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Original Research Article

# Study of Various Risk Factors Leading to Mortality in Severe Pneumonia among Children 1 Month to 5 Years

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**Abstract**

**Introduction:** Understanding the diverse array of risk factors contributing to mortality in severe pneumonia among children aged one month to five years is essential for devising targeted interventions to reduce mortality rates and improve overall child health outcomes. By dissecting various risk factors, including demographic, socio-economic, and environmental influences, our research aims to pave the way for targeted interventions and improved health outcomes for vulnerable children worldwide.

**Material and Methods:** The study, conducted at a tertiary care center in Gujarat from March 2021 to September 2022, focused on children aged 1 month to 5 years admitted to the Pediatric Intensive Care Unit (PICU) with severe pneumonia. Severe pneumonia cases were clinically diagnosed according to WHO classification criteria. Inclusion criteria encompassed children meeting the specified age range admitted to the PICU with severe pneumonia, while exclusion criteria included known cases of congenital heart disease, asthma, COPD, and tuberculosis. Detailed clinical assessments, socioeconomic profiling, and investigations including chest X-ray and blood culture were conducted. All patients received antibiotics, and statistical analysis was performed to discern significant differences and associations.

**Results:** Our investigation into severe pneumonia among children aged one month to five years, encompassing a total of 240 subjects, reveals several critical insights into the disease's dynamics. Notably, limited parental education and a history of exclusive breastfeeding (72.9%) emerged as prominent risk factors. Clinical symptoms such as fever (65.4%), cough (12.5%), and feeding refusal (42.9%) showed no significant correlation with mortality. However, malnutrition, particularly Severe Acute Malnutrition (SAM), demonstrated a strong association with mortality, with SAM children experiencing the highest fatality rate (40.4%). Physiological parameters including hypoxia (90.4%), low blood pressure (97.9%), pallor (32.5%), and leukocytosis (32.9%) were significant predictors of mortality. Additionally, chest X-ray findings, oxygen supplementation, and mechanical ventilation needs were indicative of mortality outcomes. Furthermore, sociodemographic and maternal factors exhibited significant associations with mortality, underscoring the need for targeted interventions to mitigate childhood pneumonia mortality.

**Conclusion:** In conclusion, our study identifies critical predictors of mortality in children with severe pneumonia aged 1 to 5 years, emphasizing the importance of prompt recognition and targeted interventions to improve outcomes in this population.

**Keywords:** Severe Pneumonia, Children, Mortality, Risk Factors.



## Introduction

Severe pneumonia continues to pose a significant threat to child health globally, particularly among children aged one month to five years, representing a critical age group vulnerable to its adverse effects. [1,2] Trends in morbidity and mortality among children serve as crucial indicators of the overall health status within developing nations. According to the World Health Organization (WHO), the global under-five mortality in 2019 amounted to approximately 5.2 million deaths, translating to over 14,000 fatalities daily. [3] Moreover, neonatal deaths worldwide reduced from five million in 1990 to 2.4 million in 2019, accompanied by a notable decline in the under-five mortality rate, plummeting by 58% from 93 deaths per 1000 live births in 1990 to 37.7 per 1000 children in 2019. [4] Understanding the diverse array of risk factors contributing to mortality in severe pneumonia among this age group is essential for devising targeted interventions to reduce mortality rates and improve overall child health outcomes. [5]

Pneumonia, characterized by inflammation of the lungs often caused by bacterial, viral, or fungal

infections, presents a complex interplay of factors influencing its severity and outcomes. [6] While effective treatment modalities exist, including antibiotics and supportive care, identifying the specific risk factors predisposing children to severe pneumonia-related mortality is paramount for tailored interventions. [7]

The significance of this study lies in its potential to inform evidence-based strategies for pneumonia prevention, early detection, and management, thereby reducing the burden of childhood mortality globally. [8] This study aims to comprehensively explore the multifactorial nature of severe pneumonia mortality among children aged one month to five years, with a focus on elucidating the intricate relationships between demographic, socio-economic, nutritional, immunological, and environmental determinants.

