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## Time to Recovery from Severe Pneumonia and Its Predictors among Children Aged 2-59 Months Admitted To Asella Referral and Teaching Hospital, Asella, Ethiopia, 2023: A Retrospective Cohort Study

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Time to Recovery from Severe Pneumonia and Its Predictors among Children Aged 2-59 Months Admitted To Asella Referral and Teaching Hospital, Asella, Ethiopia, 2023: A Retrospective Cohort Study

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## Abstract

**Objective:** To determine the time to recovery from severe pneumonia and its predictors in children aged 2-59 months admitted to Asella Referral and Teaching Hospital, Ethiopia.

**Methods:** An institution-based retrospective cohort study was conducted on 424 children aged 2– 59 months. Medical records of eligible children were selected using a simple random sampling technique. The data were gathered using a structured checklist. Data were analyzed using STATA Version 17. The Kaplan-Meier curve and log-rank test were used to describe the survival function. Independent predictors of recovery time were identified using Cox regression analysis, and the model assumption was checked using Schoenfeld and Cox-Snell residuals. The 95% confidence interval of the hazard ratio with a corresponding p-value of 0.05 was used to declare statistical significance.

**Results:** The median recovery time was 5 days. The incidence density of recovery was 16 (95% CI: 14.44–17.76) per 100-person-day observation. Being a rural resident (AHR: 0.68, 95% CI: 0.57-0.82), aged 36-59 months (AHR: 0.70, 95% CI: 0.50-0.98), being Underweight (AHR: 0.75, 95% CI: 0.59-0.95), the presence of danger signs (AHR: 0.31, 95% CI: 0.24-0.39), and having comorbidity (AHR: 0.38, 95% CI: 0.30-0.48) were significant predictors of time to recovery in children aged 2–59 months.

**Conclusion**: In this study, the median recovery time was longer than that reported in similar studies. Age, residence, underweight, danger signs and comorbidities were significant predictors. Therefore, proper nutrition and management of children with danger signs at admission, and management of medical co-morbidities are necessary for promoting fast recovery.

Keywords: Asella, recovery, retrospective cohort, severe pneumonia, children under five.

# Strengths and limitations of the study

- A survival model was employed to analyze data that considered censoring of the study participants.
- The study employed five consecutive years of subject records which increased the generalizability of the results.

- However, due to the retrospective nature of the investigation and the use of secondary data, the study was unable to explore potential predictors of time to recovery, such as parental, sociodemographic, and environmental factors.
- Future research should collect primary data or use a prospective study to incorporate potential predictors of recovery time.

## Introduction

Pneumonia is the leading cause of death in children worldwide, more than AIDS, malaria, and measles.<sup>1,2</sup> Pneumonia continues to be a significant cause of death in children worldwide. It claimed the lives of 740180 children under the age of five in 2019 alone. This translates to a staggering 14% of all deaths in children under five and 22% of all deaths in children aged 1 to 5 years. <sup>3</sup> Children under the age of five are particularly vulnerable to this disease. In low- and middle-income countries, approximately 7 million children under the age of five are hospitalized with pneumonia each year, necessitating emergency oxygen therapy to ensure their survival. <sup>4</sup> Pneumonia presents a significant challenge for children residing in sub-Saharan Africa and Asia, where the highest numbers of fatalities are concentrated in countries such as the Congo, Nigeria, Ethiopia, India, and Pakistan. Shockingly, these countries account for more than half of all child deaths under the age of five.<sup>5</sup>

It is estimated that 3,370,000 children are diagnosed with pneumonia annually in Ethiopia, contributing to 18% of all causes of death, killing 40,000 under-five children.<sup>6</sup> According to health and health-related indicators (HHRI), pneumonia was the primary cause of death in Ethiopia in 2021, constituting 9.6% of all cases and 4.5% of cases in children under five years of age. Pneumonia has a major impact on Ethiopia's health and economy, especially among children. The medical expenses for pneumonia treatment range from \$8 for outpatient visits to \$64 for severe inpatient visits. Non-medical expenses such as transportation costs averaged \$2. Severe pneumonia has pushed 7% of households below the extreme poverty threshold, with the Ethiopian government spending \$13.9 million annually on treatment.<sup>7,8</sup>

Recovery time from severe pneumonia varies worldwide. A median recovery time of 2 days has been reported in Britain and Nepal, while a median recovery of 5 days was reported in India.<sup>9-12</sup> Studies conducted in Africa also reported a median recovery time of 3–10 days.<sup>13,14</sup> In Ethiopia,

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the recovery time varies between 3 and 4 days. Evidence showed that age, nutritional status, duration before seeking care, danger signs at admission, drug regimens, antibiotic change, severity of signs, and symptoms of pneumonia, mode of infancy feeding, formula feeding, vaccination status, and co-morbidity are all factors that influence the rate of recovery of children from severe pneumonia.<sup>15-20</sup>

Some studies conducted in Ethiopia have explored the time to recovery in children with severe pneumonia and its predictors. However, these studies have presented conflicting findings regarding certain predictors. For example, a study conducted in Gondar and Debre Markos found that older age was associated with prolonged recovery, whereas a study in Hossana indicated that older age was associated with early recovery. <sup>16,18,20</sup> Similarly, a study in Gondar found that rural residency prolonged recovery time, whereas a study in Bahirdar reported that rural residency increased the likelihood of early recovery <sup>17,21</sup>. Lastly, a study in Gondar found that the severity of signs and symptoms of pneumonia was associated with early recovery, which contradicts other findings. <sup>16</sup> Without resolving these contradictions, a clear picture of the predictors of time to recovery from severe pneumonia would not be adequately described. This shows the need for further investigation of predictors of recovery time from severe pneumonia. In addition, this problem was not addressed in the study area.

