Predictors of mortality in children due to severe and very severe pneumonia

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ABSTRACT

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Background: Mortality due to pneumonia in children is more than any other illness. Limited data is available to predict mortality in children with pneumonia from central India. **Aim:** To study predictors of mortality in children aged 1-59 months hospitalised with severe and very severe pneumonia. **Materials and Methods:** Present study was observational longitudinal study that was done in a tertiary care hospital of central India. Two hundred and ninety children, aged 1-59 months, presented with severe and very severe pneumonia were enrolled in this study. Outcome and predictors of mortality were studied. Data was analysed with Chi-square test, univariate and multivariate regression analysis. **Results:** Out of 270 enrolled study subjects, maximum (108, 37.24%) were belonged to 1-6-months age group. Proportion of mortality was maximum (16, 64.00%) in that age group. Overall case fatality rate was 8.62%. Among significant variables, delayed hospital referral [adjusted odds ratio (OR)-52.09, 95% confidence interval (CI)- 6.74-402.39], incomplete immunisation (OR-12.28, 95% CI-2.15-69.93), severe malnutrition (Z score < −3) (OR-15.51, 95% CI- 2.04-117.83), refusal to feed (OR- 30.57, 95% CI- 2.47-378.26), and hypoglycaemia (OR- 6.98, 95% CI- 1.05-46.30) were found significant independently on multivariate regression analysis. Conclusion: Delayed hospital referral, incomplete immunisation, severe malnutrition, refusal to feed, and hypoglycaemia were independent predictors of mortality in children with severe and very severe pneumonia.

Key words: Children, mortality, predictors, severe pneumonia, very severe pneumonia

INTRODUCTION

Pneumonia is estimated to kill 410,000 children in India every year. In India, recent estimates in under-fives suggest that 13% of deaths and 24% of National Burden of Disease is due to pneumonia.[1] To reduce mortality, the World Health Organisation (WHO) initiated the Acute Respiratory Infection (ARI) control program in 1983 which led to a decline in the infant mortality rate and under-fives mortality.[2] Case fatality rates in hospitalised children are reported to be between 8.7 and 47%.[3-5]

Although predictors of mortality were studied in developed countries, it can not be used in developing countries due to differences in aetiology and treatment resources available. Very few studies have evaluated the predictors of mortality in children with pneumonia in developing countries.[3,6,7] More studies are required to analyze the factors predicting mortality in hospitalised children.

Hence, this study was planned to study predictors of mortality in children aged 1-59 months hospitalised with severe and very severe pneumonia.

MATERIALS AND METHODS

The present observational longitudinal study was carried out in a tertiary care teaching hospital of central India. Duration of the study was 2 years (2010-2012). Ethical clearance was sought for from institutional ethical committee before start of the study. Children who were diagnosed as severe and very severe pneumonia[2] of either sex between age group 1-59 months admitted in a hospital were enrolled in the study.

Severe Pneumonia[2]: Rapid respiration with lower chest indrawing.

Very Severe Pneumonia[2]: rapid respiration with severe chest indrawing/ central cyanosis/ difficulty breastfeeding/ unconsciousness, or head nodding.

For diagnosing the child as tachypneic or rapid respiration, the WHO guidelines followed that is: For age <2 months is respiratory rate >60/min; age 2-12 months is respiratory rate >50/min and age >1yr is respiratory rate >40/min.

Children diagnosed with asthma, aspiration pneumonia, children with WHO-defined pneumonia, immune-compromised children and children with other comorbidities such as meningitis and congenital heart disease were excluded. They were followed up for outcome measurement till their discharge from the hospital or death.

Consecutive convenient sampling technique was adopted in this study. Minimum sample size required was 288, derived from published study.[7] Power of study is 80% and level of significance is 5%. Total 290 children were enrolled and as per WHO case definition were divided into two groups, severe pneumonia and very severe pneumonia. Any child reaching hospital after 3 days of illness was considered as delayed referral. Demographic data, clinical details and laboratory parameters of the enrolled cases were recorded in a predesigned pretested proforma. Variables studied are age, sex, urban slum, weight for age, delayed hospital referral, lack of exclusive breast feeding, incomplete immunisation (as per national immunisation programme), respiratory rate ≥70/minute, cyanosis, grunting, chest retractions, altered consciousness, refusal to feed, shock, pallor, mechanical ventilation, hypoglycaemia at admission (random blood sugar level <50 mg/dl), SpO_2 <90%, and total leucocyte count (TLC) >20000/mm³. They were treated with appropriate therapy and the outcome recorded was discharge or death. Statistical analysis was conducted using STATA version 10.0. Categorical variables were compared between deaths and discharges by performing Chi-square test. All tests were two sided and $P < 0.05$ is considered significant. Univariate and multivariate regression analysis was done in this study.

