RESEARCH PAPER

Risk of Hospitalization in Under-five Children With Community-Acquired Pneumonia: *A Multicentric Prospective Cohort Study*

JAVEED IQBAL BHAT,[1] BASHIR A CHAROO,[1] APARNA MUKHERJEE,[2] RIDWANA AHAD,[1] RASHMI R DAS,[3] JAGDISH PRASAD GOYAL,[4] BHADRESH VYAS,[5] VINOD H RATAGERI,[6] RAKESH LODHA[7] AND ATU GROUP*

*From Departments of Pediatrics, [1]Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir; [2]Indian Council of Medical Research, New Delhi; [3]All India Institute of Medical Sciences, Bhubaneswar, Odisha; [4]All India Institute of Medical Sciences, Jodhpur, Rajasthan; [5]MP Saha Medical College, Jamnagar, Gujarat; [6]Karnataka Institute of Medical Sciences, Hubballi, Karnataka; [7]All India Institute of Medical Sciences, New Delhi. *Full list of ATU Group provided in Annexure I. Correspondence to: Dr Javeed Iqbal Bhat, Department of Pediatrics, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir, India. drjaveediqbal@gmail.com*

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Objective: To evaluate factors associated with risk of hospitalization in children with community-acquired pneumonia (CAP).

Design: Prospective cohort study.

Setting: Multi-site hospital based study.

Intervention: A separate acute respiratory tract infection (ARI) treatment unit (ATU) was established. The revised WHO case definition for ARI was used across all the study sites to ensure uniformity in management of ARI patients (2-59 months). Clinical history, examination findings and investigations of enrolled patients were recorded on a predesigned case record form. Children were followed up at 1 week (± 1 day).

Main outcome measure: Risk factors for hospitalization among pneumonia patients.

Results: A total of 7026 children with the diagnosis of ARI were enrolled. Pneumonia was diagnosed in 938 (13.4%) patients (median (IQR) age: 15 (8, 25) months; 63.5% boys). Hospitalization was needed in 56.8% of pneumonia patients. On multivariate analysis, factors associated with risk of hospitalization were: Oxygen saturation on pulse oximetry (SpO_2) <92% in room air (OR 7.04; 95% CI 1.6, 30.8, *P*=0.01), procalcitonin level >0.5 ng/mL (OR: 7.5, 95% CI: 1.0, 57.7, *P*=0.05), and lower weight for height *z*-score (OR 0.8; 95 % CI: 0.6, 0.9, *P*=0.02).

Conclusion: Present study found SpO_2 <92% at room air, serum procalcitonin level >0.5 ng/mL and lower weight for height *z*-score to be predictors for risk of hospitalization in under-five children presenting with community acquired pneumonia. These factors can be utilized to assess a child with CAP regarding the need of hospitalization.

Keywords: *Hypoxia, Outcome, Procalcitonin, Underweight.*

Community-acquired pneumonia (CAP) is one of the leading causes of morbidity and mortality in under-five children [1]. CAP is more common in the developing world, accounting for 95% of all cases [2]. In India, an estimated 4 lakh pneumonia deaths occur annually [3]. Efficient case management is a cornerstone of pneumonia control strategies. Simple clinical signs like rapid breathing, chest in drawing and general danger signs have been used by WHO to classify the severity of pneumonia in under-five children [1].

WHO revised case definition for CAP in under-five children has two categories – 'pneumonia', which is treated at home with oral amoxicillin and 'severe pneumonia, which requires hospitalization and parental antibiotics. Despite the improvement in case management of childhood pneumonia, mortality and morbidity still remains high, especially in resource-constrained settings. The early identification of important risk factors for hospitalization among these patients could help to prioritize the management and potentially increase their likelihood of surviving. This prospective study was conducted to evaluate the factors associated with risk of hospitalization in children with CAP.