## Material and Method

The study was conducted at a tertiary care center located in Gujarat from March 2021 to September 2022. Children aged 1 month to 5 years who were admitted to the Pediatric Intensive Care Unit (PICU) with severe pneumonia were eligible for enrollment. Severe pneumonia was clinically diagnosed based on the World Health Organization (WHO) classification. [9]

Inclusion criteria encompassed children aged 1 month to 5 years admitted to the PICU with severe pneumonia, whose parents or legal guardians provided informed consent. Exclusion criteria included known cases of congenital heart disease, asthma, Chronic Obstructive Pulmonary Disease (COPD), and Tuberculosis.

A detailed history was taken, noting presenting symptoms including fever, cough, rapid breathing, refusal of feeds, and wheezing. Thorough physical examinations, including anthropometry, were conducted with emphasis on assessing the general condition of the child, respiratory rate, presence of fever, cyanosis, and pallor. Detailed systemic examinations of the respiratory, cardiovascular, and central nervous systems were performed, and any associated illnesses such as septicemia, meningitis, and congestive cardiac failure were noted.

Socioeconomic histories were recorded, including the type of housing, family size, sanitary facilities, and cooking fuel type. Socioeconomic status was classified according to modified Prasad's classification. Detailed histories regarding immunization and feeding practices were taken. The degree of malnutrition was recorded according to IAP classification. [10]

Patients were classified into severe pneumonia and very severe pneumonia according to WHO ARI criteria. Risk factors for severe and very severe pneumonia were studied for analytical purposes. Investigations including hemoglobin, total WBC count, differential WBC count, ESR, chest X-ray, and blood culture were conducted in all patients. Investigations were repeated according to need during treatment to assess prognosis and treatment effectiveness.

All patients received antibiotics, with the majority receiving first-line antibiotics (ampicillin with gentamicin) except those with complications. Patients who failed to respond to first-line antibiotics within 48 hours received second-line antibiotics. Cloxacillin was administered in case of empyema/massive consolidation. All children were evaluated during their hospital stay, and response to treatment was noted.

Statistical analysis was performed using Microsoft Excel. The Chi-Square test was utilized to determine significant differences between groups, and odds ratios were determined whenever required. Significance for the statistical tests was predetermined at a probability value of 0.05 or less ($p < 0.05$).

## Results

A total of 240 subjects were included in the study. A total of 240 subjects were included and the socio demographic and risk factor data were as per mentioned in Table 1.

**Table 1: Sociodemographic and risk factor among study subjects**

| Category | Frequency (%) |
|---|---|
| **Age (months)** | |
| 2-6 | 138 (57.5%) |
| 6-12 | 49 (20.4%) |
| 12-24 | 24 (10.0%) |
| >24 | 29 (12.1%) |
| Female | 89 (37.1%) |
| Male | 151 (62.9%) |
| **Socioeconomic Status** | |
| Upper, Upper middle, Lower Middle, Upper Lower, Lower | 0 (0%), 16 (6.7%), 40 (16.7%), 169 (70.4%), 15 (6.3%) |
| **Risk Factors** | |

| | |
|---|---|
| Education | |
| Illiterate, Primary School, Middle School, High School, Post High School | 140 (48.3%), 64 (26.7%), 17 (7.1%), 11 (4.6%), 8 (3.3%) |
| Exclusive Breast Feeding | 175 (72.9%) |
| Smoking in Family | 116 (48.3%) |
| H/o Covid Contact | 62 (25.8%) |
| Use of biomass fuel | 95 (39.6%) |
| Delay in seeking care | |
| <72 hr, 72 hr-7days, >7days | 185 (77.1%), 30 (12.5%), 25(10.4%) |
| Delay in Transport | 87 (36.3%) |

