Original Article

Lower RTI

Predisposing Factors Associated with Longer Hospital Stay in Children Less Than 5 Years of Age with Severe Lower Respiratory Tract Infection

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ABSTRACT

Objective: To determine the predisposing risk factors associated with longer duration of hospitalisation of children aged 2-59 months with severe Lower respiratory tract infection (LRTI).

Study Design: Observational / descriptive / cross sectional study

Place and Duration of Study: This study was carried out in the Children Hospital, Islamabad from October 2011 to March 2014.

Materials and Methods: We enrolled 606 children aged 2-59 months with severe LRTI and at enrolment, complete history of present illness, physical examination, and necessary laboratory investigations were done. Enrolled children were managed according to the hospital's standard protocols. Multivariate logistic regression analyses was conducted to determine the independent factors associated with longer duration of hospitalisation.

Results: The mean (sd) age of children was 7.45 (8.41) months and 63% were male. Of 606 children, 241 (40%) had longer hospital stay (>3 days).Children whose mothers used biomass energy as fuel for cooking at home (AOR 3.63, p<0.0001), children who had history of vomiting (AOR 1.74, p=0.014), had duration of illness before presenting to hospital was >7 days (AOR 1.90, p=0.040), were unvaccinated (AOR 2.54, p=0.001), had lower mean serum calcium levels (AOR 0.08, p<0.0001), had positive CRP (AOR 4.67, p<0.0001), were severely anaemic (AOR 6.28, p=0.017) or were underweight (AOR 1.64, p=0.013) had significantly longer hospitalisation compared to their counterparts.

Conclusion: The current study identified independent risk factors which lead to longer hospitalisation in children aged 2-59 months with severe LRTI. Findings of the current study would help paediatricians for better management of severe LRTI in under 5 children.

Key Words: Lower respiratory tract infection, Hospitalisation, Predisposing factors, Child, Biomass energy

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INTRODUCTION

Almost half of the annual 6.3 million under-five deaths occur in five countries including Pakistan[1]. The current under-five mortality rate in Pakistan is 89/1,000 livebirths[2]. Most of the under-five deaths (64%) are contributed to the infectious diseases including lower respiratory tract infection (LRTI)[3], which is the number one killer of under-five[3]. The disease burden is present in younger age as 81% of deaths attributed by LRTI is in children <2 years[4].

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Further, childhood LRTI is the major reason for hospitalization in developing countries[4]. The management of LRTI primarily consists in eradicating the organism. Empirical antibiotic treatment given is based on the pathogens that commonly cause LRTI. There is a need for early identification of children with severe LRTI who are at high risk for longer hospitalisation for aggressive management. We conducted this study to determine the predisposing factors resulting in longer hospitalisation in children aged 2-59 months with severe LRTI.

MATERIALS AND METHODS

We conducted a prospective cohort study at the Children Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad Pakistan. Children with LRTI were screened to been rolled at the time of admission. Children with LRTI were ranked from mild to severe LRTI based on the clinical score system[5] as given in Table 1. 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. We included children aged 2-59

months diagnosed to have severe LRTI. Children who had LRTI with congenital heart disease, cerebral palsy, chromosomal defects (Down's syndrome), Edward's syndrome, spinal muscular atrophy or storage disorder were not included. We calculated the data between October 2011 and March 2014.

Ethics: We obtained informed verbal consent from parents/care givers of each child enrolled in the study. The study protocol was approved by the Hospital Ethics Committee, PIMS Islamabad.

Data collection procedure: We screened all children with LRTI based on clinical severity score. We counted the respiratory rate for aminutetwice, within 5 minutes when the child was quiet, feeding or asleep. We considered the average value of two readings for each child. Each child was evaluated for audible and auscultatory wheeze, and the general condition at the time of enrolment. In case of wheezing, we provided inhaled salbutamol and reassessed the child after up to three cycles of bronchodilator therapy, which were repeated (if necessary) at 20 minute interval[6]; and often given injectiblesteroids. We calculated the clinical severity score again and a child whose score was decreased from severe LRTI to moderate LRTI was then discharged from the hospital with oral antibiotics and/or salbutamol. Those children who had severe LRTI even after inhalation, were enrolled in the current study.