METHODS

This was a multisite prospective cohort study conducted from June, 2016 to May, 2018 in following tertiary care hospitals of India: *i*) Sher-e-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, *ii*) All India Institute of Medical Sciences (AIIMS), Jodhpur, *iii*) AIIMS, Bhubaneswar, *iv*) Karnataka Institute of Medical Sciences, Hubballi, and *v*) MP Saha Medical College, Jamnagar. AIIMS, New Delhi was a coordinating center for the study. Prior ethical approval was obtained from institutional Ethics Committee of AIIMS, Delhi and all other five study sites.

Previously healthy children, 2 to 59 months of age, with acute respiratory infection (ARI) of less than 2 weeks duration were assessed for inclusion in the study. Children

suffering from chronic respiratory diseases (asthma, cystic fibrosis, bronchopulmonary dysplasia (BPD), airway anomalies), congenital heart disease, gastroesophageal reflux disease (GERD)/recurrent aspirations, suspected/ known immunodeficiency, patient living outside the city where the study site was based, history of radiologically confirmed pneumonia in last 2 months, and very sick child requiring immediate ICU care, were excluded.

A separate acute respiratory tract infection treatment unit (ATU) was established to manage all ARI patients. The ATU team comprised of a pediatrician and a trained nurse. All children between 2 months to 59 months of age with history of ARI were directed to attend ATU during working hours of the hospital. The revised WHO case definition for ARI was used across all the study sites to ensure uniformity in management of ARI patients. The revised classification includes two categories of pneumonia; 'pneumonia' with fast breathing and/or chest in drawing, and 'severe pneumonia,' pneumonia with any general danger sign [1]. Children were enrolled in the study after obtaining written, informed consent from parents or legal guardians. A detailed history was taken, and physical examination, including respiratory rate, presence of chest in drawing, pulse, temperature, oxygen saturation by pulse oximetry and anthropometry was done by the research nurse under the supervision of research officer. Each child's respiratory rate was counted for a full minute when the child was calm and quiet. If the child presented with fever and fast breathing, appropriate paracetamol dose was given and respiratory rate was reassessed after 30 minutes. Children presenting with wheeze and fast breathing were administered salbutamol nebulization (0.15 mg/kg single dose) and respiratory rate was reassessed after 10-15 minutes. Weight was measured to the nearest 0.1 kg using calibrated electronic scales, and height was measured to the nearest 0.1 cm using a standardized stadiometer. If a child was less than 2 years of age, recumbent length was measured by using an infantometer. Clinical history and examination findings of enrolled children were recorded on a predesigned case record form.

Every fifth child with ARI underwent a chest *X*-ray. The chest radiographs were interpreted by site investigator at the time of enrolment, thereafter, either original films or digital copies were sent to the coordinating centre at AIIMS, New Delhi. All chest *X*-rays were read by two independent pediatricians, who were blinded for the clinical diagnosis of the patient. In case of disagreement about the presence or absence of pathology, chest *X*-rays were read by a third pediatrician without knowledge of the previous evaluations and final findings matching for two of them were considered for purpose of analysis. Patients with suspected pneumonia underwent serum quantitative procalcitonin (PCT) estimation. All children were followed till 7 days (±1 day) after enrolment. Parents were given reminder telephone call one day prior to the anticipated follow-up. All admitted patients were examined daily until discharge.

Management of children with pneumonia was done according to the WHO recommendations [1]. Any child with severe pneumonia was hospitalized; the treating physicians' assessment was the deciding factor in other cases.

The aim was to enrol about 4000 children per site giving a total data of about 20000 children across all the sites. Of these 30-40% may be because of respiratory problems. Approximately 6000-8000 children with ARI, i.e approximately 1200-1500/site were expected to be enrolled. About 10% children with acute respiratory infection may develop pneumonia. As the primary aim of the ATU project was to improvise clinical case definition (combine clinical features) of CAP with a sensitivity and specificity of 80% (sensitivity of tachypnea with/without chest indrawing is about 69%) and precision of 5%, we needed a total of 256 children with pneumonia. We expected that this sample size could be easily achieved.

