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# EVALUATION OF RISK FACTORS FOR MORBIDITY AND MORTALITY IN CHILDREN AGED 6 MONTH- 5 YEARS PRESENTING WITH LOWER RESPIRATORY TRACT INFECTION TO A REFERRAL HOSPITAL

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**Abstract**
Acute lower respiratory tract infection in children is a major cause of mortality and morbidity worldwide. A simple clinical score predicting the probability of death and poor outcome in a young child with lower respiratory tract infection (LRTI) could aid clinicians in case management and provide a standardized severity measure during epidemiologic studies. Therefore, our study was aimed to assess the usefulness of one such scoring model, the RISC score, in an urban setting in eastern part of India and also to determine significant risk factors for LRTI in young children
Our study concluded that the RISC score maybe used as an index of severity in children with LRTI, as a complementary tool to the current IMCI framework, to ensure appropriate treatment and hospitalization in children, who are most in need. Also, recognizing the risk factors at presentation, may facilitate decisions about the most appropriate site of treatment (i.e., home vs. hospital) or the need for additional supportive care (i.e., supplemental oxygen or intensive care).
**Keywords:** Morbidity, Mortality in Children, Lower Respiratory Tract Infection, LRTI, etc.

## Introduction

Acute lower respiratory tract infection (LRTI) is the single largest cause of death in children in most developing countries. It accounted for 2, 53,877 of death of children aged 1-59 months and 24% of all the deaths in children <5 years in India, according to the official data by WHO [1], for the year 2010. Children can be protected from LRTI, as it can be prevented by simple interventions and treated with low-cost and low-tech medication and care, especially if detected early. [2] Hence, the identification and evaluation of risk factors for both morbidity and mortality in LRTI in young children is one of the most important steps in ensuring optimal utilization of scarce resources so that effective preventive strategies and early appropriate therapy can be instituted.

Clinical prediction scores have been developed and validated to aid clinicians in managing and treating adult patients with community-acquired pneumonia and other LRTIs. There are various scoring systems for the pediatric population too, namely, PSI (Pneumonia severity index) and PRISM score (Pediatric risk of mortality) [3], which are however complicated to an extent and prognosticate complicated hospitalized patients. A simple pediatric severity score like the Respiratory Index of Severity in Children (RISC) [4] score can help in more specific discrimination of children with LRTI, at presentation and follow-up, based on their risk of mortality may help refine decisions about case management.

Respiratory index of severity in children (RISC) score is a composite score that uses the oxygen saturation, ability to feed, presence of chest in drawing and nutritional status. The score ranges from zero to six, with six being the poorest score. This will further lead to maximal utilization of resources and minimize cost in a resource-limited country by complimenting the current IMCI framework by predicting the probability of death in a child who presents with respiratory illness or provide a standardized means of quantifying severity among children during vaccine trials and other epidemiologic studies. Furthermore, it needs to be emphasized that this a simple scoring model, which does not need any laboratory parameters and can be easily done in both emergency setting and in OPD, and since it is an objective score, it helps in follow-up and can be applied by different observers.

Therefore, this study attempts to ascertain its ability to predict mortality and morbidity in respiratory illnesses by evaluating the performance and accuracy of the scoring model in the context of Indian children.

The study was undertaken with specific aims and objectives as stated below:

Aims:

1. To assess the severity of LRTI in children aged 6 month-5 years using the RISC scoring system in the hospital setting and to evaluate the prognosis of these children using this scoring model.

2. To evaluate which are the risk factors that consistently predict mortality and morbidity in LRTI in young children aged 6 month – 5 years.

Objectives:

1. Describe the RISC scores of children aged 6 month- 5 years hospitalized with acute lower respiratory tract infections.
2. Assess short-term treatment outcomes.
3. Determine the relationship between the RISC score and poor outcomes.
4. To make suitable recommendations based on the outcome of the study.

