 18 months from November 2013 to March 2015 conducted in pediatrics ward of a tertiary care hospital. The study was conducted after obtaining Institutional Ethics Committee's approval, and patients were enrolled after receiving written consent of the parents/legally acceptable representatives. A total of 300 children of either sex between 2 and 59 months of age with the WHO-defined severe and very severe pneumonia were enrolled in the study [10]. Children having other comorbid conditions such as severe malnutrition, congenital malformations, congenital heart disease, meningitis, severe anemia (hemoglobin <7 gm% or as per the

WHO cutoffs for age-based value of hemoglobin for severe anemia [11]), chronic respiratory disease (e.g., asthma, cystic fibrosis, bronchopulmonary dysplasia, and previously diagnosed case of tuberculosis), diarrhea with dehydration, and pulmonary Koch's were excluded from the study. Patients who were admitted in other hospitals prior to presentation and who have wheeze and improved after nebulization with beta-agonists (salbutamol) thrice at 20 min interval were also excluded from the study.

After recruitment, details of personal, demographic profile, signs and symptoms, and relevant past and family history were enquired and recorded. Overcrowding was determined by calculating the number of family members per room. A child who was not found to be in the following norm was labeled as staying in overcrowded house. (a) 1 room - 2 persons, (b) 2 rooms - 3 persons, (c) 3 rooms - 5 persons, (d) 4 rooms - 7 persons, and (e) 5 or more rooms - 10 persons (additional 2 for each further room). Immunization status was assessed by verifying the immunization records or asking the parents. Details of breastfeeding and addition of top feeds were also recorded. Thorough clinical examination was done, and the findings were noted in pre-designed proforma.

Chest radiographs were performed in all patients. Results of the investigations including complete blood count, chest X-ray, blood culture, serum electrolytes (normal sodium=135-145 mEq/L and potassium=3.5-5.5 mEq/L), and arterial blood gas (ABG) analysis were recorded. Total leukocyte count (TLC) is considered normal if it is in the range of 4000-11000 cells/mm^3 of blood. The treatment given and progress note were recorded at 48 h, 5^{th} day, or as required. Patients were observed till the day of discharge or death. Treatment was started as per the WHO standard protocol, and antibiotics were changed if there was no improvement or worsening of symptoms within 48 h of admission. Patients were discharged when respiratory rate reduced below the age-specific cutoff, with absence of hypoxemia, chest in-drawing, and fever for at least 24 h.

Associations of severity of pneumonia with sociodemographic and family background of patients and associations between survival from severe and very severe pneumonia (outcome) and various clinical symptoms were assessed using Chi-square test first and then through logistic regression models. Association of sociodemographic, family, and clinical characteristics with change in antibiotics, duration of hospital stay, and complications was assessed separately in radiologically proven pneumonia and children with normal chest X-ray using Chi-square test. The associations were considered statistically significant at 5% level of significance (i.e., $p \leq 0.05$). SPSS software version 17.0 was used for all the statistical analyses.

RESULTS

Out of the 300 children enrolled as per the inclusion criteria, 147 (49%) children had severe pneumonia and 153 (51%) had very severe pneumonia. In our study, 69.3% of the children were male and majority (55.7%) was below 1 year of age. Mothers of 120 (40%) and fathers of 50 (16.7%) children were illiterate. About 245 children (81.7%) came from overcrowded families, 21 (7%) were having pets at their home, and 80 (26.7%) belonged to the families where liquefied petroleum gas (LPG) was not used for cooking fuel. About 65 (21.7%) children were partially immunized, 9 (3%) were unimmunized, and 207 children (69%) received exclusive breast milk up to 6 months (Table 1).

At the time of presentation, 133 (44.3%) children were unable to feed/drink, 84 (28%) were lethargic, 64 (21.3%) were having wheezing, 25 (8.3%) had altered sensorium, 23 (7.7%) had head