Statistical analysis: A data entry program in Microsoft Access was developed at AIIMS, New Delhi. The data from all the study sites were sent to AIIMS for analysis. Children with CAP (as per WHO criteria) needing hospitalization were compared to those who did not, by univariate analysis, followed by multivariate analysis using a logistic regression model; the dependent criteria was whether hospitalization occurred or not, independent covariates were the ones which emerged statistically significant in univariate analysis. The *z*-scores for weight for age, height for age and weight for height were calculated using the WHO Anthro software.

RESULTS

A total of 18159 under-five children were screened; 7026 (39% of screened) children assessed to have ARI were enrolled in the study. Using the WHO criteria, pneumonia was diagnosed in 938 (13.4%) patients; remaining 6088 patients were labelled as having upper respiratory tract infection. Hospitalization was needed in 533 (56.8%) children with pneumonia including 7 patients who were initially given ambulatory treatment and were later admitted in view of deteriorating respiratory distress. Four hundred and five (43.2%) children with pneumonia received ambulatory treatment. The baseline demo-graphic and clinical characteristics of the study population are shown in **Table I**. Amongst children with pneumonia, reportable chest *X*-rays were available in 563 cases (total *X*-rays 571).

Factors associated with hospitalization in children with pneumonia were younger age, lower weight- and height-for-age *z*-scores, higher PCT levels, lower SpO_2, and higher

percentage of significant pathology in chest-*X*-rays as compared to those receiving ambulatory treatment (**Table II**).

On multivariate analysis, factors associated with hospitalization were SpO_2 <92% in room air [OR (95%CI) 7.04 (1.6-30.8); *P*=0.01], PCT level > 0.5 ng/mL [OR (95%CI) 7.5 (1.0-57.7); *P*=0.05] and low weight for height *z*-score [OR (95%CI) 0.8 (0.6-0.9); *P* = 0.02].

DISCUSSION

In this multi-site prospective observational study, hospitalization was needed in 56.8% of patients diagnosed with pneumonia as per current the WHO criteria. Risk factors associated with hospitalization were SpO_2 < 92% on room air, serum PCT levels >0.5 ng/mL, and lower weight for height *z*-score.

Majority of the patients of ARI can be managed safely in the community [5,6]. Hospital admission in revised WHO case definition for CAP management in under-5 children is recommended when the child is brought with general danger signs like not able to drink, persistent vomiting, convulsions, lethargy or unconsciousness, stridor in a calm child or severe malnutrition [1]. The WHO recommendations; however, do not include several parameters which have been proven to predict severity of pneumonia in under-five children more accurately [7,8]. Studies from different parts of the world have observed that hypoxic children are more likely to die than adequately oxygenated children [9,10]. In a systematic review, the median prevalence of hypoxemia in WHO-defined severe and very-severe pneumonia was 13% [11]. The British Thoracic Society guideline recommends that SpO2 below 92% in childhood CAP warrants hospital admission and optimal management [5]. We have utilized pulse oximetry for measurement of SpO2 in our study, which has been recommended as a standard point of care for SpO2 monitoring in children with pneumonia [12,13]. A recent meta-analysis also concluded that the pulse oximetry is a useful tool for hypoxemia screening and optimal oxygen supplementation to prevent pneumonia deaths in children [14]. Our study findings corroborates with these observations. Detection of hypoxemia by pulse oximetry should be an important component for assessment of a child with CAP so that a decision regarding the severity of pneumonia and need for hospitalization can be taken.

Serum PCT level > 0.5 ng/mL had a higher odds of hospitalization in our cohort of children with CAP. Multiple studies in both adults and children have shown that serum PCT is a surrogate tool to differentiate between viral and bacterial pneumonia, and the latter has higher probability of hospitalization [15,16]. Serum PCT levels can be used as a point of care diagnostic tool to assess severity of pneumonia in children with CAP as this investigation is becoming increasingly available even in smaller hospitals in our country.