RESULTS

Table 1 shows that total 290 children aged 1-59 months were enrolled and maximum subjects (108, 37.24%) were from 1 to 6-months age group. Mortality was maximum (16, 64.00%) in 1-6-months age group and least (2, 8.00%) in 25-59-months age group. Out of 290 enrolled subjects, 65.86% (191) were male and rest were female; however, difference in mortality between them was not statistically significant ($P = 0.518$). Majority (254, 87.59%) of them were from lower socio-economic class and mortality was almost same in upper and lower socio-economic class.

Mortality was significantly higher in children with lack of exclusive breast feeding (16, 68.00%, $P = 0.013$), incompletely immunised (10, 40.00%, $P = 0.020$), severe malnutrition (Z score < −3) (9, 36.00%, $P = 0.008$), refusal of feed (16, 64.00%, $P = 0.010$), respiratory rate ≥ 70/minute (16, 64.00%, $P = 0.020$), delayed hospital referral (22, 66.66%, $P = 0.022$), hypoglycaemia (8, 32.00%, $P = 0.014$) and TLC <20000/mm³ (10, 47.61%, $P = 0.021$).

Table 1: Socio-demographic, clinical and laboratory variables and outcome of pneumonia

Variables	Present/Absent	No (%)	Death (%)	Survival (%)	*P*-value
Age (months)	1-6	108 (37.24)	16 (14.81)	92 (85.18)	0.004
	7-12	92 (31.72)	4 (4.34)	88 (95.66)	0.077
	13-24	51 (17.58)	3 (5.88)	48 (94.12)	0.044
	25-69	39 (13.44)	2 (5.12)	37 (94.88)	0.404
Sex	Male	191 (65.86)	15 (7.85)	176 (92.15)	0.518
	Female	99 (34.14)	10 (10.10)	89 (89.90)	
Socioeconomic status	Upper	36 (12.41)	3 (8.33)	33 (91.77)	0.947
	Lower	254 (87.59)	22 (8.66)	232 (91.44)	
Exclusive breast feeding	Yes	161 (55.55)	8 (4.96)	153 (95.04)	0.013
	No	129 (44.48)	17 (13.17)	112 (86.83)	
Weight for age (Z score)	> −2	190 (65.51)	8 (4.21)	182 (95.79)	0.008
	−2 to −3	51 (17.58)	8 (15.68)	43 (84.32)	
	< −3	49 (16.89)	9 (18.36)	40 (81.64)	
Respiratory rate	<70/minute	168 (57.93)	9 (5.35)	159 (94.65)	0.020
	≥70/minute	122 (42.06)	16 (13.11)	106 (86.89)	
Refusal of feed	Present	118 (40.68)	16 (13.55)	102 (86.45)	0.010
	Absent	172 (59.32)	9 (5.02)	163 (94.98)	
Delayed hospital referral	Yes	162 (55.87)	22 (13.58)	140 (86.42)	0.000
	No	128 (44.13)	11 (8.59)	117 (91.41)	
Incomplete immunisation	Yes	63 (21.72)	10 (15.87)	53 (84.13)	0.005
	No	227 (78.27)	15 (6.60)	212 (93.40)	
Hypoglycaemia	Present	44 (15.17)	8 (18.18)	36 (81.82)	0.014
	Absent	246 (84.82)	17 (6.91)	229 (93.09)	
Total leucocyte count (mm³/L)	<20000	248 (85.51)	11 (4.43)	237 (95.57)	0.021
	>20000	42 (14.49)	10 (23.80)	32 (76.20)	

Table 2 reveals that out of 290 subjects, 221 (76%) were of severe pneumonia and 69 (23.79%) were of very severe pneumonia. Among them, 25 children died while providing treatment, hence an overall case fatality rate (CFR) was 8.62%; however, CFR was 6.33% and 15.94% in severe pneumonia and very severe pneumonia, respectively.

By univariate analysis, variables found significant were age, urban slum, weight for age, delayed hospital referral, lack of exclusive breast feeding, incomplete immunisation, respiratory rate ≥70/minute, cyanosis, grunting, chest retractions, altered consciousness, refusal to feed, shock, pallor, mechanical ventilation, hypoglycaemia, SpO$_2$ <90%, and TLC >20000/mm^3. On multivariate regression analysis, delayed hospital referral [adjusted odds ratio (OR)-52.09, 95% confidence interval (CI)- 6.74-402.39], incomplete immunisation (OR-12.28, 95% CI-2.15–69.93), severe malnutrition (Z score < −3)(OR-15.51, 95% CI- 2.04-117.83), refusal to feed (OR-30.57, 95% CI-2.47-378.26), and hypoglycaemia (OR-6.98, 95% CI-1.05-46.30) were found significant independently, while rest were found insignificant [Table 3].