It is essential to study the time to recovery from severe pneumonia and its predictors in children for several reasons. First, understanding the factors that influence recovery time can help healthcare providers optimize treatment strategies and improve outcomes in children with severe pneumonia. Second, identifying predictors of longer recovery times can facilitate resource allocation, ensuring that children receive prompt and appropriate care. In addition, studying recovery time predictors can inform clinical decision-making, allowing healthcare providers to identify children at a higher risk for prolonged illness and intervene accordingly. Moreover, data on recovery times and predictors can inform public health planning efforts, leading to improved health outcomes and reduced healthcare costs. Finally, studying recovery times and predictors can contribute to a growing body of knowledge on severe pneumonia in children, guiding future research efforts to improve treatment and prevention strategies.

# **Study Design**

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## Study Setting, Study Design, and Period

An institution-based retrospective cohort study was conducted in ARTH from June 14 to July 5, 2023. ARTH is located in the Oromia Region, Arsi Zone, in Asella Town. Asella Town is located in the Arsi Zone of the Oromia Region, 126 km (78 mi) south of Addis Ababa. The hospital has 297 beds and acts as a medical referral center for a population of 3.5 million inhabitants in the Arsi Zone and its surroundings. It is one of Ethiopia's university teaching hospitals. Asella Teaching and Referral Hospital provides services (inpatient and outpatient) to the community.

# Population

All children with severe pneumonia aged 2-59 months admitted to Asella Referral and Teaching Hospital were the source population. All eligible children with severe pneumonia aged 2 to 59 months who were admitted to this Hospital pediatric ward from January 2018- December 2022 were the study population.

## **Eligibility Criteria**

All medical charts of children with severe pneumonia aged 2-59 months, who were treated in the pediatric ward, were included. However, incomplete information regarding the date of admission, and discharge, children whose recovery, death, transfer out, and refusal were not recorded and children who had been readmitted were excluded.

## **Sample Size Determination**

To estimate sample size, the Schoenfeld DA formula was used.<sup>22</sup> Assuming a 5% level of significance with a 2-sided critical value of 1.96, and 80% power with a table value of 0.84. From a previous similar study done on time to recovery from severe pneumonia, we considered the probability of recovery rate of 0.93 with the proportion of exposed 93% and the hazard ratio (HR: 0.56) for the underweight variable.<sup>23</sup>

$$E = \frac{(Z_{\alpha/2} + Z_{\beta})^2}{(lnHR)^2 P(1 - P)} = \frac{(1.96 + 0.84)^2}{(ln0.56)^2 0.93(1 - 0.93)} = \frac{7.84}{0.336 * 0.93 * 0.07} = 358.22$$
$$n = \frac{E}{\Pr(recovery)} = \frac{358}{0.93} = 385$$

To compensate for the missing/dropout rate, a 10% rate was added and the final sample size was 424.

## **Sampling Procedures**

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A total of 2423 children were recorded in the registration book at ARTH during the study period from January 1, 2018, to December 31, 2022. Patients who did not meet the inclusion criteria were excluded, whereas those who met the criteria were identified and recorded using their unique medical registration numbers. Using computer-generated random numbers, 424 records were randomly selected. Twenty-three randomly selected records were incomplete for nearly all independent variables and were thus excluded from the analysis.

## **Data Collection Tools and Procedure**

A pre-tested structured data collection checklist was used to extract routinely recorded data from patients with severe pneumonia. Data collection tools and study variables were selected after an extensive review of the literature. The data were gathered by two well-trained BSc pediatric nurses and one supervisor.

## **Study Variables**

## **Dependent Variable**

Time to recovery from severe pneumonia

## **Independent Variables**

Socio-demographic factors: Residence, age, sex, treatment-related factors (medication used, Nutritional status: history of exclusive breastfeeding, wasting, and stunting) Comorbidity status (HIV infection, heart failure, congenital heart diseases, asthma, Down syndrome, diabetes mellitus, hyperactive airway disease, SAM, anemia, and rickets) Danger signs during admission (Head nodding, abnormal body movement, severe chest in drawing, grunting, and vomiting) Duration before seeking care (1-3 days, 4-7 days, and more than 7 days) and Others variables (Vaccination status and sunlight exposure).

## **Operational Definition**

**Severe pneumonia:** defined as having a cough or difficulty in breathing with oxygen saturation < 90% or central cyanosis, severe respiratory distress, and signs of pneumonia with a general danger sign. The admission criteria for severe pneumonia in children under the age of five at Asella Referral and Teaching Hospital include the following symptoms: difficulty in breathing or fast breathing (respiratory rate of 60 breaths per minute or more in children aged 2-11 months, or 50

breaths per minute or more in children aged 1-5 years), cyanosis, severe chest in drawing, inability to breastfeed or drink, signs of respiratory distress (e.g. nasal flaring, grunting, stridor), history of high fever (39°C or higher), signs of poor general condition or severe illness, a child is unable to stay awake or alert, comorbidities such as HIV infection, severe anemia, or other underlying medical conditions, and history of not improving after initial treatment at home or in outpatient settings.

**Recovery time:** The period from admission until the child was released from the hospital because of improvement in symptoms was calculated as the number of days.

**The median recovery time:** was defined as the time at which half of the study participants had recovered.

**Censored**: A child admitted with severe pneumonia whose outcome status was either selfdischarged, transferred, unknown, dead, or not yet recovered up to the end of the study.

Event: Recovery from severe pneumonia

**Recovered**: A child released from the hospital as a result of clinical improvement confirmed by a doctor.

**Danger signs:** If the child has a loss of consciousness, abnormal body movement, vomiting everything, grunting, and severe chest in drawing.

