

Risk Factors for Mortality in Community –Acquired Pneumonia Among Children Aged 1-59 Months Admitted in a Referral Hospital

PADMANABHAN RAMACHANDRAN, KRISHNAMOORTHY NEDUNCHELIAN, APPASAMY VENGATESAN AND SARADHA SURESH

From the Institute of Child Health and Hospital for Children, Egmore, Chennai, Tamilnadu.

Correspondence to: Dr P Ramachandran, G3 Murugan Apartments, #18 Sivasailam Street, T Nagar, Chennai, Tamilnadu 600 017, India. ramachandran_dr@rediffmail.com

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Objective: To determine the case fatality rate and factors for death in community acquired pneumonia among children aged 1 month to 59 months admitted in a referral Hospital.

Design: Hospital based retrospective study.

Setting: Institute of Child Health and Hospital for Children, Chennai.

Patients: Case records of children aged 1 month to 59 months of age with pneumonia (clinically diagnosed pneumonia, radiologically diagnosed pneumonia, and clinically and radiologically diagnosed pneumonia), from January 2006 to December 2008.

Outcome measures Case fatality rate (CFR) was calculated. Risk factors for mortality analyzed were young age of 1 to 6 months old, female sex, wheeze, respiratory rate ≥ 70 /min, chest indrawing, altered level of consciousness, convulsions, shock, associated heart disease, recent measles, weight for age < -2 Z

score and need for assisted ventilation. The association of risk factors to mortality was arrived at for all three categories of pneumonia cases separately.

Results: Case fatality rate was 8.2% (95% CI: 7.37- 8.99%). There was no significant difference in the CFR among the three study groups. Need for assisted ventilation alone was found to be an independent risk factor for mortality in children with pneumonia among all the study groups. Other risk factors like young age, weight for age < -2 Z score, altered level of consciousness, and congenital heart disease were also observed among these groups.

Conclusion: Among 1 month to 59 months old hospitalized children with pneumonia, CFR was 8.2%. Need for assisted ventilation was a significant risk factor associated with mortality.

Key words: *Case fatality rate, Children, Community acquired pneumonia, Risk factors.*

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Pneumonia is one of the leading causes of mortality among under five children in most developing countries. It is estimated to cause 1.9 million deaths each year [1]. According to official estimate from the WHO for the year 2000, two thirds of all these deaths were in just 10 countries and were maximum in India [2]. More than 20% of world's pneumonia deaths still occur in India, resulting in greater than 370,000 child deaths annually [3]. Different studies, both community as well as hospital based, have highlighted a variety of factors contributing to mortality in childhood pneumonia such as young age, low birth weight, under nutrition, anemia, lack of parental education, overcrowding, pollution at home, lack of exclusive breast feeding, lack of measles immunization, and severe disease at presentation [4-9]. With socio-economic progress and improvement in health awareness and referral services, an increasing proportion of pneumonia deaths will occur in hospitals [7]. Hence, the profile of pneumonia in tertiary care centers is likely to

reflect the burden in the community. Only a few studies have performed such an evaluation in developing countries [4, 9-11]. More studies are required to analyze the contributing factors for mortality in childhood pneumonia in young children. This information may help in optimal utilization of scarce resources for the most effective preventive and early management strategies.

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Data on pneumonia from sentinel centres may also serve as baseline information to assess the trend when some of the vaccines such as pneumococcal and *H. influenzae* type b vaccines are introduced in the national immunization program. We conducted a retrospective study on pneumonia among children aged 1 month to 59 months admitted in a tertiary care hospital, to determine the case fatality rate and factors responsible for death.