We gathered and reported the information about demographic features, vaccination status, feeding pattern, family history of asthma, and a complete history of current illness at the time of enrolment. We recorded the actual temperature and the anthropometry measurements using the standard technique from each enrolled child. We weighed children aged <2 years with minimum clothing using a digital baby scale, with a 16 kg capacity and a sensitivity of 10 grams. We measured their lengths in decubitus dorsal on a flat surface with an anthropometric rule scaled in centimetres up to a maximum of 1 millimetre. We weighed children aged ≥2years with a minimum of clothing using an adult scale accurate to 100 grams. We measured the height of the children while standing upright against a vertical rule with a metric scale, reading up to 150 centimetres, marked off in centimetres and fixed to the wall[7]. We assessed the nutritional status 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). The nutritional status was categorised based on 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)[8].

We obtained a blood sample for full blood count, C reactive protein (CRP) and serum calcium concentrations and sent to the Department of Pathology for analysis. We managed all children based on the hospital's standard protocols. To summarised, all the enrolled children were kept nil by mouth and we provided them intravenous rehydration. We also given them oxygen inhalation through nasal prongs. In addition, we also provided them inhaled salbutamol at 6-8 hourly intervals, if necessary. We also provided first line injectible antibiotics - Ampicillin and Amikacin at 8-12 hourly intervalsto all the enrolled children and then we followed up them at 12 hourly intervals till the time of discharge. At the time of follow up,we calculated the clinical severity score of each child and noted on the performa. We decided to discharge a child from hospital with oral medication when clinical severity scores was reduced to <9 (moderate to mild disease). At the day of discharge we calculated the days of hospitalisation of child.

Potential risk factors and study outcome: The potential factors assessed for duration of hospitalisation were: age and gender, socio-economic status (middle class monthly income >Rs.6000, lower class monthly income ≤Rs. 6000), history of fever, cough, difficult breathing, poor feeding, vomiting, fits, duration of present illness (in days), vaccination till date (fully vaccinated, partially vaccinated, unvaccinated), feeding practices (exclusive breastfeeding <6 months of age, non-exclusive breastfeeding <6 months of age, any feeding after 6 months of age), family history of asthma, presence of wheeze, lethargy, respiratory rate (breaths/min), actual temperature (in ^{0}F), nutritional status of a child (underweight <-2 WAZ, stunting <-2 HAZ, and wasting <-2 WHZ), CRP, serum calcium concentrations, and anaemic condition of a child based on WHO criteria as child whose serum haemoglobin level was ≥11 g/dl was categorised as no anaemia; whose serum haemoglobin level was 10-10.9 g/dl was classified as mild anaemia; whose serum haemoglobin level was 7-9.9 g/dl wasclassified as moderate anaemia: and whose serum haemoglobin level was <7 mg/dl was classified as severe anaemia[9].

The outcome measures were duration of hospitalisation categorised as shorter hospital stay if a child was discharged within 3 days of admission and longer hospital stay if a child was discharged after 3 days of admission, based on clinical severity score.

Sample size and statistical analysis: We used the standard formula for single proportion(10) to calculated the sample size. We assumed 10% prevalence of children aged 2-59 months with severe LRTI would be admitted at the Children Hospital (based on annual hospital admission data) and considered that absolute precision at 2.4%, and with 95% confidence level, the required sample size was 600 children aged 2-59 months with severe LRTI.

We used STATA 13.1 (Stata-Corp, College Station, TX, USA) software to analyse the data. For categorical variables we calculated frequencies and percentages. For continuous variables we calculated the mean (±Standard deviation) with median (interquartile range).To identify predisposing factors resulting in

longer hospitalisation, logistic regression was performed. First, univariate or bi-variate regression analyses to identified potential risk factors was performed. Later, multivariate logistic model by considering all variables, which showed p value of <0.2 at univariate analyses, was constructed using a backward elimination technique. We presented results as adjusted odds ratio (OR), 95% confidence interval (CI) and p-value. The significant level was considered at 5%.

RESULTS

Trial profile: During the study period, a total of 11,713 children presenting with respiratory tract infection visited the hospital and of those, 888 (7.6%) children were diagnosed to have LRTI and were admitted. Out of 888, 606 (68.2%) children aged 2-59 months had severe LRTI. Of 606 children with severe LRTI, 365 (60%) children had shorter hospitalisation (≤3 days) while 241 (40%) had longer hospitalisation (>3 days).