Table 1: Association between demographics of child and outcome

Characteristics	Outcome		p-value
	Discharge	Death	
	n (%)	n (%)	
Age (year)			
<1	145 (86.8)	22 (13.2)	0.175
1-2	71 (92.2)	6 (7.8)	
2-5	53 (94.6)	3 (5.4)	
Sex			
Male	188 (90.4)	20 (9.6)	0.539
Female	81 (88.0)	11 (12.0)	
Maternal education			
Illiterate	92 (76.7)	28 (23.3)	<0.001
Up to 7^{th}	73 (98.6)	1 (1.4)	
$8\text{-}10^{th}$	71 (98.6)	1 (1.4)	
$<10^{th}$	33 (97.1)	1 (2.9)	
Paternal education			
Illiterate	42 (84.0)	8 (16.0)	<0.001
Up to 7^{th}	54 (81.8)	12 (18.2)	
$8\text{-}10^{th}$	97 (90.7)	10 (9.3)	
$<10^{th}$	76 (98.7)	1 (1.3)	
Maternal age (years)			
<18	1 (33.3)	2 (66.7)	<0.001
≥18	268 (90.2)	29 (9.8)	
Paternal age (year)			
<21	1 (100.0)	0 (0.0)	0.734
≥21	268 (89.6)	31 (10.4)	
Overcrowding at home			
Yes	215 (87.8)	30 (12.2)	0.022
No	54 (98.2)	1 (1.8)	
Pets at home			
Yes	19 (90.5)	2 (9.5)	0.899
No	250 (89.6)	29 (10.4)	
Cooking fuel			
LPG	206 (93.6)	14 (6.4)	<0.001
Other	63 (78.8)	17 (21.3)	
Immunization			
Complete	208 (92.0)	18 (8.0)	0.50
Partial	53 (81.5)%	12 (18.5)	
Unimmunized	8 (88.9)	1 (11.1)	
Feeding			
EBM upto 6 months	199 (96.1)	8 (3.9)	<0.001
Other	70 (75.3)	23 (24.7)	

LPG: Liquefied petroleum gas, EBM: Expressed breast milk

nodding, 12 (4%) had cyanosis, and 1 (0.33%) had convulsion. On examination, 254 children (84.7%) had a temperature above 38°C, 5 (1.7%) had temperature below 35°C, and 29 (9.7%) had O_2 saturation below 92%. Investigations showed increased TLC in 170 (56.7%) and decreased TLC in 6 (2%) children, while 134 children (44.7%) had decreased hemoglobin. In 188 (62.7%) children, chest radiograph showed consolidation or infiltrates (Table 2). In our study, 86 (28.7%) children stayed in hospital for more than 5 days, 18 (6%) patients progressed from severe to very severe pneumonia, 113 (37.7%) needed change in antibiotics, 24 (8%) developed complications (5% effusion and 3% pneumothorax), 49 (16.3%) required mechanical ventilation, and 31 (10.3%) expired.

In this study, younger age, lower maternal education, overcrowding, cooking fuel other than LPG, and non-exclusive breastfeeding were significantly associated with increasing severity of pneumonia ($p<0.05$). However, on multiple logistic regression analysis, younger age, cooking fuel other than LPG, and non-exclusive breastfeeding remained significantly associated with an increasing severity of pneumonia. With respect to mortality, lower parental education, increasing maternal age, overcrowding, cooking fuel other than LPG, and breastfeeding for <6 months were significantly associated with an increased mortality ($p<0.05$). Hence, timely intervention in these children can reduce mortality. On multivariate analysis, female children had significantly 65% (odd ratio [OR]=0.35) less chance to survive due to pneumonia as compared to male children ($p<0.05$). In addition, those who were not exclusively breastfed up to 6 months had 83% (OR=0.17) less chances of survival as compared to those who were exclusively breastfed till 6 months ($p<0.05$).

Among clinical features and laboratory parameters, sensorium, head nodding, lethargy, inability to feed/drink, hypothermia, hyperthermia, cyanosis and decreased oxygen saturation (<92%) at presentation and increased or decreased TLC, anemia, abnormal chest X-ray, electrolyte imbalance, and blood culture positivity were significantly associated with poor survival ($p<0.05$). However, on including all the variables in the model, the net effect of only head nodding and cyanosis was statistically significant on survival.

In this study, we found that both change in antibiotics and prolonged duration of stay were significantly associated with radiologically proven pneumonia. Nearly 48.4% of the children required change in antibiotics with abnormal chest X-ray as compared to 19.6% of those who had normal chest X-ray ($p<0.001$). It is presumed that radiologically proven pneumonia is mostly due to bacterial cause. About 37.8% of the children with radiologically proven pneumonia required prolonged hospitalization in comparison to 13.4% with normal chest X-ray ($p<0.001$). This further shows that radiologically proven pneumonia should require a more aggressive approach in management.