Table 2: Case fatality rate in severe and very severe pneumonia

Diagnosis as per WHO criteria	Deaths	Discharged	Case fatality rate (CFR) (%)
Severe pneumonia (*n*=221)	14	207	6.33
Very severe pneumonia (*n*=69)	11	58	15.94
Total (*n*=290)	25	265	8.62

DISCUSSION

Decreasing pneumonia deaths will significantly contribute to achieving Millennium Development Goal 4 (MDG 4) of reducing under 5-years mortality. This study was conducted to identify the demographic, clinical and laboratory variables associated with deaths in hospitalised children aged 1-59 months with diagnosis of severe and very severe pneumonia. Although various variables are studied until now, we tried to study variables which can be interpreted even at primary or secondary health care level and can be used to treat intensively or to refer early to tertiary care hospital.

In the present study, most children (37.24%) were from 1 to 6 months age group and this observation is similar to previous published studies.[7-9] In the developing nations, boys are treated with priority, leading to the high reporting of the males to the hospital. Thus, in the present study, 59.65% males were enrolled and similar observation were reported by previous study.[10] There was no significant difference in mortality between male and female; and between lower class and upper class in the present study. This can be explained by small sample size.

Association of lack of exclusive breast feeding with mortality in pneumonia is well described in previous studies[3,11,12] and we also found higher mortality in children with lack of exclusive breast feeding. Breast milk protects child by multiple mechanisms like maturational, anti-inflammatory, immuno-modulatory and antimicrobial action.[13] We found higher mortality in subjects with incomplete immunisation. SPEAR Study Group[14] has reported incomplete immunisation as an

Table 3: Predictors of mortality in children with severe and very severe pneumonia

Variables	Univariate analysis		Multivariate analysis	
	No. of deaths/total	*P*-values	*P*-value	Adjusted odds ratio and 95% CI
Age <6 months	16/108	0.029		
Urban slum	15/99	0.004		
Delayed hospital referral	22/162	0.022	0.000	52.09 (6.74-402.39)
Weight for age Z score < −3	9/40	0.008	0.008	15.51 (2.04-117.83)
Lack of exclusive breast feeding	17/112	0.013		
Incomplete immunisation	10/53	0.020	0.005	12.28 (2.15-69.93)
Fever duration <3 days	16/89	0.042		
Respiratory rate ≥70/min	16/106	0.020		
Cyanosis	14/89	0.025		
Grunting	15/92	0.012		
Chest retractions	12/60	0.014		
Altered consciousness	19/132	0.012		
Refusal to feed	16/102	0.010	0.008	30.57 (2.47-378.26)
Shock	20/148	0.019		
Pallor	16/107	0.022		
Mechanical ventilation	13/65	0.003		
Hypoglycaemia	8/36	0.014	0.044	6.98 (1.05-46.30)
SpO$_2$ <90%	11/52	0.014		
Total leucocyte count >20000/mm^3	10/32	0.021		

independent risk factor for predicting treatment failure in pneumonia.

Similar to previous studies,[5,15] presence of severe malnutrition was observed as independent risk factors for predicting mortality. A systematic review[16] has reported high mortality in children with pneumonia with severe malnutrition than moderate malnutrition. Similar to previous study,[17] we found delayed hospital referral as a significant risk factor for mortality. This can be due to delayed start of treatment in these patients. Presence of respiratory rate ≥70/minute was a significant, independent risk factor for mortality in the present study. Recent retrospective Indian study[7] also found chest indrawing as a risk factor for mortality in pneumonia.

Hypoglycaemia was found as independent predictor of mortality. Previous study[18] has reported association of hypoglycaemia with death in children and adults hospitalised for pneumonia. Spontaneous hypoglycaemia has numerous causes like severe systemic illness, severe malnutrition, medications, and malignancy. Contrary to our observation on TLC, previous published studies from India[3,6] and other developing country[19] found bandemia and abnormal leucocyte count as a significant independent risk factor for mortality.

We found overall CFR of 8.62% compared to 3.9% for an all-cause mortality in this age group. CFR of childhood pneumonia in various Indian studies ranges from 8.9% to 47%[3-6] and 3.4% to 12% in other developing countries.[9,17,20] This can be due to differences in aetiology, immunisation and treatment resources available.

In the present study, on multivariate regression analysis, delayed hospital referral, incomplete immunisation, severe malnutrition, refusal to feed, and hypoglycaemia were found significant predictors of mortality independently. A recent study from India[7] reported weight for age < –2 Z score and need for assisted ventilation as independent risk factors for mortality.

Limitation of the study was that we could not find out the aetiology of pneumonia. The study may have referral bias since many enrolled cases were referred from peripheral centres and findings can not be generalised. Strength of the study was the study period of 2 years preventing the effect of epidemic outbreak. There is a need to carry out extensive multi-centric studies involving both rural and urban areas to identify the predictors of mortality.

CONCLUSIONS

Case fatality rate among children aged 1 to 59 months hospitalised with severe and very severe pneumonia was 8.62%. Delayed hospital referral, incomplete immunisation, severe malnutrition, refusal to feed, and hypoglycaemia

were independent predictors of mortality. Children with these predictors of mortality should be monitored and treated intensively to decrease mortality.

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