Malnourished children have a higher incidence and severity of CAP. Mortality increases proportionately with severity of malnutrition [18]. We also found significantly increased risk of hospitalization among children with

Table I Demographic and Clinical Details of Children with Community-acquired Pneumonia (*N*=938)

Characteristics	*Values*
Age, mo[a]	15 (8,25)
Boys	596 (63.5)
Weight for age *z*-score[a]	-1.34 (-2.5, -0.18)
Height for age *z*-score[a]	-1.2 (-2.6, 0.12)
Weight for height *z*-score[a]	-0.77 (-1.96, 0.3)
Respiratory rate /min, mean (SD)	54 (11)
Chest indrawing present	455 (48.5)
SpO_2 %, mean (SD)	94.3 (5.1)
Procalcitonin level, ng/mL (*n*= 12)[a]	0.1 (0.05, 0.44)
Significant pathology in CXR (*n*=563)	331 (58.8)

Values in no. (%) or [a]median (IQR). CXR: chest X-ray.

Table II Factors Associated With Hospitalization in Community-acquired Pneumonia (*N*=938)

Characteristics	*Hospitalized children (n=533)*	*Ambulatory treatment (n=405)*
Age, mo[a]	12 (7,20)	18 (9,35)
Boys, *n* (%)[b]	342 (64.2)	254 (62.7)
Weight for age *z*-score[a]	-1.67 (-2.75, -0.53)	-0.84 (-2.02, 0.22)
Height for age *z*-score[a]	-1.37 (-2.72, -0.12)	-0.9 (-2.46, 0.6)
Weight for height *z*-score[a]	-1.11 (-2.36, 0.03)	-0.27 (-1.43, 0.54)
Significant pathology in CXR, *n* (%)[c]	268 (63.9)	63 (43.7)
Procalcitonin level, ng/mL[d]	0.14 (0.05, 0.54)	0.05 (0.05,0.07)
SpO_2 %, mean (SD)	93 (5.9)	95.9 (3.1)

Values are expressed as median (IQR) unless specified. All P<0.001 except [a]P=0.008 and [b]P=0.65. [c]Chest X-ray available in 563 (419 inpatients and 144 out patients; [d]procalcitonin levels available in 312 (284 inpatients and 28 outpatients).

WHAT IS ALREADY KNOWN?

- Delayed hospitalization in children with severe community-acquired pneumonia is associated with increased mortality.

WHAT THIS STUDY ADD?

- Hypoxia (SpO2 <92% in room air), higher serum procalcitonin levels (>0.5 ng/mL) and lower weight for height *z*-score can predict hospitalization in under-five children with community-acquired pneumonia.

undernutrition. The variable used was weight for height *z*-score. With one unit increase in weight for height *z*-score, the odds for hospitalization was 0.8. Our study has some limitations. Since the readmission rate was very low in our study, no meaningful analysis of factors determining hospitalization after starting ambulatory treatment could be done.

To conclude, our study found SpO2< 92% by pulse oximetry, serum procalcitonin level >0.5 ng/mL, and low weight for height *z*-score as important predictors for risk of hospitalization in under five children presenting with CAP. Routine monitoring of SpO_2 by pulse oximetry and serum PCT levels can be used to identify high risk patients who would require inpatient care.

Contributors: JIB, BAC, RA: involved in data collection and manuscript writing; AM,RL: involved in development of protocol, supervision of the study, data analysis; JPG, RRD,VHR,BV: data collection, manuscript review. All authors approved the final version submitted.

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ANNEXURE I

***Members of The ATU (Acute Respiratory Infection Treatment Unit) Group**

Daisy Khera, *Department of Pediatrics, AIIMS, Jodhpur, Rajasthan;* Deepak Singhal: *Department of Pediatrics, AIIMS, Jodhpur, Rajasthan;* KR Jat, *Department of Pediatrics, AIIMS, New Delhi;* Kuldeep Singh, *Department of Pediatrics, AIIMS, Jodhpur, Rajasthan;* Partha Sarathi Ray, *AIIMS, Bhubneshwar, Odisha;* Prawin Kumar, *Department of Pediatrics, AIIMS, Jodhpur, Rajasthan*; Samarendra Mahapatro, *AIIMS, Bhubaneswar, Odisha;* SK Kabra, *Department of Pediatrics, AIIMS, New Delhi.*