In our study, severe pneumonia exhibited higher prevalence among patients with limited parental education, with 48.3% of cases in individuals whose parents were illiterate and 26.7% in those educated up to primary school level. Additionally, a significant proportion, 72.9%, had a history of exclusive breastfeeding. Among clinical features, fever was present in 65.4% and cough in 12.5% of patients. Feeding refusal was noted in 42.9%, with 46.3% diagnosed with Moderate Acute Malnutrition (MAM) and 33.8% with Severe Acute Malnutrition (SAM). Physiological parameters indicative of severity included hypoxia in 76.7% of cases, blood pressure below the 90th centile in 97.9%, temperature >100°F in 53.8%, and pallor in 32.5%. Leukocytosis was observed in 32.9%, while a majority had serum calcium levels <8 mg/dL (56.1%).

In our study, the majority of patients (86.3%) required oxygen supplementation. The need for mechanical ventilation within specific time frames of admission was observed in 11.7% within 6 hours, 10.8% between 6-12 hours, and 11.3% beyond 12 hours. Among the 240 children aged between 1 month to 5 years with severe pneumonia, 51 (21.7%) succumbed to the illness. The mortality rate among children within this age group with severe pneumonia was determined to be 21.7%.

In our study, children's age and sex were not associated with mortality in severe pneumonia cases, but socioeconomic status (SES) emerged as a significant predictor. The majority of deceased children belonged to the upper lower class (51.9%), while mortality rates were 17.3% in the lower class and 5.8% in the upper middle class ($p < 0.001$). Maternal risk factors found in our study were as per in Table 2.

**Table 2: Maternal risk factors for outcome**

| Risk factors | | Outcome | | Total | P value |
|---|---|---|---|---|---|
| | | Death | Discharge | | |
| Education | Illiterate | 33 (63.5) | 107 (56.9) | 140 (48.3) | 0.396 |
| | Primary School | 11 (21.2) | 53 (28.2) | 64 (26.7) | |
| | Middle School | 5 (9.6) | 12 (6.4) | 17 (7.1) | |
| | High School | 3 (5.8) | 8 (4.3) | 11 (4.6) | |
| | Post High School | 0 (0) | 8 (4.3) | 8 (3.3) | |
| Exclusive Breast Feed | No | 33 (63.5) | 32 (17) | 65 (27.1) | <0.001 |
| | Yes | 19 (36.5) | 156 (83) | 175 (72.9) | |
| Smoking in Family | No | 20 (38.5) | 104 (55.3) | 124 (51.7) | 0.031 |
| | Yes | 32 (61.5) | 84 (44.7) | 116 (48.3) | |
| H/o Covid Contact | No | 21 (40.4) | 157 (83.5) | 178 (74.2) | <0.001 |
| | Yes | 31 (59.6) | 31 (16.5) | 62 (25.8) | |
| Use of bio-mass fuel | No | 16 (30.8) | 129 (68.6) | 145 (60.4) | <0.001 |
| | Yes | 36 (69.2) | 59 (31.4) | 95 (39.6) | |
| Delay in seek-ing care | <72 hr | 26 (50) | 159 (84.6) | 185 (77.1) | <0.001 |
| | 72 hr-7days | 10 (19.2) | 20 (10.6) | 30 (12.5) | |
| | >7 days | 16 (30.8) | 9 (4.8) | 25 (10.4) | |
| Delay in Transport | No | 21 (40.4) | 132 (70.2) | 153 (63.7) | <0.001 |
| | Yes | 31 (59.6) | 56 (29.8) | 87 (36.3) | |

In our study, factors such as fever (p=0.320), cough (p=0.438), and refusal to feed (p=0.594) did not show significant association with mortality, while malnutrition emerged as a significant predictor. Severe Acute Malnutrition (SAM) children had the highest mortality (40.4%), compared to 13.5% among Moderate Acute Malnutrition (MAM) children. Among laboratory parameters, hypoxia (80-91% oxygen saturation) (90.4%; p<0.001), blood pressure < 90th centile (90.4%; p<0.001),

presence of pallor (40.5%; p<0.001), and leucocytosis (61.5%; p<0.001) were significant predictors of mortality. Analysis of chest X-rays revealed mortality rates of 17.3%, 25%, and 11.5% in children with consolidation, diffuse infiltrates, and effusion, respectively (p<0.001). Mortality was higher in children requiring oxygen (92.3%) compared to those who did not (p=0.001). Mechanical ventilation also predicted mortality, with the highest mortality (36.5%) observed in children requiring it within 6 hours of admission, followed by 34.6% within 6-12 hours, and 18.8% beyond 12 hours of admission (p<0.001).