METHODS

Institute of Child Health and Hospital for Children,

Chennai is a referral pediatric institute and a 537 bedded multi-specialty hospital attached to Madras Medical College, Chennai. It caters to health needs of children up to 12 years of age from the city of Chennai and neighbouring districts. We conducted a retrospective chart review of all children in the age group of 1 month to 59 months admitted between January 2006 and December 2008 in our hospital with a final diagnosis of pneumonia. These cases were classified in to 3 groups (i) clinically diagnosed pneumonia {WHO diagnostic criteria for pneumonia (fast breathing defined by respiratory rate ≥ 60 /min in < 2 months of age, ≥ 50 /min in 2- 11 months of age and ≥ 40 /min in 12-59 months of age) or severe pneumonia (pneumonia with chest retraction) as per IMCI guidelines} [12], (ii) radiologically diagnosed pneumonia (based on the consensus finding of chest infiltrate(s) by a qualified radiologist and treating clinician), and (iii) clinically and radiologically diagnosed pneumonia (when both criteria were present). Children whose final diagnosis was tuberculous pneumonia or chemical pneumonitis following kerosene ingestion were excluded. Those in whom the data were incomplete (discharged against medical advice, absconded) were also excluded.

A pre-designed proforma was used to record the demographic profile (age and sex), symptoms (fever, cough, difficulty in breathing, altered sensorium, convulsions, inability to feed and wheezing), physical findings (weight, temperature, level of consciousness, cyanosis, shock, respiratory rate, chest retraction, grunting, auscultatory signs such as crackles and wheeze, associated congenital heart disease), radiologic findings (chest radiograph findings were available for all cases), oxygen saturation, need for assisted ventilation and final outcome. The possible outcomes were "Discharged" (those children who recovered) as per the treating physician or "Death". Risk factors for mortality analyzed were young age of 1-6 months, female sex, presence of wheeze, respiratory rate ≥ 70 /min, chest retraction (lower chest indrawing), altered level of consciousness (ALOC) as denoted by unresponsiveness to voice or pain, convulsion at the time of presentation, shock as defined by Pediatric Advanced Life Support (PALS) guidelines [13], associated congenital heart disease (CHD) confirmed by echocardiogram, measles infection within past three months, weight for age < -2 Z score, and need for assisted ventilation at the time of presentation. Need for assisted ventilation was based on the treating clinician's decision. Nutritional status was recorded by using the Z score as per WHO standards of weight for age [14]. Risk factors for all the three study groups of pneumonia were analyzed separately.

Statistical analysis: Data collected from hospital records were entered in case report forms. These data were entered in SPSS 11.5 for statistical analysis. After entering the data, they were checked for accuracy and also checked statistically and inconsistencies were resolved with the raw data. For the analysis of pneumonia related mortality, comparison was carried out among the above described three groups. Cases and controls (discharged) in the ratio of 1:2 were selected by arranging the discharged cases serially according to admission among the three groups and every 5th discharged child was included as a control. The calculated sample size was 1320 in each group based on the previous reported least Odds Ratio of 1.4 for the risk factor of age less than six months, with 80% power and 95% confidence, assuming 40% of exposure in control group. Chi square test was used to study the association between the contributory factors and outcome (mortality). The association was studied by univariate analysis by Pearson Chi square test initially and risk was assessed by using Odds Ratio with 95% Confidence Interval [OR (95% CI)]. Stepwise multiple regression analysis was used to identify independent factors associated with the outcome. To find out the association of the various grades of under nutrition, with mortality, Chi Square test for trend was applied. All hypothesis testing was two tailed and P value of ≤ 0.05 was considered statistically significant.

RESULTS

In the period between January 2006 and December 2008, there were 4976 children admitted in the age group of 1 month to 59 months with a final diagnosis of pneumonia. 4375 children (42% girls) were included in the study after excluding those with chemical pneumonitis or tuberculous pneumonia and those in whom the data were incomplete. There were 1536 children who were diagnosed to have pneumonia based on clinical features alone, 1020 children who were diagnosed by radiological findings alone and 1819 children who had clinical as well as radiological evidence of pneumonia (**Fig. 1**). Total cases of pneumonia constituted 8% of hospital admissions in this period. There were 1176, 1670 and 1529 children with pneumonia in the years 2006, 2007 and 2008, respectively.

Majority of the children (2175; 48%) were in the age group 1-6 months (**Table I**). 357 children died providing an over all case fatality rate of 8.2 % (95% CI: 7.37 - 8.99%). The all cause mortality in the age group of 1 month to 59 months was 3.9% in this period as per the hospital statistics.