**Co-morbidity:** If the child had any disease condition (acute or chronic) present during admission in addition to severe pneumonia including, HAAD (childhood asthma), anemia, severe acute malnutrition, rickets, RVI, CHF, CHD, acute gastroenteritis, measles, pertussis, bronchitis, meningitis, and others.

**Vaccination status:** Full vaccination status was defined as children who had completed all forms of vaccinations

Partially vaccinated: children who had taken at least one dose of PCV

Non-vaccinated: children who had never been vaccinated against PCV or other vaccines.

Up to date: children who had completed vaccination up to their age

## **Data Quality Control**

To ensure the quality of the data, a pre-test was performed on 5% of the total study population at JUMC to ensure agreement with the data abstraction format. The data collectors were trained prior to the data collection. Supervision and verification were performed to ensure completeness and consistency. The gathered data were examined for completeness and consistency during data extraction. The collected data were entered into the Epi data entry software, which includes control mechanisms such as range, must enter, and jump.

## **Data Analysis Procedure**

The extracted data were checked for completeness, entered into Epi-Data version 4.6, and exported to STATA software Version 17 for further cleaning, management, and statistical analysis. Descriptive statistics were used to summarize categorical variables. The results were summarized as frequency, percentage, mean, median, standard deviation, and IQR. The Kaplan-Meier (KM) survival curve and log-rank test were used to describe the survival function. Univariate Cox proportional hazards regression was performed to screen candidate variables for multivariable analysis. All covariates associated with the time to recovery (TTR) with a p-value of 0.25 or less were entered into the multivariable model. The independent predictors of TTR were analyzed using a multivariable Cox proportional hazards model to control for confounding effects. Adjusted hazard ratios (HRs) with a 95% Confidence Interval (CI) were estimated, and a p-value less than 0.05 was used to declare the presence of a significant association between time to recovery and covariates. Independent predictors of recovery time were identified using Cox regression analysis. A global test was conducted to verify the proportional hazard assumption. The p-value for the global test of the Schoenfeld residual test for the Cox regression model was 0.908, indicating that the proportionality assumption was valid. The interaction effects of the variables on time to recovery were examined; however, no variable showed a multiplicative effect. Therefore, the final model accounted only for the main effect. In time-to-event analysis, negative outcomes such as death and disease progression are usually evaluated. In our case, recovery was a positive event, and a hazard ratio of less than one implied a lower rate of recovery or a longer recovery time, which is a negative outcome.

# Results

## **Socio-demographic Characteristics**

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The study included records of under-5-year-old children with severe pneumonia admitted for five consecutive years from 2018 to 2022 in ARTH, Asella, Ethiopia. Of the 424 selected medical charts, 401 were completed, with a response rate of 94.6%. More than half (58.1%) were males, and 284 (70.8%) were urban residents (**Table 1**).

Table 1: Sociodemographic characteristics of children with severe pneumonia admitted to ARTH, Asella, Ethiopia, (N = 401)

Variable	Category	Recovered N (%)	Censored N (%)
Age	2-11 month	194 (91.1)	19 (8.9)
	12-35 month	124 (89.9)	14 (10.1)
	36-59 month	42 (84.0)	8 (16.0)
Sex	Male	213 (91.4)	20 (8.6)
	Female	147 (87.5)	21 (12.5)
Residence	Urban	106 (90.6)	11 (9.4)
	Rural	254 (89.4)	30 (10.6)

## **Nutritional and Vaccination Status**

Most children (73.57%) were exclusively breastfed. To classify the children's nutritional status, anthropometric measurements were compared with the WHO child growth standards. Of all study participants, 100 (24.94%) were categorized as underweight, 121 (30.7%) were stunted, and 88 (21.95%) were wasted (**Supplementary Table 1**).

## **Clinical Characteristics**

During admission, 294 (73.3%) patients were febrile and 140 (34.9%) had a high-grade fever. Among all observations, 249 (62.1%) had danger signs during admission. During admission 371 (92.5%) study participants had fast breathing, while 30 (7.5%) had normal breathing, and oxygen support was provided to 337 (84%) children (**Supplementary Table 2**).

## The median Recovery Time

Of the 401 study participants, 360 (89.78%) were recovered and the remaining, 41 (10.22%), were censored. The minimum and maximum length of hospital stay was 1 and 29 days, respectively. The time to recovery of children with severe pneumonia was estimated using the Kaplan-Meier

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survival curve and as shown in the overall Kaplan-Meier curve at the crossing broken lines, the median recovery time was 5 days with an IQR of 3-7. The graph tends to decline rapidly within the first ten days, implying that most children recovered from their illness within this time frame **(Figure 1).** 

## **Comparison of Recovery Status among Categorical Predictors**

The recovery time among the categories of various covariates was compared using a log-rank test and Kaplan-Meier plot. Depending on this test, recovery time among various groups of covariates such as age group, residence, nutritional status, comorbidity, danger signs, drug regimen, history of asthma, and ARTI, were significantly different at 5% level of significance. However, we prefer to present some of the variables in the figure below. The median recovery time for children with comorbidities was 7 days (IQR: 5–11), whereas for children without comorbidities was 4 days (IQR: 3-5). The median recovery time of children with danger signs during admission was 6 days (IQR: 5–9), and that of children without danger signs was 3 days (IQR: 2-4) (Figures 2 and 3).

