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Original Article

Paediatrics Section

Risk Factors and Outcome of Respiratory Disease in Children Aged between 2 Months to 5 Years: A Prospective Observational Study

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ABSTRACT

Introduction: Acute Respiratory Infection (ARI) constitutes a leading cause of morbidity and mortality in children. It is one of the major causes of under-five mortality in the world and in India. India is improving its position in ranking following the recent measures it has made toward improving access to child health interventions like Haemophilus influenzae type b (Hib) and pneumococcal vaccination, promoting exclusive breast feeding as well as strengthening critical care services to protect children from severe disease

Aim: To assess the risk factors associated with respiratory disease and detect mortality and morbidity among children between the age of 2 months to 5 years.

Materials and Methods: The study was conducted in the Department of Paediatrics, SCB Medical and Hospital, Cuttack, Odisha, India. A total of 306 cases of acute respiratory diseases between the age group of 2 months to 5 years admitted during the period from September 2018 to September 2019 were enrolled. After detailed history and examination, the risk factors were compiled. Morbidity was assessed in the form of need for ventilation, prolonged Paediatric Intensive Care Unit (PICU) stay and hospital stay. Chi-square test for categorical data and Kruskal-Wallis test for non parametric data was used to identify whether various risk factors for morbidity and mortality of ARI cases were statistically significant.

Results: Out of 2793 children between 2 months to 5 years of age, 306 (10.95%) had ARI. Of these, 288 (94.12%) children survived and 18 (5.88%) died. Most of them were males 186 (60.78%) but mortality was more among females, 10 (8.33%) Children who were not exclusively breastfed were 173 (56.54%) and who were from low socio-economic class (24,79.41%), inadequately immunised were 191 (62.4%), or had bad child rearing practices were 175 (57.2%), had higher risk of ARI were 12 (66.67%) and mortality 18 (100%) was also higher in this group. Sepsis 18 (100%), malnutrition 14 (77.78%) and need for mechanical ventilation 18 (100%) were significant risk factors for mortality.

Conclusion: Low socio-economic status, malnourishment and lack of exclusive breastfed for 1st six months of age have significant bearing on the occurrence of ARI. Children between 2-12 months are most vulnerable. Very severe pneumonia and bronchiolitis had a poor outcome.

Keywords: Acute respiratory infection, Mortality, Pneumonia, Undernutrition

INTRODUCTION

The Acute Respiratory Infection (ARI) are one of the common causes for which people seek health care services especially among under five age group [1,2]. Each year, about 1.3 million children under five years of age die from ARIs worldwide [3]. The ARO constitute one third of the deaths in under five age group in low income countries [4]. As per the World Health Organisation (WHO) respiratory infections account for 6% of the total global burden of disease; this is a higher percentage compared with the burden of diarrhoeal disease, cancer, Human Immunodeficiency Virus (HIV) infection, ischaemic heart disease or malaria [5].

Each year ARIs account for over 12 million hospital admissions in children less than five years [6]. India ranks third, the lowest compared to the 15 other high burden countries for its Global Action Plan for Pneumonia and Diarrhoea (GAPPD) score. The goal is to end preventable childhood deaths due to pneumonia and diarrhoea by 2025 [7].

There are several risk factors that predispose younger age group of children to ARI. Majority of these risk factors are modifiable. The environmental factors such as wet season, secondary exposure to smoke, and housing standards such as rural or urban residence, overcrowding, use of smoking chulhas play a major role in acquiring ARI among children [8]. Children are more affected especially in developing countries because of low-birth weight and malnutrition [9]. Vaccination status could also affect the burden of ARIs in a particular region.

Despite a large number of hospital admissions of ARI cases in the under five age group, data regarding factors associated with ARI from eastern India is lacking. A recent systematic review identified the lack of evidence on epidemiology and aetiology of pneumonia. This was highlighted as a barrier to effective planning and execution of pre-emptive measures [10].

Study done by Krishnan A et al., discussed explicitly about the epidemiology of the disease with ALRI incidence in the under five age group being higher among boys and boys had 2.4 times higher ARI-related hospitalisation rate as compared to girls [11]. Jain N et al., studied a rural northern Indian community and found that ARIs account for 20-40% of outpatient and 12-35% of inpatient attendance in a general hospital [12].

Since, majority of risk factors causing ARI are modifiable and there is lack of studies highlighting such causes in this region, the present study was carried out with the aim to assess prevalence pattern of various associated risk factors and outcome of ARI admitted in a tertiary hospital in Odisha, India.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Paediatrics, SCB Medical College and Hospital, Cuttack, Odisha, India. All cases of acute respiratory diseases between the age group of 2 months to 5 years admitted to the hospital during the period September 2018-September 2019 were enrolled for the study. The study was approved by the Institutional Ethics Committee with Ethical Committee (ID No. 904/14.10.2019) and informed consent was obtained from the parents.