Table No.1: Description of clinical severity score used in the current study

Sign/ symptoms	0 point	1 point	2 points	3 points
Respiratory rate (breaths/min)	<30	31–45	46–60	>60
Wheezing	None	Terminal expiratory or heard only with a stethoscope	Entire expiration or audible on expiration without a stethoscope	Inspiration and expiration without a stethoscope
Retractions	None	Subcostal	Intercostal or tracheosternal	Severe with nasal flaring
General condition	Normal		Irritable	Lethargic, poor feeding

Baseline characteristics*:* The baseline characteristics of children aged 2-59 months had severe LRTI and outcome measures are presented in Table 2. The mean (sd) age of children was 7.45 (8.41) months with an interquartile range of 2 to 9 months. The mean (sd) duration of illness before presentation was 4.39 (3.48) days with an interquartile range of 2 to 5 days. Substantial majority of children were fully vaccinated (79.9%). On examination, 157 (25.9%) had wheeze (either audible or auscultatory), and 34 (5.6%) had signs and symptoms suggestive of rickets. The mean (sd) respiratory rate was 63.0 (9.14) breaths per minute and mean (sd) temperature at the time of enrolment was 99.0 $(5.86)^0$F. The mean (sd) serum calcium concentrations was 1.12 (0.21). Ninety seven (16%) children had positive CRPand 405 (66.8%) children were anaemic. The nutritional status of children showed that the mean (sd) values of WAZ, HAZ and WHZ were -1.42 (1.66), -1.53 (2.00) and -1.18 (1.79), respectively. Of 606, 213 (35.2%), 217 (35.8%) and 69 (11.4%) children were underweight, stunted and wasted, respectively. The mean (sd) duration of hospitalisation was 4.19 (3.44) days with interquartile range of 2 to 5 days.Out of 606, 365 (60%) children has shorter hospitalisation (≤3 days), whereas,241 (40%) children had longer hospitalisation (>3 days).

Table No.2: Baseline characteristics and outcome measures of children age 2-59 months with severe LRTI (n=606)

Variables	n (%)
Age categories	
2 to 5 months	408 (67.3)
6 to 11 months	95 (15.7)
12 to 59 months	103 (17.0)
Gender	
Male	379 (62.5)
Female	227 (37.5)
Fuel used for cooking at home	
Natural gas/ electricity/ LPG	417 (68.8)
Biomass energy	184 (30.4)
Missing	5 (0.8%)
Vomiting	
No	472 (77.9)
Yes	134 (22.1)
Duration of symptoms categories (in days)	
Upto 7 days	547 (90.3)
>7 days	59 (9.7)
Vaccination status	
Fully vaccinated	484 (79.9)
Partially vaccinated	51 (8.4)
Unvaccinated	70 (11.5)
Missing	1 (0.2%)
Wheezing	
No	449 (74.1)
Yes	157 (25.9)
Signs and symptoms suggestive of rickets	
No	572 (94.4%)
Yes	34 (5.6%)
Serum calcium levels	
Mean (SD)	1.12 (0.21)
Median (IQR)	(0.58 – 1.25)
C-reactive protein	
Negative	509 (84.0%)
Positive	97 (16.0%)
Anaemic status	
No anaemia	201 (33.2)
Mild anaemia	162 (26.7)
Moderate anaemia	231 (38.1)
Severe anaemia	12 (2.0)
Underweight (WAZ <-2)	
No	393 (64.8)
Yes	213 (35.2)
Stunting (HAZ <-2)	
No	389 (64.2)
Yes	217 (35.8)
Wasting (WHZ <-2)	
No	537 (88.6)
Yes	69 (11.4)

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

Table No.3: Predisposing factors associated with longer hospital stay in children <5 years of age with severe lower respiratory tract infection: findings of univariate and multivariate regression analyses (n=606)