## Predictors of Time to Recovery from Severe Pneumonia

The variables age, sex, residence, vaccination status, exclusive breastfeeding, weight for age, height for age, weight for height, duration before seeking care, history of asthma, history of acute respiratory tract infection, drug regimen, presence of danger signs during admission, presence of comorbidity and oxygen saturation during admission were associated with recovery time in a Univariable Cox regression analysis. Stepwise variable selection techniques were used to determine which variables should be included or excluded in the model. The decision was based on a p-value of 0.05 in the multivariable Cox regression model. Finally, in this multivariable Cox regression model, age category, residence, weight for age, presence of danger signs during admission, and presence of comorbidities were significant predictors of time to recovery in children aged 2–59 months.

Being a rural resident (AHR: 0.68, 95% CI: 0.57-0.82), aged 36-59 months (AHR: 0.70, 95% CI: 0.50-0.98), being underweight (AHR: 0.75, 95% CI: 0.59-0.95), the presence of danger signs (AHR: 0.31, 95% CI: 0.24-0.39), and having comorbidities at the time of admission (AHR: 0.38, 95% CI: 0.30-0.48) were significant predictors of recovery time (**Table 2**).

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Table 2: Predictors of recovery time in children with severe pneumonia admitted to Asella Referral and Teaching Hospital, Asella, Ethiopia, (N=401)

Variable	Recovered	Censored	CHR[95%CI]	AHR[95%CI]	P-value
Age categories					
2-11 months	194	19	1	1	
12-35 months	124	14	0.83[0.68-1.02]	0.93[0.76-1.13]	0.458
36-59 months	42	8	0.60[0.43-0.85]	0.70[0.50-0.98]	0.038*
Residence					
Urban	106	11	1		
Rural	254	30	0.73[0.59-0.91]	0.68 (0.57-0.82)	0.000**
Weight for age					
Normal	276	25	1	1	
Underweight	84	16	0.61[0.49-0.75]	0.75[0.59-0.95]	0.019*
Danger sign					
No	140	12	1		
Yes	220	29	0.27[0.22-0.34]	0.31 (0.25-0.39)	0.000**
Comorbidity					
No	219	18			
Yes	141	23	0.31[0.25-0.39]	0.38 (0.30-0.48)	0.000**

Abbreviations: AHR: adjusted hazard ratio; CI: confidence interval; CHR: crude hazard ratio; \*, \*\* indicates the significance of the variables

## Schoenfeld residual test and Cox-Snell residual plot

The Schoenfeld residual chi-square test was 2.74 with a corresponding p-value of 0.908, greater than 0.05, indicating that the proportional hazard assumption was satisfied.

The Cox-Snell Residual plot showed that the overall goodness of fit of the multivariable coxregression model for time to recovery from severe pneumonia was a good fit for the data, which is on the straight line at 45° (Supplementary Figure 1).

# Discussion

This study aimed to determine the recovery time from severe pneumonia and its predictors in children aged 2-59 months admitted to ARTH. The study followed 401 children for 2259 persondays. The study revealed that the overall recovery rate from severe pneumonia was 16 per 100person day observation with a median recovery time of 5 days. Rural residency, aged 36-59 months, being underweight, the presence of danger signs, and comorbidity were found to be significant predictors of recovery time.

The overall recovery was 16 per 100 person-days. This finding is fairly identical to the finding of the study in Debre Markos, in which the rate of recovery was 16.25 per 100 person-days, <sup>18</sup>and lower than the findings of the studies conducted in Gondar, Hossana, and Central and North Gondar Zones, in which the incidence of recovery was 21.3, 24.6, and 26.7 per 100 person-days, respectively. <sup>19,23,24</sup> Differences in sociodemographic and clinical characteristics of the study participants may explain the discrepancy among studies or it may be due to differences in treatment regimens and availability of quality healthcare services.

The overall median time to recovery from severe pneumonia was 5 days. The findings of this study are almost identical to those of the study carried out in the rural health center of the Gambia and Benshangul-Gumuz, which revealed that the average recovery time was 4.5 and 5 days, respectively.<sup>14,25</sup> This finding is lower than the study findings in Poland, which reported 8.2-10.1 days, and the study conducted in Tanzania, which reported 10 days.<sup>26,27</sup> This disparity could be due to the time difference between studies and the type of analysis employed by both studies, which does not consider subject censoring. In contrast to studies conducted in Nepal, Britain, Gondar, Hossana, Bahirdar, the Central and North Gondar Zones, and Jimma where the median recovery time was 2-4 days, the median recovery time was longer. <sup>10,16,18,19,28,29</sup> This variation could be brought about by socioeconomic differences between research areas, variations in study times, variations in treatment and care practices, and variations in clinical characteristics of the study population, as this study included a larger number of children who had danger signs and comorbidities.

This study showed that residency significantly predicted the recovery time of children admitted with severe pneumonia; children residing in rural areas had a longer recovery time than their counterparts. The result of the current study is supported by a study carried out in Central and North Gondar Zones .<sup>19</sup> This finding contradicts a study done in Bahirdar, Ethiopia, which found

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that rural residency increases the chance of early recovery.<sup>17</sup> This could be explained by the fact that children who are rural residents often face economic poverty, limiting access to care and quality healthcare services and causing delayed child care. Malnutrition is more prevalent in rural areas, which has a substantial negative impact on children's immunity, which in turn affects recovery time.<sup>30-32</sup>