The difference in mortality due to pneumonia among

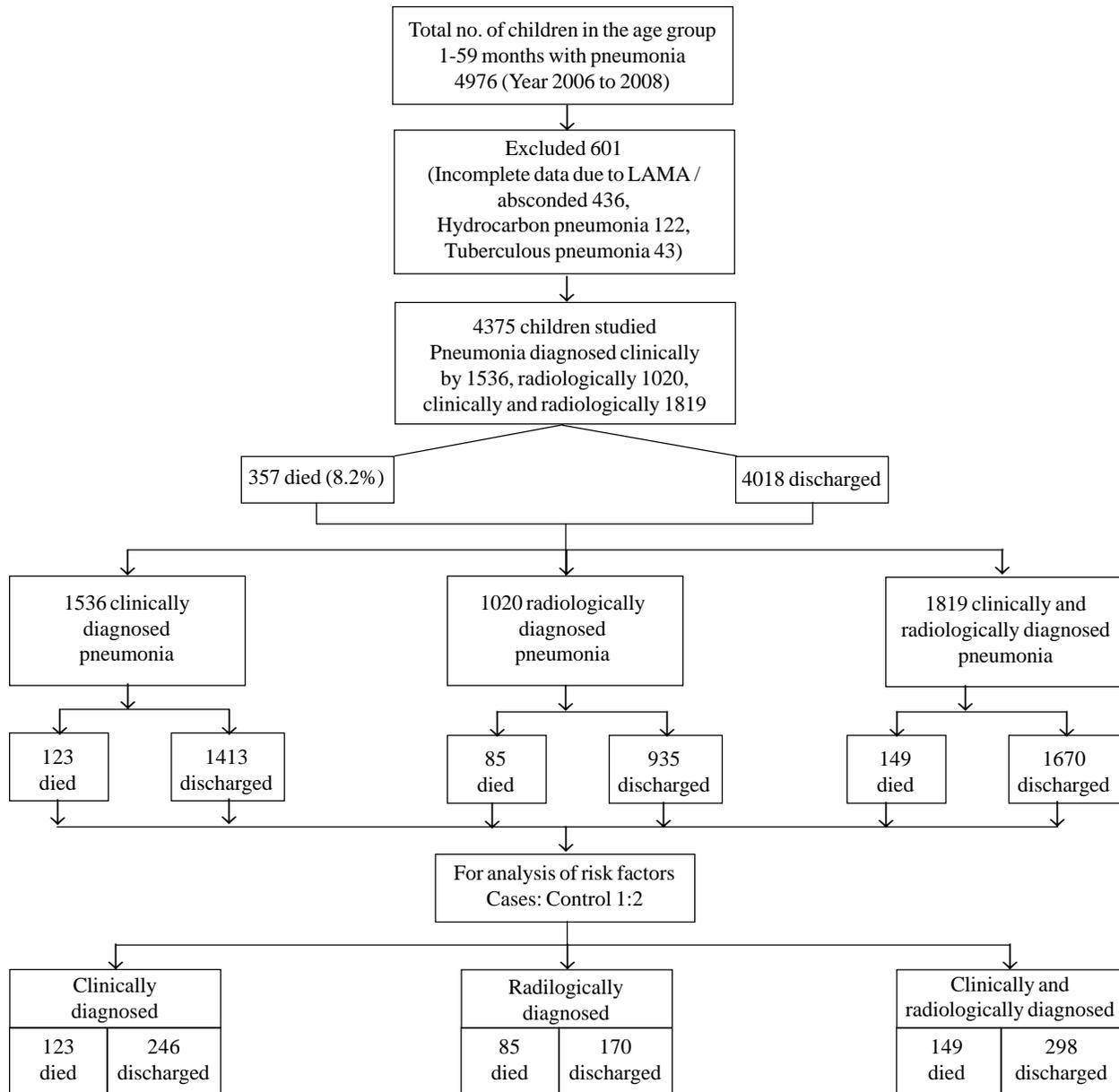


FIG.1 Flow chart of study subjects.

male and female children was not statistically significant ($P=0.12$). The mortality rate was lower in older children as compared to younger ones ($P=0.001$) (**Table I**). The difference in CFR among the three study groups was not significant, except in clinically and radiologically diagnosed cases in the age group of 24 to 59 months, which was higher compared to clinically diagnosed and radiologically diagnosed cases (**Table II**).