**Discussion**

Childhood clinical pneumonia is caused by a combination of exposure to risk factors related to the host, the environment and infection. In present study risk factors amongst severe and very severe pneumonia like appropriate immunization for age, presence of anemia, previous history of similar illness, Protein Energy Malnutrition (PEM) grade 3 and 4, poor housing conditions and indoor environmental pollutions were studied.

The present study included children with WHO-defined symptoms and other signs to define pneumonia and severe pneumonia. [11] The other included signs which were part of the initial assessment, and whose values were ascertained by other studies, were cyanosis, toxic look, severe pallor (Hb<7 gm/dL), severe dehydration, shock, and meningeal irritation. [12]

Severe pneumonia was more prevalent in the age group of 2-6 months (57.5%). There were 20.4% children who had been between 6-11 months and 10% had age between 12-24 months and 12.1% were older than 24 months. In a recent Indian study [13], severe pneumonia was more common in children between two and 12 months of age compared with children between 13 and 60 months of age. The global prevalence of pneumonia is highest in the age group of 1–4 years. [14] On comparing the outcome among the children with severe pneumonia with Sociodemographic parameters it was revealed that age and sex of the children with severe pneumonia were not associated with the mortality.

In our study, severe pneumonia was more common in males (62.9%) compared to females (37.1%). Majority of the children with severe pneumonia belong to upper lower class (70.4%).

However, the socio economic status of children was a significant predictor of mortality in our study. Majority of the children who died belong to upper lower class (51.9%) whereas a quarter (25%) of the children who died belongs to lower middle class. Mortality rate in lower class of children was 17.3% whereas mortality rates in upper middle class was 5.8%. The association between mortality and SES was significant with p value of <0.001.

In Shah et al. [15] study, shows that nearly 60% of cases were male with male: female ratio was 1.45. Male children were predominant in the severe pneumonia group (63%) in Nasrin et al. [16] study. Yet in the pneumonia group their proportion reached 56% as well; overall male children thus were more affected significantly by severe pneumonia corroborating findings of other studies. [17,18] The cause behind the high susceptibility of male children could be either genetic, or higher reporting for male children by the mothers due to gender bias, which potentially causes mothers to notice symptoms due to a higher attention to male children particularly for seeking health care much earlier than female children. [19] Nevertheless, boys have greater likelihood of being affected or of care seeking in general for common acute respiratory illness than girls, as reported in several studies from India. Another possibility of male children to be in the high risk of infection could be the testosterone suppressing the immune response. [12] However, clarification of this trend is multifaceted, as the role of social determinants of health, such as sex, socio-economic status (SES), and water, sanitation, and hygiene (WASH) practices, with disease are often not included in studies.

In present study, severe pneumonia was more common in patients whose parents were illiterate (48.3%) and had education till primary school (26.7%). However, maternal education has no role in determining the mortality in present study (p=0.396). There was no relationship found between the educational status of the mothers and the incidence of pneumonia in children in Sutriana et al. study. [20] According to Machmud, one might anticipate higher morbidity and mortality among the less well-educated mothers because the children may not be receiving adequate food or appropriate health care. [21] Fatmi and White [22] identified no significant relationship between the education of parents with the incidence of pneumonia in children. The study of Tiewsoh et al. [23] reached much the same conclusions. Nonetheless, these findings are in contrast to the results presented by Nirmolia et al. [24] which showed that lack of maternal education is significantly correlated with the incidence of pneumonia. Additionally, the use of health care facilities was directly related to knowledge regarding pneumonia symptoms. As such, we can conclude that even mothers with relatively low levels of formal education might be educated in the signs and symptoms of pneumonia, so that proper steps might be taken toward seeking treatment for pneumonia as necessary.