Children's age was another important socio-demographic predictor that had a significant impact on recovery time. The recovery time of the children aged 36-59 months was longer than that of the children aged 2-11 months. This finding is supported by similar studies.<sup>16,18</sup> The current findings are not consistent with other findings. For instance, older age was associated with early recovery in a study conducted in Hossana and Nepal.<sup>10,20</sup> The observed variation could be attributed to the differences in age groups among the studies. A study conducted in Nepal focused solely on children aged 2-35 months. Additionally, the inconsistency could also be due to the differences in the baseline clinical conditions and treatment protocols across the study areas. Being underweight was a significant predictor of recovery time. The recovery time of underweight children was longer than that of their counterparts. These findings are consistent with those of similar studies. <sup>14,16,20</sup> This is because the nutritional status of a child plays a crucial role in their overall health, encompassing their growth and development, physical activity, and capacity to combat severe illnesses. Undernutrition can impair T-cell function, cytokine production, and the lymphocytes' ability to respond adequately to cytokines, thereby affecting both acquired immunity and innate host defense mechanisms.<sup>33</sup>

The presence of comorbidities was another significant predictor that substantially affected recovery time. The recovery time of children admitted with comorbidities was longer than that of their healthy counterparts. This may be because children with comorbid diseases may already experience complications from the underlying condition or may have a compromised immune system, which places additional stress on their bodies and makes them vulnerable to delayed recovery. The current finding is supported by a study carried out in Debre Markos, Central and North Gondar Zones, and Gambia.<sup>18,19,34</sup> Danger signs during admission were also predictors that substantially affected median recovery time. The recovery time was shorter in patients with no danger signs during admission. This finding is supported by similar studies.<sup>18,19,34</sup> This could be explained by the fact that children with danger signs have more severe disease, and the time needed

to recover from it is longer. Furthermore, the presence of danger signs may indicate complications that further delay treatment and recovery. This finding contradicts a study conducted in Gondar, which stated that the recovery time of children who had severe signs and symptoms of pneumonia was shorter than their counterparts.<sup>24</sup>

# CONCLUSION

The findings of this study revealed that the median recovery time was longer than that reported in similar studies. The variables children aged 36–59 months, rural residence, underweight in weight for age, presence of danger signs, and presence of comorbidity were statistically significant predictors of time to recovery in children aged 2–59 months. Therefore, proper nutrition and management of children with danger signs at admission, and management of medical comorbidities are necessary for promoting fast recovery. Further prospective studies need to be conducted to incorporate other potential predictors such as parental factors, environmental and other clinical-related factors.

# **Consent for Publication**

All authors declared that they have agreed to publication.

# **Competing Interests**

The Authors have declared no conflicts of interest in this work.

# Funding

There is no funding to report.

# Availability of data and material

The datasets used for this study are available from the corresponding author upon reasonable request.

# **Ethical Considerations**

Ethical approval was obtained from the Ethical Review Board (IRB) of Jimma University a Ref.

No. JUIH/IRB/367/23 and official permission were secured from the Health Department at Asella

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Referral and Teaching Hospital. As we stated in the methods section, we used secondary data retrieved from the patient cards/databases that had already been collected for the patients' registration cards in the Hospital. The names of the study participants were not recorded to maintain confidentiality, instead, their medical registration numbers were used to distinguish the study participants' information, and all data collected were kept confidential. The hospital database management department had consented to each study participant or caregiver to use the data for research purposes in a confidential way at the time of initiation.

# Authors' contributions

**T.M.:** Conceptualizations, Data curation, Formal analysis, Investigations, Methodology, Supervision, Validation, Visualization, Writing an original draft, and Writing Review and editing the manuscript.

**A.L.:** Formal analysis, Investigations, Methodology, Supervision, Visualization, Writing Review, and editing the manuscript.

**A.K.:** Formal analysis, Investigations, Methodology, Supervision, Visualization, Writing Review, and editing the manuscript.

## Acronyms and abbreviations

ACSH: Ayder Comprehensive Specialized Hospital, AGE: Acute gastroenteritis, AHR: Adjusted Hazard ratio, ARTH: Asella Referral and Teaching Hospital, ARTI: Acute respiratory tract infection, CHD: Congenital heart disease, CHR: Crud Hazard ratio, CI: Confidence interval, DM: Diabetes mellitus, DS: Down syndrome, HAAD: Hyperactive airway disease, HHRI: Health and health-related indicators, Hib: Hepatitis B vaccine, HIV: Human immune virus, JUMC: Jimma University Medical Center, PCV: Pneumococcal vaccine, PIV1: Parainfluenza type-1, NEMMCSH: Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital, RVI: Retroviral infection, SAM: Severe acute malnutrition, SCAP: Severe community-acquired pneumonia, SRS: Simple random sampling, TB: Tuberculosis, TTR: Time to recovery, UGCSH: University of Gondar Comprehensive Specialized Hospital, UNICEF: United Nations Children's Fund, and WHO: World Health Organization