**Methodology:**

The present study was planned in Patna Medical College & Hospital, Patna, Bihar, India. All children between the ages of 6 month and 5 years attending the OPD/emergency between the defined study period & satisfying the inclusion criteria, were recruited for the study. There were 132 such cases, out of which 3 did not give consent & 25 were lost to follow up. So, the total numbers of cases were 104. Children aged 6 month - 5 years either hospitalized or brought to the OPD/Emergency of our hospital with symptom complex of fever, cough, rapid breathing and/or difficulty in breathing. These cases of LRTI were included in the study.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

INCLUSION CRITERIA: Children aged 6 month- 5 years either hospitalized or brought to the OPD/Emergency of our hospital with symptom complex of fever, cough, rapid breathing and/or difficulty in breathing. These cases were included in the study and the LRTIs were classified in the following categories15:

EXCLUSION CRITERIA:

1. Children with a final diagnosis of tuberculous pneumonia or chemical pneumonitis.
2. Those in whom the data was incomplete (discharge against medical advice, absconded or incomplete follow-up)
3. Those children whose parents did not give consent.
4. Children with known HIV infection.
5. Those children with known heart disease, asthma and hypertension.

**Results & Discussion:**

Our study included a total of 104 subjects with LRTI, who satisfied the inclusion criteria. There were a total of 59 males (56.7%) and 45 females (43.3%). Proportion of males was higher in the whole study population and in each group. None of the subjects had underlying heart disease, hypertension, and bronchial asthma and HIV infection.

**Table 1**: Sex wise distribution of cases

| Sex | No. of subjects | % of subjects |
|---|---|---|
| Male | 59 | 56.7 |
| Female | 45 | 43.3 |

Age of the subjects ranged from 6 to 60 months, with a mean age of 25.3 months.

**Table 2:** Age wise distribution of population under study

| Age (Months) | No. (%) |
|---|---|
| 06 – 12 | 33 (31.73%) |
| 13 - 24 | 29 (27.88%) |
| 25 - 36 | 18 (17.30%) |
| 37 - 48 | 12 (11.53%) |
| 49 - 60 | 12 (11.53%) |

**Table 3:** Risk Factors for Prolonged hospitalization (Length of stay in hospital ≥ 5 days)

| Risk Factors | Prolong hospitalization (Length of Stay more than 5 days)# | Odds Ratio ( 95% CI) | P value |
|---|---|---|---|
| Age < 8 months | 7 (63.64%) | 3.86 (1.080, 15.728) | 0.042338** |
| Sex (Male) | 20 (33.90%) | 0.93 (0.411, 2.113) | 0.860 |
| Z score ≤ -2 | 15 (42.86%) | 1.71 (0.734, 3.999) | 0.21 |
| Tachypnea | 36 (39.56%) | 2.78e+07 (3.66e-35, n/a) | 0.988 |
| Hypoxemia | 16 (100%) | 3.93e+08 (2.63e-49, n/a) | 0.99 |
| Refusal of Feeds | 31 (47.69%) | 6.2 (2.31, 19.87) | 0.00072** |
| CXR + | 33 (66.00%) | 33 (10.23 149.94) | 1.45e-07** |
| Wheezing | 0 (0.00%) | 3.53e-08 (n/a 4.87e+31) | 0.9871 |
| Hypoxemia | 16 (100%) | 81 (18.27, 591.26) | 2.53e-07** |

# Out of total cases (In patient + Outpatient) ** P value less than 0.05

Simple logistic regression shows "Age less than 8 months" [odds ratio 3.86, 95% confidence interval (1.080, 15.728)], "Refusal of feeds" [odds ratio 6.2, 95% CI (2.31, 19.87)], "Positive CXR" [odds ratio 33, 95% CI (10.23 149.94)] and "Hypoxemia" [odds ratio 81, 95% CI (18.27, 591.26)] are factors significantly associated with prolonged hospitalization (more than 5 days) with p values 0.042338 (<0.05), 0.00072 (<0.05), 1.45e-07 ( < 0.05) and 2.53e-07 (<0.05) respectively.

