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Original Research Article

Prospective Cohort Study to Assess the Risk Factors for the Development of Pneumonia and Severe Pneumonia in Children in Northern Bihar

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Abstract

Aim: To identify the risk factors for pneumonia and severe pneumonia in children.

Material & Methods: This study was a prospective cohort study carried out at Darbhanga Medical College & Hospital, Laheriasarai, Darbhanga, Bihar, India from October 2020 to May 2021.

Results: A total of 990 children were included, and 603 (60.9) boys with ARI were enrolled. Among them, 938 (11.8%) and 772 (77.9%) had 'pneumonia. younger age and low weight for height were considered as an independent risk factor for pneumonia. In the case of Hib vaccination, positive vaccination history increased the odds of developing community acquired pneumonia.

Conclusion: Young age and under nutrition (low weight for height/length) in children are significant independent risk factors for pneumonia.

Keywords: Acute respiratory infection treatment unit, under nutrition.

Introduction

Community-acquired pneumonia (CAP) remains the most common reason for pediatric clinical visits and the major cause of pediatric mortality, posing a significant burden to the health system worldwide [1,2]. According to a report by the World Health Organization (WHO), CAP killed 808,694 children in 2017, accounting for 15% of all deaths of children under 5 years old [3]. The status quo is even worse for developing countries like China, where more than 20 million new pediatric CAP cases are reported annually [4].

CAP is a pulmonary infectious disease acquired outside of the hospital, with viruses and bacteria as the most common pathogens [5]. Its severity varies dramatically from one person to another. Mild cases could recover swiftly even without specific treatment, whereas severe ones might end up with a dismal outcome even with intensive care [6]. In the era of

precision medicine, we do not want to over treat the mild cases or risk missing out on the severe disease, which might behave exactly like a mild disease at an early stage and early initiation of intensive treatment is critical in controlling its progression. Even with the advancement of modern medicine, there is no substantial improvement in the management strategy and treatment outcome of pediatric CAP, which is significantly ascribed to the inability to accurately predict disease severity and administer early intensive treatment or prophylactic therapies to high-risk cases [7].

There is a wide variation in the risk factors for pneumonia in the published studies. Most of the studies for risk factors of pneumonia were hospital-based and represented only a small proportion of pneumonia cases. Few studies had focused on the risk factors that were associated with progression to severe or very severe pneumonia [8].

The identified risk factors for childhood pneumonia are under nutrition, incomplete immunization, and use of solid fuels in the household, over-crowding, lack of exclusive breastfeeding, low degree of maternal education, and limited access to secondary care. These risk factors are characteristics of low socioeconomic status and are interrelated. However, due to the linear relation of these risk factors, it is difficult to estimate their individual risk [9].

To study this problem, we conducted a large multi-center prospective study to determine the risk factors for the development of pneumonia and severe pneumonia in under five children.

Material & Methods:

This study was a prospective cohort study that was designed to develop acute respiratory infection treatment units (ATUs) and assess their utility in improving healthcare and research in pneumonia-related morbidity and mortality in India. The study was carried out at Darbhanga Medical College & Hospital, Laheriasarai, Darbhanga, Bihar, India from October 2020 to may 2021

Previously healthy children of either gender, 2 months to 59 months of age attending the Pediatrics outpatient department were recruited over a period of two years with ARI – defined as any cough and/or breathing difficulty, for less than 2 weeks. Children with any of the following were excluded from the study, a) Patients with chronic respiratory diseases (such as asthma, cystic fibrosis, Broncho pulmonary dysplasia, airway anomalies), diagnosed in a health care facility; b) Patients with congenital heart disease (suspected based on the history of the suck-rest-suck cycle and cyanosis) – confirmed by echocardiography or presence of murmur; c) Patients with GER/ recurrent aspirations (based on the history of choking or coughing while feeding or barium swallow/GER scan); d) Known or suspected HIV positive/ immunocompromised patient – based on the history of recurrent, documented multisite infection or on immunosuppressive therapy; e) Place of residence outside the city where the study site is based; f) Unable to attend follow up; g) History of radiologically confirmed pneumonia in the last 2 months; h) Terminally sick children - impending respiratory failure, cyanosis at room air and shock.

All children who fulfilled the case definition of ARI, were enrolled in the study after written informed consent from parents or legally authorized representative. Children were assessed for a history of cough or breathing difficulty by counting respiratory rate and presence of chest in drawing by a trained study staff nurse under the supervision of the doctor. A detailed clinical history and examination findings of the enrolled patient were

recorded on a pre-designed case record form before any radiological investigation. An X- ray film of the chest was obtained in every fifth child assessed to have ARI.

The outcome variable was the diagnosis of pneumonia defined by WHO criteria as cough or difficulty breathing and age-specific tachypnea (>60 breaths per minute for children less than 2 months of age, >50 breaths per minute for children 2-11 months of age and >40 breaths per minute for children 1-5 years of age). Severe pneumonia was defined as oxygen saturation <90%, severe respiratory distress, inability to drink or breastfeed or vomiting everything, altered consciousness, and convulsions. Variables examined as risk factors were age, gender, nutritional status, and immunization status.