	Shorter stay (≤3 days)	Longer stay (>3 days)	Unadjusted		Adjusted	
Variable	n (%)	n (%)	OR (95% CI)	p	OR (95% CI)	p
Fuel used for cooking at home						
Natural gas/ electricity/ LPG	266 (72.9)	151 (62.7)	1.00 (reference)		1.00 (reference)	
Biomass energy	94 (25.8)	90 (37.3)	1.69 (1.19, 2.40)	0.003	3.63 (2.29, 5.76)	<0.0001
Vomiting						
No	296 (81.1)	176 (73.0)	1.00 (reference)		1.00 (reference)	
Yes	69 (18.9)	65 (27.0)	1.58 (1.08, 2.33)	0.020	1.74 (1.12, 2.71)	0.014
Duration of symptoms categories (in days)						
Upto 7 days	337 (92.3)	210 (87.1)	1.00 (reference)		1.00 (reference)	
>7 days	28 (7.7)	31 (12.9)	1.78 (1.04, 3.05)	0.037	1.90 (1.04, 3.49)	0.040
Vaccination status						
Fully vaccinated	305 (83.6)	179 (74.3)	1.00 (reference)		1.00 (reference)	
Partially vaccinated	33 (9.0)	18 (7.5)	0.92 (0.51, 1.70)	0.812	1.48 (0.73, 2.99)	0.268
Unvaccinated	26 (7.1)	44 (18.3)	2.88 (1.72, 4.84)	<0.0 001	2.54 (1.43, 4.49)	0.001
Serum calcium levels						
Mean (SD)	1.17 (0.23)	1.06 (0.15)		<0.0 001	0.08 (0.03, 0.22)	<0.0001
C-reactive protein						
Negative	329 (90.1)	180 (74.7)	1.00 (reference)		1.00 (reference)	
Positive	36 (9.9)	61 (25.3)	3.10 (1.97, 4.85)	<0.0 001	4.67 (2.79, 7.83)	<0.0001
Anaemic status						
No anaemia	109 (29.9)	92 (38.2)	1.00 (reference)		1.00 (reference)	
Mild anaemia	105 (28.8)	57 (23.6)	0.64 (0.42, 0.98)	0.042	0.67 (0.41, 1.08)	0.099
Moderate anaemia	148 (40.5)	83 (34.4)	0.66 (0.45, 0.98)	0.038	0.75 (0.48, 1.15)	0.185
Severe anaemia	3 (0.8)	9 (3.7)	3.55 (0.94, 13.5)	0.063	6.28 (1.39, 28.3)	0.017
Underweight (WAZ <-2)						
No	250 (68.5)	143 (59.3)	1.00 (reference)		1.00 (reference)	
Yes	115 (31.5)	98 (40.7)	1.49 (1.06, 2.09)	0.021	1.64 (1.11, 2.42)	0.013

CI: Confidence interval. OR: Odds ratio. NS: Non-significant. Adjusted for all baseline characteristics

Univariate and Multivariate analysis*:* Table 3 presents the findings of uni-and multi-variate analyses of comparison of baseline characteristics of children aged 2-59 months with severe LRTI between shorter and longer hospitalisation. Our multivariate analysis showed that children whose mother used biomass energy as fuel for cooking at home (AOR 3.63, 95%CI 2.29, 5.76, p<0.0001), who had history of vomiting (AOR 1.74, 95%CI 1.12, 2.71, p=0.014), had duration of current illness for <7 days (AOR 1.90, 95%CI 1.04, 3.49, p=0.040),were unvaccinated (AOR 2.54, 95%CI 1.43, 4.49, p=0.001), had lower mean serum calcium levels (AOR 0.08, 95%CI 0.03, 0.22, p<0.0001), had positive CRP (AOR 4.67, 95%CI 2.79, 7.83, p<0.0001), were severely anaemic (AOR 6.28, 95%CI 1.39, 28.3, p=0.017) or were underweight (AOR 1.64, 95%CI 1.11, 2.42, p=0.013) at the time of enrolment had significantly longer hospital stay compared to their counterparts without these factors after adjusted for other baseline characteristics.

DISCUSSION

LRTI is one of the major killer of under-five[3] and it is one of the major contributor for paediatric hospitalisation in developing countries[4]. The current study was conducted to determine the predisposing factors contributing to longer hospitalisation in children aged 2-59 months with severe LRTI. The findings of the current study are important for paediatricians in our local areas for the better management of the children with severe LRTI. These findings are comparable with other studies as well.