**Table 4:** Risk factors for Prolonged Hospitalization (Length of Stay more than 5 days)

| Risk Factors | Adjusted Odds Ratio (95% CI) | P value |
|---|---|---|
| Age < 8 months | 1.254 (0.113, 15.098) | 0.850 |
| Hypoxemia | 1.51e+08 (1.38e-65, n/a) | 0.990 |
| Refusal of Feeds | 2.454 (0.681, 9.844) | 0.181 |
| CXR + | 2.516 (6.295, 170.763) | 5.97e-05 ** |

Multiple logistic regression with "Age less than 8 months", "Refusal of feeds", "Positive CXR" and "Hypoxemia" shows "Positive CXR" (odds ratio 2.516, 95% CI (6.295, 170.763)), is the only factor significantly associated with prolonged hospitalization (more than 5 days) with P value 5.97e-05 (<0.05) respectively.

**Table 5:** Risk factors for treatment under ventilation

| Risk Factors | Under Ventilation | Odds Ratio ( 95% CI) | P value |
|---|---|---|---|
| Age < 8 months | 3 (27.27%) | 8.343 (1.443, 44.966) | 0.0124 ** |
| Sex (Male) | 3 (5.08%) | 0.549 (0.103, 2.619) | 0.448 |
| Z score ≤ -2 | 4 (11.43%) | 2.839 (0.592, 15.153) | 0.189 |
| Tachypnea | 7 (7.69%) | 9.64e+06 (9.245e-88, n/a) | 0.993 |
| Hypoxemia | 7 (43.75%) | 1.81e+09 (2.257e-149 , n/a) | 0.995 |
| Refusal of Feeds | 7 (10.77%) | 3.79e+07 (3.176e-82, n/a) | 0.992 |
| CXR + | 7 (14.00%) | 1.39e+08 (6.18e-117, n/a) | 0.994 |
| Wheezing | 0 (0.00%) | 1.025e-07 (n/a, 3.936e+83) | 0.993 |

** P value less than 0.05

Simple logistic regression shows "Age less than 8 months" [odds ratio 8.343, 95% CI (1.443, 44.966)] is the sole factor significantly associated with treatment under ventilation with P value 0.0124 (<0.05).

The RISC score wise distribution of cases is shown in Table no. 6. There was almost a uniform distribution of scores from -2 to 3. However, there were only a few cases with scores of 4 & 5 and no case with a score of 6.

**Table 6:** RISC Score wise distribution of LRTI cases

| RISC Score | Pneumonia | Severe Pneumonia | Very severe Pneumonia | Acute Bronchiolitis | Wheezing | Acute Bronchitis |
|---|---|---|---|---|---|---|
| -2 | 1 (5.88%) | 0 (0.00%) | 0 (0.00%) | 7 (41.18%) | 7 (41.18%) | 2 (11.76%) |
| -1 | 0 (0.00%) | 1 (7.69%) | 0 (0.00%) | 7 (53.85%) | 4 (30.77%) | 1 (7.69%) |
| 0 | 8 (61.54%) | 0 (0.00%) | 0 (0.00%) | 2 (15.38%) | 2 (15.38%) | 1 (7.69%) |
| 1 | 0 (0.00%) | 1 (7.14%) | 1 (7.14%) | 10 (71.43%) | 0 (0.00%) | 2 (14.29%) |
| 2 | 1 (9.09%) | 3 (27.27%) | 2 (18.18%) | 4 (36.36%) | 1 (9.09%) | 0 (0.00%) |
| 3 | 0 (0.00%) | 2 (9.52%) | 16 (76.19%) | 3 (14.29%) | 0 (0.00%) | 0 (0.00%) |
| 4 | 0 (0.00%) | 0 (0.00%) | 8 (100%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) |
| 5 | 0 (0.00%) | 1 (14.29%) | 6 (85.71%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) |