Children who received excessive breast feeding, mortality reported in 36.5% of them. In our study, severe pneumonia was more common in patients had exclusive breast feeding (72.9%). Recent research in the United States and the United Kingdom showed children who are breastfed exclusively become ill much less frequently than children who are not breastfed. [25] Research from the group of Lamberti et al. [26] showed children who are not breastfed optimally or exclusively have a higher risk for morbidity and mortality secondary to pneumonia at all age levels. Pneumonia mortality was highest among children who were not breastfed exclusively, notably in the age range of 0–5 months. Breast milk contains colostrum, which is ~16% protein and contains immunoglobulin A, lactoferrin, and white blood cells that contribute to the prevention of infections. [27] Similar research featuring a cohort from Brazil found that children who were not breastfed were 17 times more likely to be hospitalized with pneumonia than were breastfed children; as such, the study concluded that breastfeeding could protect children from the most severe forms of pneumonia, especially in the first month of life. [28]

In present study, mortality was significantly more with family history of smoking (61.5%) as compared to those who had no smoker in the family. History of Covid Contact (59.6%; p<0.001), use of biomass fuel (69.2%; P <0.001)), delay in seeking care for more than 7 days (30.8%) and between 72 hours to 7 days (19.2%; P<0.001)) and delay in transport (59.6%; p<0.001) are the significant predictor of mortality in present study. Children who live with high levels of indoor air pollution have more than a 7-fold higher risk of contracting pneumonia than do infants and toddlers who live in homes without this condition. Most of the indoor air pollution was directly attributed to family members who were smoking cigarettes inside the house. Smoking inside the house, and also the use of mosquito coils and/or firewood stoves will have a direct impact on the quality of inhaled air. Mukono et al. [29] defined 5 sources of indoor pollution based on the results of an examination by The National Institute of Occupational Safety and Health; these include cigarette smoke, pesticides, and kitchen fumes. Greenberg et al. [30] showed that children under 5 years of age who are exposed to secondhand smoke are at a higher risk of pneumonia than children who are not exposed to cigarette smoke (P=0.016). Cigarette smoke in the home is also associated with bacterial infections including Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenza which are the most common bacterial pathogens which cause respiratory infections.

Among the clinical features, fever was present in 65.4% and cough in 12.5% patients and delay in transport was an important risk factor in 36.3% patients. On the World Pneumonia Day on Nov 12, 2015, action was sought to improve the early identification and treatment of childhood pneumonia at community and outpatient level to reduce disease severity and deadly outcomes. [31] It was apparent that the case–mortality rate in untreated children with pneumonia is high, sometimes reaching as high as 20%, and deaths can occur as early as 3 days after illness onset. [31] A study by Nasrin et al.6 also found that duration of illness at home for 3 days or more was significantly associated with the likelihood of disease progression to severe pneumonia. The same observation was reported from Kenya. [32] In Nasrin et al. [16] study fever was significantly associated with severe pneumonia. Studies in diverse LMICs like South Africa, Papua New Guinea, and Indonesia reported no association between fever and pneumonia severity. [33–35] However, one study in USA indicated temperature to be associated with severe pneumonia (not defined by WHO classification) [36] and another study reported duration of fever (at day 6) was associated with severity. [37] Although WHO did not consider fever in their pneumonia severity criteria, the British Thoracic Society (BTS) includes fever in their guideline. [38]

Our study revealed that 42.9% of patients who had refused to feed whereas 46.3% had MAM and 33.8% had SAM. In present study SAM children had maximum mortality (40.4%) whereas 13.5% of the MAM children had mortality. Refusal to feed (p=0.594) did not have any significant association with mortality whereas malnutrition among the children was a significant predictor for mortality. Furthermore, Fatmi and White reported that the impact of nutritionally-related short stature on the growth and development of lung function is not yet known.[22] However, stunted growth did increase the risk of treatment failure and is associated with longer recovery in children with pneumonia. The relationship between nutritional status (WHZ) and the incidence of pneumonia in our cohort is in line with the research of Tiewsoh et al. [23] which reported that malnutrition is the most important risk factor for pneumonia in childhood. These findings are also similar to those of the Caulfield et al. [39] which indicated that malnutrition in childhood contributes significantly to the global burden of disease, specifically that 52.3% of child deaths due to pneumonia are directly related to malnutrition.