In the case control analysis by univariate analysis of risk factors contributing to mortality, young age of 1-6 months, altered level of consciousness, weight for age

<-2 Z score, shock, CHD and need for assisted ventilation were significantly associated with mortality among the clinically diagnosed pneumonia cases. Among radiologically diagnosed cases, convulsion was found to be an additional factor. In clinically and radiologically diagnosed pneumonia cases, wheeze was found to be more commonly seen among those who got discharged when compared to those who died. The proportion of female children and those who had measles in the past, presence of chest retraction and respiratory rate ≥ 70 /min were similar among 'discharged' as well as 'died' in all the three study groups.

TABLE I AGE AND CASE FATALITY RATE AMONG PNEUMONIA CASES

Age group	Clinical death, n (%)	Radiological death, n (%)	Clinical and radiological death, n (%)	Total death, n (%)
1-6 m	83/735 (11.3)	49/404 (12.1)	96/1036 (9.3)	228/2175 (10.5)
7-<12 m	13/244 (5.3)	16/219 (7.3)	20/335 (6.0)	49/798 (6.1)
12-<24 m	14/324 (4.3)	9/201 (4.5)	11/270 (4.1)	34/795 (4.3)
24-59 m	13/233 (5.6)	11/196 (5.6)	22/178 (12.4)	46/607 (7.6)
Total	123/1536 (8.0)	85/1020 (8.3)	149/1819 (8.2)	357/4375 (8.2)

TABLE II COMPARISON OF CASE FATALITY AMONG STUDY GROUPS

	Clinically vs radiologically diagnosed pneumonia		Clinically vs clinically and radiologically diagnosed pneumonia		Radiologically vs clinically and radiologically diagnosed pneumonia	
	OR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
1-6 months	0.92 (0.62-1.37)	0.67	1.25 (0.90-1.72)	0.16	1.35 (0.92-1.98)	0.10
7 -<12 months	0.71 (0.31-1.61)	0.38	0.89 (0.41-1.91)	0.74	1.24 (0.60-2.57)	0.53
12 - < 24 months	0.96 (0.38-2.46)	0.93	1.06 (0.45-2.56)	0.88	1.10 (0.41-2.93)	0.83
24 -59 months	0.99 (0.41-2.44)	0.99	0.42 (0.19-0.90)	0.01**	0.42 (0.19-0.95)	0.02*
Total	0.96 (0.71-1.29)	0.77	0.98 (0.75-1.26)	0.84	1.02 (0.76-1.36)	0.89

On multivariate analysis, need for assisted ventilation was found to be the only independent risk factor for death among all the three study groups of pneumonia. In addition young age of 1-6 months, weight for age < - 2Z score, altered level of consciousness (ALOC) and CHD among clinically diagnosed pneumonia cases; ALOC and

CHD among radiologically diagnosed pneumonia cases; and weight for age <-2Z score among clinically and radiologically diagnosed pneumonia cases were found to be significant independent risk factors for death (**Tables III, IV and V**).