Lower parental education, overcrowding, cooking fuel other than LPG, incomplete immunization, breastfeeding <6 months, increasing severity of pneumonia, inability to feed/drink, anemia,

Table 2: Association between clinical symptoms of child and outcome

Characteristics	Outcome		p-value
	Discharge	Death	
	n (%)	n (%)	
Sensorium			
Normal	265 (96.4)	10 (3.6)	<0.001
Altered	4 (16.0)	21 (84.0)	
Wheezing			
Present	63 (98.4)	1 (1.6)	0.009
Absent	206 (87.3)	30 (12.7)	
Head nodding			
Present	8 (34.8)	15 (65.2)	<0.001
Absent	261 (94.2)	16 (5.8)	
Lethargy			
Present	62 (73.8)	22 (26.2)	<0.001
Absent	207 (95.8)	9 (4.2)	
Convulsion			
Yes	0 (0.0)	1 (100.0)	0.003
No	269 (90.0)	30 (10.0)	
Inability to feed/drink			
Present	102 (76.7)	31 (23.3)	<0.001
Absent	167 (100.0)	0 (0.0)	
Pulses			
Normal	149 (99.3)	1 (0.7)	<0.001
Tachycardia	120 (80.0)	30 (20.0)	
Bradycardia	0 (0.0)	0 (0.0)	
Absent	269 (89.7)	31 (10.3)	
Temperature			
>38°C	227 (89.4)	27 (10.6)	<0.001
<35°C	1 (20.0)	4 (80.0)	
In between	41 (100.0)	0 (0.0)	
Cyanosis			
Present	2 (16.7)	10 (83.3)	<0.001
Absent	267 (92.7)	21 (7.3)	
TLC			
Normal	123 (99.2)	1 (0.8)	<0.001
Increased	145 (85.3)	25 (14.7)	
Decreased	1 (16.7)	5 (83.3)	
Hib			
Normal	164 (98.8)	2 (1.2)	<0.001
Decreased	105 (78.4)	29 (21.6)	
CXR			
Normal	112 (100.0)	0 (0.0)	<0.001
Infiltrates	63 (100.0)	0 (0.0)	
Consolidation	94 (75.2)	31 (24.8)	
O_2 saturation			
≥92%	261 (96.3)	10 (3.7)	<0.001
<92%	8 (27.6)	21 (72.4)	
ABG			
Hypoxia	103 (96.3)	4 (3.7)	<0.001
Acidosis	0 (0.0)	0 (0.0)	

(Contd...)

Table 2: *(Continued)*

Characteristics	Outcome		p-value
	Discharge	Death	
	n (%)	n (%)	
Both	12 (30.8)	27 (69.2)	
Normal	154 (100.0)	0 (0.0)	
Blood culture			
No growth	255 (91.7)	23 (8.3)	<0.001
Staphylococcus	4 (44.4)	5 (55.6)	
Acinetobacter	3 (100.0)	0 (0.0)	
Streptococcus	7 (70.0)	3 (30.0)	
No	269 (89.7)	31 (10.3)	
Electrolyte imbalance			
Yes	3 (50.0)	3 (50.0)	0.001
No	266 (90.5)	28 (9.5)	

TLC: Total leukocyte count, ABG: Arterial blood gas

and hypoxia in ABG were significantly associated with change in antibiotics among radiologically normal children ($p<0.05$). In addition to these variables, wheezing, head nodding, lethargy, and SpO_2 <92% at admission were also significantly associated with change in antibiotics among radiologically proven pneumonia cases ($p<0.05$).

Factors significantly associated with prolonged hospitalization were parental education, overcrowding, cooking fuel other than LPG, non-exclusive breastfeeding, severity of pneumonia, inability to feed/drink, tachycardia, anemia, leukopenia or leukocytosis, and hypoxia in ABG ($p<0.05$). In addition, pets at home and incomplete immunization were also significantly associated with prolonged hospitalization in radiologically proven pneumonia cases. We observed a mortality rate of 10.3% in our study population.