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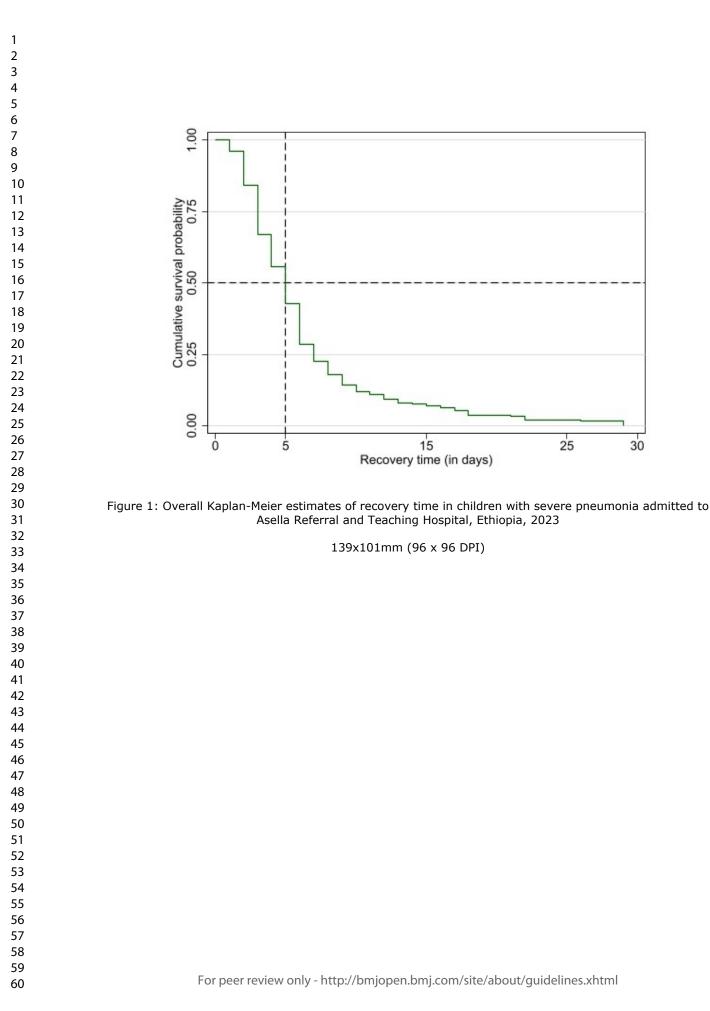
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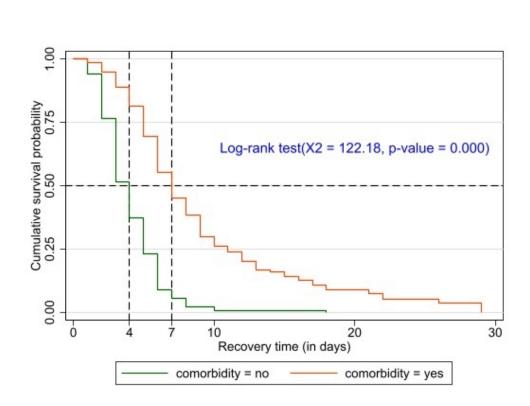
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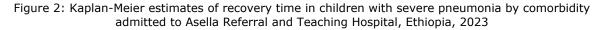
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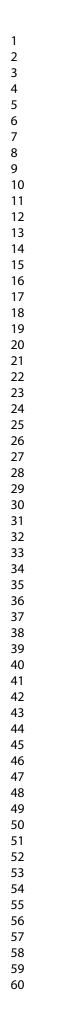






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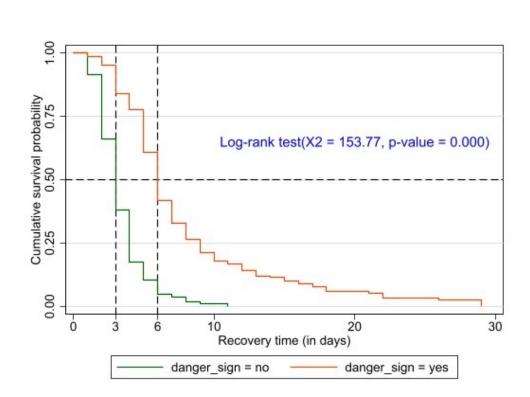


Figure 3: Kaplan-Meier estimates of recovery time in children with severe pneumonia by danger signs admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023

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Variable	Category	Recovered N (%)	Censored N (%)
Weight for age	Normal	276 (91.7)	25 (8.3)
	Underweight	84 (84.0)	16 (16.0)
Height for age	Normal	254 (90.7)	26 (9.3)
	Stunted	106 (87.6)	15 (12.4)
Weight for height	Normal	280 (89.5)	33 (10.5)
	Wasted	80 (90.9)	8 (9.1)
Exclusively breastfed	Yes	265 (89.8)	30 (10.2)
	No	95 (89.6)	11 (10.4)
Sunlight exposure	Yes	327 (90.1)	36 (9.9)
	No	33 (86.8)	5 (13.2)
Vaccination status	Fully vaccinated	129 (89.0)	16 (11.0)
	Partially vaccinated	27 (81.8)	6 (18.2)
	Up to date	182 (91.5)	17 (8.5)
	None vaccinated	22 (91.7)	2 (8.3)

Table 1: Nutritional and vaccination status of children with severe pneumonia admitted to ARTH, Asella, Ethiopia, (N = 401)

Table 2: Clinical characteristics of children with severe pneumonia admitted to ARTH, Asella, Ethiopia, N = (401)

Variable	Category	Recovered N (%)	Censored N (%)
Oxygen saturation	>=90	125 (87.4)	18 (12.6)
	<90	235 (91.1)	23 (8.9)
Oxygen support	Yes	304 (90.2)	33 (9.8)
	No	56 (87.5)	8 (12.5)
Respiratory rate	Normal	29 (96.7)	1 (3.3)
	Fast breathing	331 (89.2)	40 (10.8)
Body temperature	Normal	97 (90.7)	10 (9.3)
	Low-grade fever	136 (88.3)	18 (11.7)
	Low grade level	150 (00.5)	10(11.7)

	High-grade fever	127 (90.7)	13 (9.3)
History of ARTI	Yes	84 (88.4)	11 (11.6
	No	276(90.2)	30 (9.8)
History of Asthma	Yes	16 (88.9)	2 (11.1)
	No	344 (89.8)	39 (10.2
Danger sign	Yes	220 (88.4)	29 (11.6
	No	140 (92.1)	12 (7.9)
DPSC	1-3 days	176 (90.7)	18 (9.3)
	4-7 days	162 (90)	18 (10.0
	>7 days	22 (81.5)	5 (18.5)
Presence of	Yes	141(86.0)	23(14.0)
comorbidities	No	219(92.4)	18(7.6)