**Table 7:** Distribution of RISC Scores, Prolonged hospitalization, Ventilation and Length of hospital stay

| RISC Score | No. of cases | Not admitted into Hospital (Out Patient) | Admitted into Hospital (In Patient) | Prolong hospitalization (Length of Stay more than 5 days)# | Under Ventilation | Average Length of Stay in Hospital (Days) |
|---|---|---|---|---|---|---|
| -2 | 17 (16.35%) | 15 (88.24%) | 2 (11.76%) | 0 (0.00%) | 0 (0.00%) | 2.00 |
| -1 | 13 (12.50%) | 8 (61.54%) | 5 (38.46%) | 0 (0.00%) | 0 (0.00%) | 2.20 |
| 0 | 13 (12.50%) | 4 (30.77%) | 9 (69.23%) | 2 (15.38%) | 0 (0.00%) | 2.67 |
| 1 | 14 (13.46%) | 1 (7.14%) | 13 (92.86%) | 0 (0.00%) | 0 (0.00%) | 3.15 |
| 2 | 11 (10.58%) | 1 (9.09%) | 10 (90.91%) | 2 (18.18%) | 0 (0.00%) | 3.50 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | 21 (20.19%) | 0 (0.00%) | 21 (100%) | 18 (85.71%) | 1 (4.76%) | 6.95 |
| 4 | 8 (7.69%) | 0 (0.00%) | 8 (100%) | 8 (100%) | 2 (25.00%) | 8.63 |
| 5 | 7 (6.73%) | 0 (0.00%) | 7 (100%) | 6 (85.71%) | 4 (57.14%) | 8.86 |

**Table 8:** Sensitivity and specificity for Prolonged hospitalisation based on RISC score (for different cut-off value) #

| RISC Score* | Sensitivity | Specificity | Positive Predictive value | Negative Predictive value | Admitted into Hospital (In patient) | Average Length of Stay in Hospital (Days) | Young's Index (J) |
|---|---|---|---|---|---|---|---|
| -2 | 100.00% | 0.00% | 34.62% | n/a | 75 (72.12%) | 5.23 | 0.00% |
| -1 | 100.00% | 25.00% | 41.38% | 100% | 73 (83.91%) | 5.32 | 25.00% |
| 0 | 100.00% | 44.12% | 48.65% | 100% | 68 (91.89%) | 5.54 | 44.12% |
| 1 | 94.44% | 60.29% | 55.74% | 95.35% | 59 (96.72%) | 5.98 | 54.74% |
| 2 | 94.44% | 80.88% | 72.34% | 96.49% | 46 (97.87%) | 6.78 | 75.33% |
| 3 | 88.89% | 94.12% | 88.89% | 94.12% | 36 (100%) | 7.69 | 83.01% |
| 4 | 38.89% | 98.53% | 93.33% | 75.28% | 15 (100%) | 8.73 | 37.42% |
| 5 | 16.67% | 98.53% | 85.71% | 69.07% | 7 (100%) | 8.86 | 15.20% |

*cut off value ≥ type # Out of total cases (In patient + Outpatient)

Young's Index =Sensitivity+Specificity-1

RISC score with cutoff value 3 (≥ 3) has high Sensitivity (88.89%) and high Specificity (94.12%) for determination of prolong hospitalization.

**Table 9:** Sensitivity and specificity for being under Ventilation

| RISC Score* | Ventilation # | Sensitivity | Specificity | Positive Predictive value | Negative Predictive value | Young's Index |
|---|---|---|---|---|---|---|
| -2 | 7 (6.73%) | 100.00% | 0.00% | 6.73% | n/a | 0.00% |
| -1 | 7 (8.05%) | 100.00% | 17.53% | 8.05% | 100.00% | 17.53% |
| 0 | 7 (9.46%) | 100.00% | 30.93% | 9.46% | 100.00% | 30.93% |
| 1 | 7 (11.48%) | 100.00% | 44.33% | 11.48% | 100.00% | 44.33% |
| 2 | 7 (14.89%) | 100.00% | 58.76% | 14.89% | 100.00% | 58.76% |
| 3 | 7 (19.44%) | 100.00% | 70.10% | 19.44% | 100.00% | 70.10% |
| 4 | 6 (40.00%) | 85.71% | 90.72% | 40.00% | 98.88% | 76.44% |
| 5 | 4 (57.14%) | 57.14% | 96.91% | 57.14% | 96.91% | 54.05% |