Statistical analysis:

Data were recorded on a pre-designed proforma and managed on an Excel spread sheet. All the entries were double-checked for any possible typographical error. Data analysis was performed using STATA 11.0 (STATA Corp). Categorical variables were analyzed using both absolute and relative frequencies; continuous variables were analyzed based on the median. Pearson chi-square and Fisher exact tests were used to compare the categorical variables. Numerical variables were analyzed using the nonparametric Mann-Whitney U test. The odds ratio with 95 % CI were calculated for risk factor for pneumonia which were identified as those with P≤0.05 in the univariate analysis.

Results:

A total of 990 children were included, and 603 (60.9) boys with ARI were enrolled. Among them, 938 (11.8%) and 772 (77.9%) had ‘pneumonia. The median (IQR) age of the enrolled children was 23 (12.3) months with baseline characteristics shown in (**Table I**).

The risk factors for pneumonia were evaluated as seen in (**Table II**). On multivariate analysis one-unit increase in age in months (OR = 0.78, 0.93, 0.95) and weight for height (OR = 0.88, 0.83, 0.80) led to a decreased odd of developing pneumonia. Therefore, younger age and low weight for height were considered as an independent risk factor for pneumonia. In the case of Hib vaccination, positive vaccination history increased the odds of developing community acquired pneumonia.

The risk factors for developing severe pneumonia were evaluated in univariate analysis (**Table III**).

Table 1: Baseline Demographic and Clinical Characteristics of Enrolled Children (N=990)

Characteristics	Value	%
Age (mo)	23 (12.3)	-
Boys [a]	603	60.91
Weight for age z-score	-0.52 (-2.79,0.53)	-
Height/Length for age z-score	-0.60 (-4.62,0.76)	-
Weight for height z-score	-0.89 (-2.22,0.68)	-
Mid upper arm circumference z-score	-2.40 (-3.63, -0.7)	-
Pneumonia	772	77.98
Cough[3]	971	98.08
Fever	804	81.21
Audible wheeze[a]	87	8.788
Fast breathing post-nebulization[a]	117	11.82

Chest in drawing [a]	3	0.303
Clinical URI [a]	880	88.89
Clinical LRTI [a]	932	94.14

Table 2: Risk factors associated with development of community-acquired pneumonia

Characteristics	No pneumonia	Pneumonia	P value[a]	OR (95%CI)	P value[b]
	n=218	n=772			
Age (mo)[c]	23 (12.3)	28 (3.6)	<0.001	0.78 (0.93,0.95)	<0.001
Boys, n (%)	(60.0)	603 (60.9)	0.03	1.30 (0.95, 1.70)	0.29
Weight for height/length z-score[c]	-0.36 (-0.96, 0.62)	-0.81 (-2.84, 0.5)	<0.001	0.88 (0.83, 0.80)	<0.001
Influenza, n (%)	20 (0.31)	33 (4.2)	0.69		
Pneumococcal, n (%)	13 (0.31)	9 (1.1)	0.09		
H. influenzae, n (%)[b]	186 (77.9)	653 (84.5)	0.01	1.90 (2.38, 3.66)	<0.001

Community-acquired pneumonia defined as per World Health Organization guideline. [a]Univariate analysis; [b]Multivariate analysis.

Table 3: Risk factors associated with severe community-acquired pneumonia

Characteristics	Pneumonia	Severe pneumonia	P value[a]	OR (95%CI)	P value[b]
	n=440	n=332			
Age, mo	27 (7.25)	22 (6.20)	0.001	0.98 (0.97, 0.99)	0.05
Male, n (%)	321 (63.8)	227 (63.9)	0.60	1.53 (0.80, 1.60)	0.74
Weight for height/length z-score	-0.96 (-2.9, 0.38)	-0.63 (-1.73, 0.50)	0.001	1.30 (1.73, 1.37)	0.001

Values are median (IQR) unless specified. [a]Univariate analysis; [b]Multivariate analysis.

Discussion:

The Pneumonia Etiology Research for Child Health (PERCH) study is a prospective multisite, case-control study to describe the etiologic distribution of pathogens among 5000–7000 children hospitalized with severe or very severe pneumonia in settings characterized by the introduction of conjugate vaccines against Haemophilus influenzae type b (Hib) and Streptococcus pneumoniae [10].

The global prevalence of pneumonia is highest in the age group of 1–4 years [11]. Children residing in rural areas were more a_ected with severe pneumonia compared with children living in urban areas, and the condition showed a marked male predilection. Similar findings have been reported in other regions of India and other neighboring countries like Bhutan and Nepal [12-13].

Biomarkers like white blood cell (WBC) count and serum C-reactive protein (CRP) concentration are commonly used to diagnose CAP and define its etiology [14].

An elevation in CRP levels is generally considered as proof of bacterial infection [15]. WBC's application in identifying bacterial and nonbacterial pediatric CAP has been proved to be less reliable by more and more recent studies [16-17]. As an indicator of nutritional status, serum albumin has been associated with the risk of progressive disease among patients with pneumonia [18-20].

Males are more vulnerable to pneumonia and are given more preference for hospitalization. Females may have a greater resistance due to their enhanced Th1 immune response [21]. Under nutrition is a significant risk factor for the development of pneumonia in children [22] as also seen by us. Under nutrition is associated with secondary immune deficiency and an increase in the risk of infections, including pneumonia [23-25].

Conclusion:

Young age and under nutrition (low weight for height/length) in children are significant independent risk factors for pneumonia. Risk factors predicting disease severity among children hospitalized with CAP vary with age. Risk factor stratification of pediatric CAP based on age-specific risk factors can better guide clinical practice.

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