In present study, hypoxaemia, a major indicator of disease severity was observed in almost 76.7% children with severe pneumonia and pallor was reported in 32.5%. 32.9% had leucocytosis whereas majority had serum calcium level <8 mg/dL

(56.1%). In Kasundriya et al. [13] study evaluated host biomarkers like the TLC count, which was useful only in the presence of moderate leukocytosis. Generally, in other studies, it was concluded that TLC and Neutrophils percentage were not useful in distinguishing pneumonia from severe disease. [40] However in our study, leucocytosis (61.5%; P<0.001) were the significant predictor of mortality in children with severe pneumonia.

In our study, presence of hypoxia (80-91% oxygen saturation) (90.4%; P<0.001) was significantly associated with mortality. Mortality was more in children requiring oxygen (92.3%) as compared to those who did not required oxygen (p=0.001). Several studies have investigated factors associated with hypoxemia, particularly clinical predictors. [23,32,33]

Mortality rate in children with age between 1 month to 5 years with severe pneumonia was 21.7% in our study. In Shah et al. [15] study, case fatality rate was 6.3% (9 cases) with 55.5% (5 cases) of the fatal cases occurred within 24 hours. Bokade et al. [41] 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% and 3.4% to 12% in other developing countries. [17,23,32,34] This can be due to differences in aetiology, immunisation and treatment resources available. Underlying congenital heart diseases (CHD) is a significant risk factor for pneumonia mortality. As in this study pneumonia with CHD is being excluded, this might be the probable reason for low case fatality rate in present study. Significant predictor for mortality was determined by comparing dead subjects with survived children. It was found that severity of pneumonia (very severe) malnutrition grade 3 and 4 and associated illness (septicemia, meningitis) were significantly associated with mortality.

Mechanical ventilation is a widely used form of respiratory support in pediatric intensive care units (PICU). However, prolonged use of mechanical ventilation causes complications and leads to mortality. [42] Need for mechanical ventilation within 6 hours of admission was reported in 11.7% whereas 10.8% need it between 6-12 hours and 11.3% need it post 12 hours. Mechanical Ventilation was a significant predictor of mortality among children with severe pneumonia. Mortality was highest in those who had required mechanical ventilation Within 6 hours of admission (36.5%) compared to 34.6% who needed mechanical ventilation within 6-12 hours of admission and 18.8% children had mortality those who needed mechanical ventilation within >12 hours of admission. The association was significant with p value of <0.001. A study revealed that children less than 5 years old were most vulnerable to major diseases and the majority of them are treated in the PICU. Worldwide statistics in all age groups indicate pneumonia remains the main cause of PICU utilization, and is also associated with a mortality rate of 29.9%. [43]

Key limitations include the absence of etiological investigation into pneumonia, single-hospital data, restricted generalizability to resource-limited settings, and exclusion of high-mortality SAM cases. Subjective case selection and limited diagnostic testing also pose potential misclassification risks.

## Conclusion

The mortality rate among hospitalized children aged 1 to 5 years with severe pneumonia was notable. Independent predictors of mortality included delayed hospital referral, severe malnutrition, feeding refusal, fever, lower socioeconomic status, family smoking history, hypoxia, low blood pressure, pallor, need for mechanical ventilation, and leucocytosis. Conversely, factors such as age, sex, and maternal education showed no association with mortality. Monitoring and intensive treatment of children exhibiting these mortality predictors are imperative to reduce mortality rates.

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