The definition of ARI was according to WHO classification of ARI [13]. Socio-economic status was considered low if the family belonged to both upper lower and lower class according to Kuppuswamy classification of 2017 [14].

Sample size calculation: Sample size was calculated according to prevalence (27%) of ARI in a pilot study [10]. The prevalence was thus taken as 27%, with a margin of error of 5% and 95% confidence interval. The calculated sample size was 303. A total of 306 cases were studied.

Inclusion criteria: All children in the age group of 2 months to 5 years admitted with acute respiratory diseases like pneumonia, bronchiolitis, bronchitis, Wheeze Associated Lower Respiratory Tract Infection (WALRI) were included.

Exclusion criteria: Children with respiratory complication due to other causes like congenital heart disease, neurological diseases, foreign body aspiration, chemical pneumonitis, drowning, Inborn Error of Metabolism (IEM), metabolic causes immunosuppressive conditions and pleural disease were excluded.

Practices such as poor hand hygiene, lack of cough etiquette, open air defecation, indoor pollution, such as improper bathing, application of black carbon, not trimming nails of child, bottle feeding were considered as bad child rearing practices [15,16]. Malnutrition was considered as weight for height below -2 SD according to WHO growth chart for the age and sex [17].

Definition of sepsis was based on International Consensus Guidelines [18]:

Systemic Inflammatory Response Syndrome (SIRS): The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count:

- Core body temperature of >38.5°C or <36°C.
- Tachycardia, defined as a mean heart rate >2 SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5 to four hour time period OR for children < 1year as: bradycardia, defined as a mean heart rate <10th percentile for the age
- Mean respiratory rate >2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anaesthesia.
- Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopenia) or >10% immature neutrophils

Infection: A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection.

Sepsis: The SIRS in the presence of or as a result of suspected or proven infection.

Procedure

Presence of one or more of the following five symptoms- cough, sore throat, nasal congestion, earache/discharge and breathing difficulty, suggested presence of ARI [10].

Children were classified as per WHO ARI protocol into "No Pneumonia"; "Non severe Pneumonia"; "Severe Pneumonia" and "Very severe Pneumonia" [Table/Fig-1] [13]. Non severe pneumonia, severe pneumonia and very severe pneumonia were jointly considered as Acute Lower Respiratory Infections (ALRI). Non serious bacterial infections and no pneumonia (only cough and cold) are grouped together as Acute Upper Respiratory Infections (AURI).

Acute Respiratory Infection (ARI)	Signs
No Pneumonia (Cough and cold only)	Respiratory rate per minute: <50 – infants 2-11 months <40 – children 12-59 months
Non severe pneumonia	Respiratory rate per minute: >50 – infants 2-11 months >40 – children 12-59 months No LCI
Severe Pneumonia	LCI with or without rapid breathing
Very Severe Disease	Unable to drink, convulsions, abnormally sleepy or difficulties waking, stridor in a calm child or clinically severe malnutrition

[Table/Fig-1]: WHO classification of ARI in children presenting with cough and/or difficulty breathing [13]
WHO: World health organisation; ARI: Acute respiratory infection; LCI: Lower chest indrawing

Pre-structured proforma was used to obtain information from the parents. After getting the consent, detailed history, clinical details and investigations were collected and entered in the proforma.

Parents were enquired about the following possible risk factors:

- Breastfeeding practices (exclusively breastfeeding till six months/formula feeding/ mixed feeding),
- Socio-economic class as per modified Kuppuswamy scale,
- Immunisation status of the child,
- Bad rearing practices (such as improper bathing, application of black carbon, not trimming nails of child, bottle feeding etc., [15,16]),
- Malnutrition (as per WHO guideline [17]) - defined as weight for height < 2 SD for the gender.

Outcome assessment was done based upon the following parameters: duration of hospital stay, need for PICU admission, needs for mechanical ventilation, death or discharge.

STATISTICAL ANALYSIS

Data collected and recorded in the proforma during the whole study period were entered in Microsoft Excel Sheet and statistically analysed using IBM Statistical Package for the Social Sciences (SPSS) version 22.0, to identify whether various risk factors for morbidity and mortality of ARI cases are statistically significant. Categorical data were analysed using chi-square test and continuous data with Kruskal-Wallis tests were used. A p-value <0.05 was considered statistically significant.