TABLE III RISK FACTORS FOR MORTALITY AMONG CLINICALLY DIAGNOSED PNEUMONIA CASES

Risk factors	Status		Unadjusted OR (95%CI)*	P value	OR (95%CI)#	P value
	Discharged (n=246) No (%)	Death (n=123) No (%)				
Age (1-6 months)	120 (48)	83 (67.5)	2.18 (1.35-3.52)	0.001	1.15 (1.06-1.24)	0.001
Female sex	94(38.2)	53 (43.1)	1.22 (0.77-1.95)	0.37		
Wheeze	18(7.3)	4 (3.2)	0.43 (0.12-1.38)	0.12		
RR (≥70 per min)	164(66.7)	81 (65.9)	0.96 (0.60-1.56)	0.87		
Chest retraction	111(45.1)	43 (35.00)	0.65 (0.41-1.05)	0.06		
Altered consciousness	8(3.2)	18 (14.6)	5.10 (2.02-13.25)	0.001	1.56(1.20-2.04)	0.001
Convulsions	9(3.7)	10 (8.1)	2.33 (0.85-6.44)	0.06		
Weight for age<-2Z score	112 (45.5)	76 (61.8)	1.80 (1.12-2.91)	0.01	1.12(1.03-1.21)	0.007
Need for assisted ventilation	4 (1.6)	61 (49.6)	59.52 (19.78-200.65)	0.001	1.97(1.77-2.19)	0.001
Measles	3 (1.2)	1 (0.8)	1.69 (0.80-3.57)	0.13		
Shock	15 (6.1)	16 (13.0)	2.30 (1.04 -5.13)	0.01		
CHD	7 (2.8)	9 (7.3)	2.70 (1.01-8.27)	0.05	1.39(1.02-1.92)	0.04

*Univariate #Multivariate; RR: Respiratory rate, CHD: Congenital heart disease.

TABLE IV RISK FACTORS FOR MORTALITY AMONG RADIOLOGICALLY DIAGNOSED PNEUMONIA CASES

Risk factors	Status		Unadjusted OR (95%CI)*	P value	OR (95% CI)#	P value
	Discharged (170) n (%)	Death (85) n (%)				
Age (1-6 months)	56 (32.9)	49 (57.7)	2.77 (1.57-4.91)	0.001		
Female sex	82 (48.2)	43 (50.6)	1.10 (0.63-1.91)	0.72		
Wheeze	6 (3.5)	2 (2.4)	0.67 (0.09-3.76)	0.62		
Altered consciousness	4 (2.4)	22 (25.9)	14.49 (4.49-51.88)	0.001	1.56 (1.24-1.87)	0.001
Convulsions	4 (2.4)	22 (25.9)	11.15 (3.38-40.59)	0.001		
Weight for age<-2Z score	76 (44.7)	49 (57.6)	1.85 (1.03-3.32)	0.02		
Need for assisted ventilation	9 (5.3)	58 (68.2)	115.89 (38.43-94.71)	0.001	1.96 (1.78-2.17)	0.001
Measles	4 (2.4)	0	–	0.15		
Shock	15 (8.8)	4 (4.7)	0.51 (0.14-1.72)	0.23		
CHD	4 (2.4)	10 (11.8)	5.53 (1.53-21.72)	0.001	1.39 (1.07-1.82)	0.016

*Univariate #Multivariate; RR: Respiratory rate, CR: Chest retraction; CHD: Congenital heart disease.

TABLE V RISK FACTORS FOR MORTALITY AMONG CLINICALLY AND RADIOLOGICALLY DIAGNOSED PNEUMONIA CASES

Risk factors	Status		Unadjusted OR (95%CI)*	P value	OR (95% CI)#	P value
	Discharged (298) n (%)	Death (149) n (%)				
Age(1-6 months)	161 (54.0)	96 (64.4)	1.54 (1.01-2.36)	0.04		
Female sex	132 (44.3)	68 (45.6)	1.06 (0.70-1.60)	0.78		
Wheeze	22 (7.4)	3 (2)	0.26 (0.06-0.93)	0.02		
RR(≥70 per min)	298 (100.0)	149 (100)	–	1.00		
Chest retraction	150 (50.3)	84 (56.4)	1.28 (0.84-1.93)	0.22		
Altered consciousness	9 (3.0)	19 (12.8)	4.69 (1.95-11.55)	0.001		
Convulsions	9 (3.0)	10 (6.7)	2.31 (0.84-6.35)	0.06		
Weight for age<-2Z score	128 (43)	85 (57)	2.00 (1.29-3.11)	0.001	1.13(1.05-1.21)	0.001
Need for assisted ventilation	7 (2.4)	70 (47)	36.84 (15.56-91.23)	0.001	2.01(1.82-2.22)	0.001
Measles	1 (0.3)	0	–	0.39		
Shock	28 (9.4)	11 (7.4)	0.77 (0.35-1.67)	0.47		
CHD	9 (3.0)	15 (10.1)	3.59 (1.44-9.15)	0.001		

*Univariate; #Multivariate; RR: Respiratory rate, CHD: Congenital heart disease.