*cut off value ≥ type # Out of total cases (In patient + Outpatient)

Young's Index = Sensitivity+Specificity-1

RISC score with cutoff value 4 (≥ 4) has high Sensitivity (85.71%) and high Specificity (90.72%) for determination of need for assisted ventilation.

LRTIs constitute a major portion of the disease burden in infants and young children around the world, the problem being the gravest in developing countries due to limited resources. The prognosis of LRTI in children ranges from rapid resolution of symptoms and full recovery of functional status to the development of severe medical complications and death. [5] Understanding the prognosis of LRTI is important from clinical, research and quality-improvement perspectives. The ability to quantify the probability of serious adverse events (i.e., severe medical complications or death) can assist physicians in their initial management decisions, such as determining the most appropriate site of treatment (home vs. hospital), the intensity of hospital management (medical floor vs. intensive care unit), and the intensity of diagnostic testing and/or antibiotic therapy. Also, the identification of risk factors of severe LRTI may help in reducing the burden of disease and in instituting early appropriate management.

We validated a clinical prediction score, the RISC score16, which uses a simple set of clinical factors to discriminate between young children with varying risks of mortality and morbidity from LRTI. Variables retained in the score represent known risk factors for severe outcomes of respiratory illness in children, including: hypoxemia, chest indrawing, refusal to feed, malnutrition and age.

Our study was a hospital based prospective study conducted in a tertiary care setting of an urban area over a period of 1 year. Study included a total of 104 cases, satisfying the inclusion criteria, of which there were 59 males (56.7%) and 45 females (43.3%). The age group was divided into 4 categories, as per the WHO classification of LRTI 4. The subjects were divided into 7 age groups, with

highest number of cases in the age group of 3-12 months (22.12%) and lowest number of subjects in the 1-2 months (5.77%) age group. The mean z score for weight for age of our study population was -0.73. Most of the children had a z score of above -2, indicating that our study population was well-nourished. This may be attributed to their affluent socio-economic background. As per our LRTI definitions, most of the children belonged to very severe pneumonia and acute bronchiolitis groups (33 cases in each group, i.e., 31.73% each). Of the total number of cases , 75 (72.1%) required hospitalisation and 29 (27.9%) were managed as outpatients. In our entire study, there was only 1 mortality (0.96% case fatality rate).

Our study included 104 subjects in the age group of 1month – 6years who attended either our OPD or emergency with varied presentations of LRTI. Various investigators like Ramachandran etal [6], Barsam et al [7], Teiwsoh et al [8], Suwanjutha et al [9], Patwari et al [10], Kumar et al [11], Broor et al [12], and several others [13-15], have studied different sets of risk factors associated with increased morbidity and mortality in children with LRTI. Our study, however, did not evaluate any of the environmental factors described in some of these studies due to insufficient data. In our study, the host factors showing statistically significant association with increased morbidity, i.e. prolonged hospital stay and need for assisted ventilation, were age less than 1year and very severe disease at presentation [respiratory distress with refusal of feeds].

A positive chest X-ray finding was also a significant risk factor for an adverse outcome. [16] This finding is in contrast to a study by Swingleret al [17], who have reported that chest radiograph does not affect clinical outcome in LRTI in children.However, this difference in observation may be a bias due to inter-observer variations in interpreting chest X-rays. [18] Young age of the child, i.e. age less than 8 months was the only risk factor, shown to be significantly associated with requirement of assisted ventilation (p value 0.0124). Factors that were documented to be insignificant risk factors were sex of the child & tachypnea. These results are at par with the study by Broor et al [12] and Shah et al [19]. Our study also could not demonstrate any significant association of malnutrition (weight for age z score <-2) with poor outcome. This may be due to an inherent sampling bias, as the incidence of malnutrition in the study population was very low.