Abbreviations: ARTI: Acute respiratory tract infection, DPSC: Duration prior to seeking care

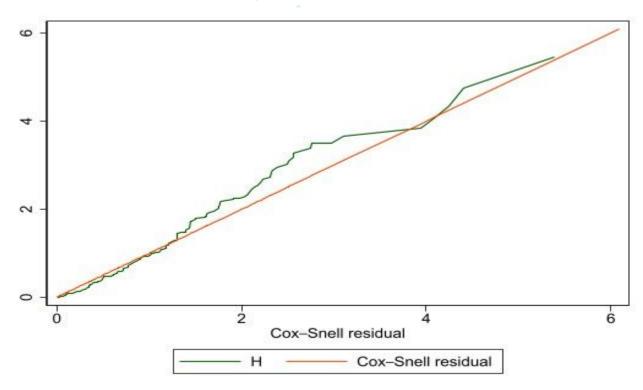


Figure 1: Cox-Snell Residual plot of the multivariable Cox-regression model for time to recovery from severe pneumonia admitted to Asella Referral and Teaching Hospital, Asella, Ethiopia



## Time to Recovery from Severe Pneumonia and Its Predictors among Children Aged 2-59 Months Admitted To Asella Referral and Teaching Hospital, Asella, Ethiopia, 2023: A Retrospective Cohort Study

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Time to Recovery from Severe Pneumonia and Its Predictors among Children Aged 2-59 Months Admitted To Asella Referral and Teaching Hospital, Asella, Ethiopia, 2023: A Retrospective Cohort Study

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## Abstract

**Objective:** To determine the time to recovery from severe pneumonia and its predictors in children aged 2-59 months admitted to Asella Referral and Teaching Hospital, Ethiopia.

**Methods:** An institution-based retrospective cohort study was conducted on 424 children aged 2– 59 months. Medical records of eligible children were selected using a simple random sampling technique. The data were gathered using a structured checklist. Data were analyzed using STATA Version 17. The Kaplan-Meier curve and log-rank test were used to describe the survival function. Independent predictors of recovery time were identified using Cox regression analysis, and the model assumption was checked using Schoenfeld and Cox-Snell residuals. The 95% confidence interval of the hazard ratio with a corresponding p-value of 0.05 was used to declare statistical significance.

**Results:** The median recovery time was 5 days. The incidence density of recovery was 16 (95% CI: 14.44–17.76) per 100-person-day observation. Being a rural resident (AHR: 0.68, 95% CI: 0.57-0.82), aged 36-59 months (AHR: 0.70, 95% CI: 0.50-0.98), being Underweight (AHR: 0.75, 95% CI: 0.59-0.95), the presence of danger signs (AHR: 0.31, 95% CI: 0.24-0.39), and having comorbidity (AHR: 0.38, 95% CI: 0.30-0.48) were significant predictors of time to recovery in children aged 2–59 months.

**Conclusion**: In this study, the median recovery time was longer than that reported in similar studies. Age, residence, underweight, danger signs and comorbidities were significant predictors. Therefore, families of children with identified predictors need counseling to prepare for the likelihood of slow recovery.

Keywords: Asella, recovery, retrospective cohort, severe pneumonia, children under five.

# Strengths and limitations of the study

- A survival model was employed to analyze data that considered censoring of the study participants.
- The study employed five consecutive years of subject records which increased the generalizability of the results.

- However, due to the retrospective nature of the investigation and the use of secondary data, the study was unable to explore potential predictors of time to recovery, such as parental, sociodemographic, and environmental factors.
- Future research should collect primary data or use a prospective study to incorporate potential predictors of recovery time.

## Introduction

Pneumonia is the leading cause of death in children worldwide, more than AIDS, malaria, and measles.<sup>1,2</sup> Pneumonia continues to be a significant cause of death in children worldwide. It claimed the lives of 740180 children under the age of five in 2019 alone. This translates to a staggering 14% of all deaths in children under five and 22% of all deaths in children aged 1 to 5 years. <sup>3</sup> Children under the age of five are particularly vulnerable to this disease. In low- and middle-income countries, approximately 7 million children under the age of five are hospitalized with pneumonia each year. <sup>4</sup> Pneumonia presents a significant challenge for children residing in sub-Saharan Africa and Asia, where the highest numbers of fatalities are concentrated in countries such as the Congo, Nigeria, Ethiopia, India, and Pakistan. These countries account for more than half of all child deaths under the age of five.<sup>5</sup>

It is estimated that 3,370,000 children are diagnosed with pneumonia annually in Ethiopia, contributing to 18% of all causes of death, killing 40,000 under-five children.<sup>6</sup> According to health and health-related indicators (HHRI), pneumonia was the primary cause of death in Ethiopia in 2021, constituting 9.6% of all cases and 4.5% of cases in children under five years of age. Pneumonia has a major impact on Ethiopia's health and economy, especially among children. The medical expenses for pneumonia treatment range from 8 USD for outpatient visits to 64 USD for severe inpatient visits. Non-medical expenses such as transportation costs averaged 2 USD. Severe pneumonia has pushed 7% of households below the extreme poverty threshold, with the Ethiopian government spending 13.9 USD million annually on treatment.<sup>7,8</sup>

Recovery time from severe pneumonia varies worldwide. A median recovery time of 2 days has been reported in Britain and Nepal, while a median recovery of 5 days was reported in India.<sup>9-12</sup> Studies conducted in Africa also reported a median recovery time of 3–10 days.<sup>13,14</sup> In Ethiopia, the recovery time varies between 3 and 4 days. Evidence showed that age, nutritional status,