In the current study, children aged 2-59 months with severe LRTI, whose mother used biomass energy as fuel for cooking at home had 3.6 times significantly higher odds of longer hospitalisationthan those whose mother used natural gas for cooking. Burning biomass fuels and coal in simple stoves with inadequate ventilation result in indoor air pollution, which is responsible for more than 1.6 million deaths annually and 2.7% of the global burden of disease[11]. A study from Ethopia reported a significantly higher odds (AOR 2.97, 95% CI 1.38, 3.87) of prevalence of LRTI in children whose mother used biomass energy for cooking compared to those whose mother used clean fuels[12]. The biomass fuel could increase the incidence of LRTI by adversely affecting specific and nonspecific host defences of respiratory tract against pathogens[13].

At the same time, severely anaemic children aged 2-59 months with severe LRTI in our study had significantly higher odds of longer hospitalisation than those without anaemia. Severe anaemia is one of the predictor of mortality in hospitalised children with severe LRTI[14].

The odds of longer hospitalisation was significantly lower in children aged 2-59 months with severe LRTI who had higher serum calcium levels compared to those who had lower serum calcium levels. Deficiency of calcium is one of the predictor of LRTI in Ethiopian children <5 years of age[15]. A study from Karachi found that 74% of children admitted with LRTI had nutritional rickets[16].

In the present study children aged 2-59 months with severe LRTI who had positive CRP had 4.7 times higher odds of longer hospitalisation than those with negative CRP. Meta-analysis of eight studies found that children with LRTI who had bacterial infection had 2.6 times higher odds of positive serum CRP concentrations than children with nonbacterial infections[17]. Differentiating bacterial from nonbacterial pneumonia in children is a major clinical challenge because of the difficulty in obtaining adequate samples for culture and the lack of reliable diagnostic methods for differentiating infection from colonization[18].

The study shows that underweight children aged 2-59 months with severe LRTI had 1.6 times higher odds of longer hospitalisation compared to those with normal weight. Severe malnutrition increases the risk of mortality in children with severe LRTI[16]. It is one of the important risk factor for treatment failure after 48 hours among Kenyan and Indian children with severe LRTI[19]. It is reported that 52% of childhood deaths as a result of pneumonia are attributable to under nutrition[20].

It was found that children aged 2-59 months with severe LRTI who had duration of illness >7 days had 1.9 times significantly higher chances of longer hospitalisationthan those who had ≤7 days of duration of present illness. Delay(between 3 and 7 days) in seeking medical treatment at a health facility is one of the major risk factor for severe LRTI in children, evident from reports from Kenya[21] and Uganda[22]. The progress of LRTI is rapid and delayed treatment can lead to increased disease severity and even death.

Children aged 2-59 months with severe LRTI who had history of vomiting stayed at hospital for longer duration than children who did not have vomiting. Several studies from Pakistan have reported history of vomiting as one of the risk factor for treatment failure in children with LRTI[23,24].

We found that the odds of children aged 2-59 months with severe LRTI who were unvaccinated was 2.5 times higher odds for longer hospitalisation compared to those who were fully vaccinated. A study from Indian found that children who were unvaccinated (primary measles) 2.6 times higher adjusted odds of longer hospital stay (>48 hours)[25].

The strengths of present study are that,firstly the current study was conducted in a tertiary care hospital which covers a wide geographic area. Secondly, an appropriate sample size was collected over the period of three years. Thirdly, multivariate logistic regression analysis was conducted and adjusted for several potential confounding factors to obtain the independent factors leading to longer hospital stay. However, one of the major limitation of the current study was enrolment of children during ARI season (that is between October and March), hence, no seasonal variation was considered during analysis.

CONCLUSIONS

The current study findings show that children aged 2-59 months whose mother used biomass energy as fuel for cooking at home, children with history of vomiting, were unvaccinated, were delayed in seeking treatment at a health facility, had lower mean serum calcium levels, had positive CRP, were severely anaemic or were underweight had significantly longer hospitalisation compared to their counterparts without these factors. These findings are important for the paediatricians of the local area, as they define a high risk group for delayed treatment response and hence resulting in longer hospitalisation. Further, there is a need to develop and implement preventive strategies such as elimination of indoor air pollution, universal coverage of vaccination and improving the nutrition status of the children to reduce the burden of disease in Pakistan. Appropriate selection of these high risk group

children with LRTI for early admission and providing them better management will reduce the mortality.

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