There was a trend of increase in death rate with worsening nutritional status (**Table VI**). Poor nutritional status was strikingly associated with mortality in children younger than 24 months of age, as mortality was seen only in children with - Z score in this age group.

DISCUSSION

Averting pneumonia deaths will significantly contribute to realizing Millennium Development Goal 4 (MDG4) of reducing under five mortality [13]. This retrospective analysis was conducted to identify the demographic and clinical variables associated with deaths in hospitalized

TABLE VI NUTRITIONAL STATUS AND OUTCOME IN PNEUMONIA

Weight for age Z score	Case fatality	OR (95%) (I)
<-3.0	127/908 (14%)	2.25 (1.66-3.04)
<-3 to -2.0	83/1120 (7.4%)	1.1 (0.8-1.54)
<-2 to -1.0	81/1200 (6.7%)	1.0
<-1 to 0	33/586 (5.6%)	0.82 (0.53-1.27)
0-1	9/246 (3.7%)	0.52 (0.24-1.1)
1-2	2/59 (3.4%)	0.48 (0.0-2.07)
2-3	1/40 (2.5%)	0.35 (0.02-2.44)

P=0.001 per trend; #Odds ratio with 95% confidence interval; *significant at P≤0.05.

WHAT IS ALREADY KNOWN?

- Identified risk factors for mortality with pneumonia are young age, low birth weight, under nutrition, anemia, illiteracy of parents, over crowding, indoor air pollution, lack of exclusive breast feeding, lack of measles immunization, congenital heart diseases, congenital anomalies, severity at presentation and altered level of consciousness.

WHAT THIS STUDY ADDS?

- The case fatality rate due to pneumonia among hospitalized children aged 1 month to 59 months during the period 2006 to 2008 was 8.2%.
- An additional risk factor independently associated with mortality in cases of childhood pneumonia is need for assisted ventilation.

children of 1 month–59 months of age with a diagnosis of pneumonia. The case fatality rate (CFR) of pneumonia was 8.2% compared to 3.9% for all cause mortality in this age group in the same period. CFR of childhood pneumonia in various Indian studies ranges between 8.9% to 47% [4,5,9,10,15,16,] and 3.4% to 12% in other developing countries [6,7,17].

The risk factors for deaths due to pneumonia vary between countries, regions and communities. Frequently studied factors are young age, low birth weight, under nutrition, anemia, lack of parental education, over-crowding, indoor air pollution, lack of exclusive breast feeding, lack of measles immunization, co-morbidities such as congenital heart diseases and other congenital anomalies and severity at presentation to hospital [4-9,11]. In this study, need for assisted ventilation was found to be independently associated with fatal pneumonia of clinically, radiologically, as well as clinically and radiologically diagnosed pneumonia cases. Need for assisted ventilation at the time of presentation is likely to indicate the severity. In another study, cyanosis and head nodding were the determining factors for mechanical ventilation [4]. Other factors like young age of 1-6 months, weight for age <-2 Z score, altered level of consciousness and CHD were found to be associated with mortality in pneumonia, even though these factors were not observed in all the three study groups. The different combination of risk factors among these groups may be due to ambiguity in clinical features for pneumonia, associated wheeze, CHD, etc. Young age has been reported to be a risk factor for mortality in studies from India and other developing countries [7-9, 11]. Malnutrition was another significant contributory factor for mortality in other studies also [9,11, 17]. Not only that malnutrition was associated with increased fatality, there was an incremental effect in pneumonia mortality with increasing degree of malnutrition when all the cases were considered together. CHD was a risk factor for pneumonia mortality in a study [7] while not so in another

study [4]. A more detailed analysis with reference to the type (cyanotic or acyanotic) and severity of CHD is needed to clarify its role in pneumonia deaths.