RESULTS

Out of 2793 inpatient admissions during the study period, total number of ARI cases were 306 and the mortality rate was 5.88% (18 out of 306).

Among the total 306 children, male preponderance was observed. Mortality was more among girls, with 55.55% deaths among the total. Most of the cases of ARI was among infants (two months to 12 months, n=133), which was 43.4% of the total cases of ARI. The highest number of cases was reported during the winter season. Mortality and ARI cases was highest among the non exclusively breast fed infants 66.67% and 56.5%, respectively. The ARI was more prevalent among low socio-economic status family (79.4%). All the deaths were observed in infancy. Malnourishment and sepsis were significant risk factors for mortality [Table/Fig-2].

Children with non severe pneumonia formed most of the inpatient admission with 38.24% followed by bronchiolitis [Table/Fig-3]. Children with severe and very severe pneumonia had a prolonged PICU stay (defined as >7 days) with 20 and 36 children, respectively. Also, it was the same category of admitted children with prolonged

Characteristics	Subcategory	N=306 (%)	Mortality	Odds ratio	p-value
Gender	Male	186 (60.8%)	8	0.643	0.143*
	Female	120 (39.2%)	10		
Age (months)	2-6	61 (19.9%)	4		0.512*
	7-12	72 (23.5%)	3		
	13-36	93 (30.4%)	8		
	37-60	80 (26.2%)	3		
Season/Period of the year	June-August	96 (31.4%)			0.023
	September-November	103 (33.6%)			
	December-February	107 (34.9%)			
Exclusive Breast Feeding till 6 months	Yes	133 (43.4%)	6	2.36	0.041#
	No	173 (56.5%)	12		
Socio-economic status	Class IV and V	243 (79.4%)	18	1.20	0.026#
	Class I, II, III	63 (20.6%)	0		
Immunisation upto date	Yes	115 (37.6%)	5	1.60	0.896#
	No	191 (62.4%)	13		
Bad rearing practices	Yes	175 (57.2%)	12	2.608	0.402#
	No	131 (42.8%)	6		
Sepsis	Yes	43 (14.1%)	18	11.52	0.001#
	No	263 (85.9%)	0		
Malnour-ishment	Weight for height <-2SD	82 (26.8%)	14	11.32	0.001#
	Weight for height > -2SD	224 (73.2%)	4		
Need for mechanical ventilation	Yes	28 (9.2%)	18	28.8	0.001#
	No	278 (90.8%)	0		
PICU admission	Yes	59 (19.3%)	14	18.9	0.001#
	No	247 (80.7%)	4		
Hospital stay >7 days	Yes	123 (40.2%)			
	No	183 (59.8%)			
Outcome	Alive	288 (94.1%)			
	Dead	18 (5.9%)			

[Table/Fig-2]: Baseline characteristics of study population.
*Kruskal-Wallis test; #Chi-square test

Diagnosis	Number of patients	Percentages
Pneumonia	**201**	**65.68%**
Non severe	117	38.24%
Severe	45	14.71%
Very severe	39	12.75%
ARI cases (diagnosis other than Pneumonia)	**105**	**34.31%**
Bronchiolitis	47	15.35%
Croup	15	4.9%
WALRI	43	14.05%

[Table/Fig-3]: Disease categorisation.
WALRI: Wheeze associated lower respiratory tract infection; ARI: Acute respiratory infection

hospital stay as well. This signifies greater morbidity in these two categories, with 43 children having severe pneumonia and 36 having very severe pneumonia admitted for more than seven days in the hospital. Both the result was statistically significant [Table/Fig-4].

As depicted in [Table/Fig-5], prognosis was poor in children with very severe pneumonia, because 15 children had died out of 39 cases. However, the death in cases of bronchiolitis was three in number and there were no deaths among children with other ARI.

Diagnosis	PICU stay >7 Days		Hospital stay >7 Days	
	Yes	No	Yes	No
Pneumonia	**56**	**145**	**105**	**96**
Non severe	0	117	26	91
Severe	20	25	43	2
Very severe	36	3	36	3
ARI cases (diagnosis other than pneumonia)				
Bronchiolitis	3	44	8	39
Croup	0	15	0	15
WALRI	0	43	10	33
	p-value=0.001		p-value=0.001	
	Kruskal-Wallis Test		Kruskal-Wallis Test	

[Table/Fig-4]: Duration of Paediatric Intensive Care (PICU) stay and hospital stay.
WALRI: Wheeze associated lower respiratory tract infection; ARI: Acute respiratory infection; p-value calculated using Kruskal-Wallis Test, p-value <0.05 considered statistically significant

Diagnosis	Prognosis	
	Death	Alive
Bronchiolitis	3	44
Croup	0	15
WALRI	0	43
Non severe pneumonia	0	117
Severe Pneumonia	0	45
Very severe pneumonia	15	24

[Table/Fig-5]: Prognosis of various disease states.
WALRI: Wheeze associated lower respiratory tract infection; p-value <0.001 (calculated using Kruskal-Wallis Test)

DISCUSSION

Knowledge regarding the burden of ARI in our community and identifying the underlying risk factors will help in better planning and implementation of community level programmes to reduce the incidence of such cases.