DISCUSSION

In our study, younger age, lower maternal education, overcrowding, cooking fuel other than LPG, and exclusive breastfeeding for <6 months were significantly associated with increasing severity of pneumonia. Similarly, lower parental education, increasing maternal age, overcrowding, cooking fuel other than LPG, and breastfeeding for <6 months were significantly associated with increased mortality ($p<0.05$) because these children are prone to develop more severe pneumonia as compared to others. Other studies also reported the same [5,9,12,13]. We observed a mortality rate of 10.3%, which is comparable to the reported CFR of 10.5%, 9.8%, and 10.45% in similar settings [1,5,12]. CFR in childhood pneumonia in various Indian studies ranges between 8.9% and 47% [1-5]. In our study, 86 (28.7%) children stayed in hospital for more than 5 days, 113 (37.7%) needed change in antibiotics, and 49 (16.3%) required mechanical ventilation while a study done by Tiewsoh et al. reported that 56.5% of the children needed a change in antibiotics, 51% stayed for more than 5 days in the hospital, and 20.5% needed mechanical ventilation [5].

As age increases, severity of childhood pneumonia decreases. In our study, adjusted results show that children aged 2-5 years were 66% less likely to suffer from very severe pneumonia (vs. severe pneumonia) as compared to children <1 year old ($p<0.05$). This can be explained by the fact that as the age increases, the respiratory passage becomes wider and respiratory defense mechanism becomes more mature.

In our study, 65.8% of the children whose mother were illiterate were suffering from very severe pneumonia as compared 47.1% children whose mothers were educated more than 10th standard ($p<0.001$). It may be due to better health awareness in literate group. Parents' education level at least up to middle school was protective against the severity of pneumonia as observed in a previous study [14].

Overcrowding at home implies a prolonged exposure to partner's pathogen. In one study, it was an independent risk factor in determining the severity of pneumonia [14] while other studies have shown variable results [15-17]. In our study, children from the houses where fuel other than LPG was used were 2-3 times more likely to suffer from very severe pneumonia. Burning of biomass in indoor releases suspended particulate matter which is likely to negatively affect the general defense mechanisms of the lungs, including its mucociliary function, which leads to increased susceptibility to respiratory diseases [18].

Duration of breastfeeding was an independent risk factor associated with the severity of pneumonia in our study. Children who were not breastfed up to 6 months were 4.1 times more likely to suffer from severe pneumonia than those who were breastfed up to 6 months in the study. In previous studies also, lack of breastfeeding has been reported to be associated with an increased risk of development of severe pneumonia by 1.5-2.6 times [14,19-21]. Breast milk seems to have effect on infant's systemic immune system through multiple mechanisms including maturational, anti-inflammatory, immuno-modulatory, and antimicrobial actions [22].

Sex difference, parental age, and immunization status of children were not significantly associated with severity of pneumonia in this study. Although a higher incidence of pneumonia was found in male children (69.3%), male gender *per se* did not appear to predispose to severity of pneumonia which is consistent with other studies [15-17]. Many vaccines provide protection against childhood pneumonia, for example, pneumococcal vaccine, Hib conjugate vaccine, and measles vaccine, but role of these vaccines to reduce severity of pneumonia is not well established.

The strength of our study is the prospective nature and good cohort, but limitations are specific etiology of pneumonia could not be identified, other comorbid conditions such as severe malnutrition, congenital heart diseases, meningitis, severe anemia, and chronic respiratory diseases were excluded, and radiological diagnosis was made by radiologists by consensus. Furthermore, the present study reflects the predictors at a tertiary care center, but whether these are different at district-level hospital where resources are limited in developing countries like India cannot be said.

CONCLUSIONS

In this study, it can be inferred that children with signs of severe respiratory distress such as head nodding, cyanosis and altered sensorium, anemia, decreased or increased TLC, and hypoxemia have a greater risk of mortality, so they should be paid more attention and preferably must be admitted in intensive care unit for more aggressive monitoring and treatment to reduce mortality. Children with severe and very severe pneumonia arriving from overcrowded house and house having indoor air pollution, lack of exclusive breastfeeding, incomplete immunization, and abnormal chest radiograph are less likely to respond to the first-line antibiotics; therefore, they should be treated aggressively with the second-line antibiotics from the beginning so that their hospital stay may be reduced.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: MD Ansari E, Kumar A, Aggarwal KC, Meena KR, Kamal M. Outcome predictors of severe and very severe pneumonia in children between 2 and 59 months of age admitted in a tertiary care hospital. Indian J Child Health. 2017; 4(1):39-43.