Our study also showed that none of the children with wheezing episode, needed prolonged hospital stay or assisted ventilation. Therefore it can be concluded that unnecessary hospitalization and over treatment may be avoided in children with acute respiratory infection and wheeze, if a simple clinical parameter like wheeze is used to refine the WHO criteria for ALRI. [20] A recent paper by Ayieko and English [21] reviewed the evidence supporting WHO case management of pneumonia but did not address the problem of wheezy children.

Reed C et al [4] developed and validated a scoring model, the RISC score, as a predictor of mortality in children with LRTI. Our study assessed the performance of this score as a determinant of poor outcome (i.e., prolonged hospitalization and need for assisted ventilation). However, its performance as a predicator of mortality could not be assessed due to the low case fatality rate observed in our study. The median and mean RISC scores recorded in our study were 1 & 1.14 respectively. Most of the children with a RISC score of <= 0, were managed as outpatients (62.79%) and all children with a RISC score of >= 3 required hospitalization. The average length of hospital stay for children with a RISC score of <= 0 was between 2 and 2.67 days, whereas those with a RISC score of >= 3 had an average hospital stay between 6.95 and 8.86 days.

In the absence of additional danger signs, children with wheeze would have a low RISC score, which supports suggestions that in many instances these young children might be successfully managed without hospitalization. [11] We found that RISC score ≥ 3 has high Sensitivity (88.89%) and high Specificity (94.12%) for determination of prolonged hospitalization. RISC score ≥ 4 has high Sensitivity (85.71%) and high Specificity (90.72%) for determination of need for assisted ventilation.

Predictive models are expected to perform better in the population in which they were developed than in other populations36. Nonetheless, our study showed the RISC score to be a good predictor of poor outcome in children with LRTI, in contrast to the finding by Maina et al. [22] However, it should be highlighted that this scoring model should be further evaluated, as our study was performed in an urban multispecialty hospital setting rather than health facilities in rural areas and this could limit the external validity of our findings. Therefore, with further validation in additional populations and refinement in other contexts, the RISC score may be a tool of high utility, in resource-limited settings, to more effectively manage LRTI in young children.

**Conclusion:**

Our study included 104 subjects (59 males and 45 females) belonging to 6 month to 5 years age group, who satisfied the inclusion criteria. The children were observed and clinically assessed using a pre-coded proforma and were followed up at 7 days. Most of the cases were aged < 12 months, followed by age < 24 months and rest almost equal distribution in the remaining age groups. The case fatality rate in our study was 0.96%. The significant risk factors for morbidity and mortality were age < 8 months,

refusal of feeds, hypoxemia (sats<90% in room air), & positive CXR findings. Some of the known risk factors which were found to be insignificant in our study were malnutrition (weight for age z score <-2), sex of the child & tachypnea.

A RISC score of >= 3 showed a high specificity and a moderately high sensitivity for both prolonged hospitalization and need for assisted ventilation. However, RISC score as a predictor of mortality in LRTI, could not be assessed in our study, as the observed mortality in our study was very low, as compared to that in the general population.

Our study concluded that the RISC score maybe used as an index of severity in children with LRTI, as a complementary tool to the current IMCI framework, to ensure appropriate treatment and hospitalization in children, who are most in need. Also, recognizing the risk factors at presentation may facilitate decisions about the most appropriate site of treatment (i.e., home vs. hospital) or the need for additional supportive care (i.e., supplemental oxygen or intensive care).

However, as our study was conducted in a tertiary care multi-specialty hospital, it might have some inherent sampling bias and therefore, larger studies in other settings, are recommended in the future.

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