Limitations of the study are that specific etiology of pneumonia could not be identified by blood culture or other methods and radiological diagnosis was by the radiologist and clinician by consensus and not as per WHO criteria [18]. Other potentially relevant risk factors such as lack of exclusive breast feeding, indoor air pollution, hypoxia, increased C-reactive protein and head nodding were not studied due to non availability of these data in view of retrospective nature of the study. The sample studied also was less than calculated sample size. A strength of the study was the study period of three years preventing the effect of epidemic outbreak and seasonality.

Case fatality rate among children 1 month to 59 months of age hospitalized with community acquired pneumonia was 8.2%. Need for assisted ventilation was found to be independently associated with mortality in children aged 1-59 months admitted with pneumonia. Young age (1-6 months), malnutrition (<-2 Z weight for age), altered level of consciousness and associated congenital heart disease are other factors and hence more aggressive monitoring and management are required in children with these risk factors.

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REFERENCES

1. Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world wide distribution of child deaths from acute respiratory infections. *Lancet Infect Dis.* 2002;2:25-32.
2. World Health Statistics Geneva WHO; 2007 available from <http://www.who.int/whosis/whostat/2007.pdf>

3. Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, *et al.* For the Child Health Epidemiology Reference Group of WHO and UNICEF. Global, Regional, and National causes of child mortality in 2008: a systematic analysis. *Lancet*. 2010; 375:1967-87.
4. Tiewsoh K, Lodha R, Pandey RM, Broor S, Kalaivani M, Kabra SK. Factors determining the outcome of children hospitalized with severe pneumonia. *BMC Pediatrics*. 2009;9:15.
5. Agrawal PB, Shendurnikar N, Shastri NJ. Host factors and pneumonia in hospitalized children. *J Indian Med Assoc*. 1995;93:271-2.
6. Suwanjutha S, Ruandkanchanasetr S, Chantarojanasini T, Ttotrakitya S. Risk factors associated with morbidity and mortality of pneumonia in children under 5 years. *Southeast Asian J Trop Med Public Health*. 1994;25:60-6.
7. Djelantik IG, Gessner BD, Sutanto A, Steinhoff M, Linehan M, Moulton LH, *et al.* Case fatality proportions and predictive factors for mortality among children hospitalized with severe pneumonia in a rural developing country setting. *J Trop Pediatr*. 2003;49:327-32.
8. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. *Bull World Health Organ*. 2008;86:408-16.
9. Sehgal V, Sethi GR, Sachdev HP, Satyanarayana L. Predictors of mortality in subjects hospitalized with acute lower respiratory tract infections. *Indian Pediatr*. 1997;34:213-9.
10. Patwari AK, Aneja S, Mandal RN, Mullick DN. Acute respiratory infections in children: a hospital based report. *Indian Pediatr*. 1988;25:613-7.
11. Deivanayagam N, Nedunchelian K, Ramasamy S, Ratnam SR. Risk factors for fatal pneumonia: a case control study. *Indian Pediatr*. 1992;29:1529-32.
12. World Health Organization. Handbook IMCI. Integrated management of childhood illness. Geneva: World Health Organization 2000.
13. Ralston M, Hazinski MF, Zaritsky AL, Schexnayder SM, Kleinman ME. PALS Provider Manual. American Heart Association, Dallas, Texas. 2006. p.66-68.
14. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards: length/height-for-age, weight-for-age-weight-for-length, weight-for-height and body mass index-for-age: methods and development. Geneva: World Health Organization, 2006.
15. Berman S, McIntosh K. Acute Respiratory infection. *In*. Walsh JA, Warren KS (eds). Strategies for primary health care. Technologies Appropriate for the control of disease in the developing world. The University of Chicago press, 1986. p.29-46.
16. Roy P, Sen PK, Das KB, Chakraborty AK. Acute respiratory infections in children admitted in a hospital of Calcutta. *Indian J Public Health*. 1991;35:67-70.
17. Banajeh SM. Outcome for children under 5 years hospitalized with severe Acute Lower Respiratory Infections in Yemen. A 5 year Experience. *J Trop Pediatr*. 1998;44:343-6.
18. World Health Organization Pneumonia Vaccine Trial Investigators Group. Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children. Geneva, WHO; 2001.