The prevalence of respiratory tract infections in the present study population was 10.9%. Both males 186 (60.78%) and females 120 (39.2%) were affected, though the difference was statistically insignificant. Out of the total number of cases, 43.4% belonged to the age group of two months to one year. This age distribution of ARI cases in the index study population was similar to observations made by Ramachandran P et al., and Islam F et al., where 48% and 38.14% of ARI cases occurred in infancy (below one year) [19,20]. Higher risk of ARI among lower age children might be due to less developed immunity. In our study, the number of ARI cases was more during December to February which was similar to observations made by Ramani VK et al., [21].

There was no significant difference in the mortality among male and females which tallies with results of Ramachandran P et al., study [19].

It was observed that the incidence of ARI cases (56.5%) was more in those babies who were not exclusively breast fed. The mortality rate was also higher (66.67%) in the same group as compared to those babies who were on exclusive breast feeding till six months. This observation was supported by several other studies. Prajapati B et al., observed decreased incidence of ARI with increased duration of breast feeding (40%, 29.2%, 27.2% respectively in babies breast fed up to three months, six months, and nine months) [22]. Savitha MR et al., observed greater incidence of ARI in patients who were started on weaning diet before four months than those after four months (37.5% vs 13.46%) [23]. Lamberti LM et al., and Mihrshahi S et al., demonstrated significant mortality following pneumonia in babies who were not exclusively breast fed for six months [24,25].

We observed that 79.4% of admitted ARI cases belonged to lower socio-economic class. In the study by Prajapati B et al., 48.3% ARI patients hailed from lower socio-economic strata of society [22]. Overcrowding, illiteracy and malnutrition could be few possible reasons for this association. All the 18 cases (5.88%) who died in the present study were born in lower socio-economic class. Islam F et al., Savitha MR et al., Nilanjan MK, Biswas A , Tupasi TE et al., and Gregory G et al., also documented significant association between poor socio-economic factors and poor outcome in ARI [20,23,26-29].

Complete immunisation was seen in 115(37.6%) cases, while a large proportion were incompletely immunised (191,72%). Prajapati B et al., Savitha MR et al., and Broor S et al., reported increased incidence of pneumonia in unimmunised population [22,23,30].

Sepsis was found to be associated in 43 patients (14.1%). Patients with associated sepsis had 12 times increased risk of mortality than those without sepsis (Odds ratio 11.52). A 26.8% patients had underlying malnutrition. The odds of mortality in patients with underlying malnutrition was 11.32 which indicated 11 times greater risk of mortality in ARI patients who were malnourished than those without associated malnutrition. Savitha MR et al., Biswas A, Tupasi TE et al., also found a significant relationship between morbidity and mortality associated with pneumonia and undernutrition [23,27,28].

In this study, 28 (9.2%) children out of 306 admitted with ARI cases needed mechanical ventilation and these cases had 28 times higher risk of mortality when compared with others not requiring ventilation. A study done in Jordan by Khuri-Bulos N et al., had 4% children with acute viral illness who were ventilated [31].

Out of 306 cases, 59 (19.3%) needed PICU admission and 14 cases died, these PICU admission had 19 times higher risk of fatality. Pneumonia, severe pneumonia, bronchiolitis, WALRI, and very severe pneumonia were the common admitted cases. The mortality was 38.5% in very severe pneumonia which was statistically significant (p-value=0.001). The overall mortality rate in the present study population (5.9%) was much less as compared to that reported by the Million Death Study [10] where 27.6% (99% CI, 31.8%- 34.1%) deaths were attributable to pneumonia among a total of 12,260 deaths in children from 1-59 months.

Limitation(s)

The aetiological evaluation of causation of ARI has not been worked up in the present study.

CONCLUSION(S)

The incidence of ARI was 10.95% and case fatality rate was 5.88%. The most vulnerable group with increased mortality were infants which (below 12 months) was 38.89% of the total mortality. Mortality was higher among infants who were not exclusively breast fed. All the deaths were observed in children with low socio-economic status. Malnutrition and sepsis had direct bearing on mortality and morbidity.

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