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duration before seeking care, danger signs at admission, drug regimens, antibiotic change, severity of signs, and symptoms of pneumonia, mode of infancy feeding, formula feeding, vaccination status, and co-morbidity are all factors that influence the rate of recovery of children from severe pneumonia.<sup>15-20</sup>

Some studies conducted in Ethiopia have explored the time to recovery in children with severe pneumonia and its predictors. However, these studies have presented conflicting findings regarding certain predictors. For example, a study conducted in Gondar and Debre Markos found that older age was associated with prolonged recovery, whereas a study in Hossana indicated that older age was associated with early recovery. <sup>16,18,20</sup> Similarly, a study in Gondar found that rural residency prolonged recovery time, whereas a study in Bahirdar reported that rural residency increased the likelihood of early recovery <sup>17,21</sup>. Lastly, a study in Gondar found that the severity of signs and symptoms of pneumonia was associated with early recovery, which contradicts other findings. <sup>16</sup> Without resolving these contradictions, a clear picture of the predictors of time to recovery from severe pneumonia would not be adequately described. This shows the need for further investigation of predictors of recovery time from severe pneumonia. In addition, this problem was not addressed in the study area.

It is essential to study the time to recovery from severe pneumonia and its predictors in children for several reasons. First, understanding the factors that influence recovery time can help healthcare providers optimize treatment strategies and improve outcomes in children with severe pneumonia. Second, identifying predictors of longer recovery times can facilitate resource allocation, ensuring that children receive prompt and appropriate care. In addition, studying recovery time predictors can inform clinical decision-making, allowing healthcare providers to identify children at a higher risk for prolonged illness and intervene accordingly. Moreover, data on recovery times and predictors can inform public health planning efforts, leading to improved health outcomes and reduced healthcare costs. Finally, studying recovery times and predictors can contribute to a growing body of knowledge on severe pneumonia in children, guiding future research efforts to improve treatment and prevention strategies. Therefore, this study aimed to determine the time to recovery from severe pneumonia and its predictors in children aged 2-59 months who were admitted to Asella Referral and Teaching Hospital in Ethiopia.

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## **Study Design**

## Study Setting, Study Design, and Period

An institution-based retrospective cohort study was conducted in ARTH from 2018-2022. ARTH is located in the Oromia Region, Arsi Zone, in Asella Town. Asella Town is located in the Arsi Zone of the Oromia Region, 126 km (78 mi) south of Addis Ababa. The hospital has 297 beds and acts as a medical referral center for a population of 3.5 million inhabitants in the Arsi Zone and its surroundings. It is one of Ethiopia's university teaching hospitals. Asella Teaching and Referral Hospital provides services (inpatient and outpatient) to the community.

## Population

All children with severe pneumonia aged 2-59 months admitted to Asella Referral and Teaching Hospital were the source population. All eligible children with severe pneumonia aged 2 to 59 months who were admitted to this Hospital pediatric ward from January 2018- December 2022 were the study population.

## **Eligibility Criteria**

All medical charts of children with severe pneumonia aged 2-59 months, who were treated in the pediatric ward, were included. However, Children were excluded if there was incomplete information regarding the date of admission, discharge, recovery, death, transfer out, refusal, or if they were readmitted.

## **Sample Size Determination**

To estimate sample size, the Schoenfeld DA formula was used.<sup>22</sup> Assuming a 5% level of significance with a 2-sided critical value of 1.96, and 80% power with a table value of 0.84. From a previous similar study done on time to recovery from severe pneumonia, we considered the probability of recovery rate of 0.93 with the proportion of exposed 93% and the hazard ratio (HR: 0.56) for the underweight variable.<sup>23</sup>

$$E = \frac{(Z_{\alpha/2} + Z_{\beta})^2}{(lnHR)^2 P (1-P)} = \frac{(1.96 + 0.84)^2}{(ln0.56)^2 0.93 (1-0.93)} = \frac{7.84}{0.336 * 0.93 * 0.07} = 358.22$$

$$n = \frac{E}{\Pr(recovery)} = \frac{358}{0.93} = 385$$

To compensate for the missing/dropout rate, a 10% rate was added and the final sample size was 424.

#### **Sampling Procedures**

A total of 2423 children were recorded in the registration book at ARTH during the study period from January 1, 2018, to December 31, 2022. Patients who did not meet the inclusion criteria were excluded, whereas those who met the criteria were identified and recorded using their unique medical registration numbers. Using computer-generated random numbers, 424 records were randomly selected. Twenty-three randomly selected records were incomplete for nearly all independent variables and were thus excluded from the analysis.

## **Data Collection Tools and Procedure**

A pre-tested structured data collection checklist was used to extract routinely recorded data from patients with severe pneumonia. Data collection tools and study variables were selected after an extensive review of the literature. The data were gathered by two well-trained BSc pediatric nurses and one supervisor. Height-for-age, weight-for-height, and weight-for-age z-scores were calculated according to the 2006 WHO Child Growth Standards. Subjects were classified as stunted if their height-for-age Z-score fell below -2 compared to the WHO Child Growth Standards median for their respective age and sex. Wasting is a weight-for-height Z-score (WHZ) below -2, indicative of acute undernutrition or rapid weight loss. Furthermore, underweight was defined as a weight-for-age Z-score (WAZ) below -2.

### **Study Variables**

## **Dependent Variable**

Time to recovery from severe pneumonia

#### **Independent Variables**

Socio-demographic factors: Residence, age, sex, treatment-related factors (medication used, Nutritional status: history of exclusive breastfeeding, wasting, and stunting) Comorbidity status (HIV infection, heart failure, congenital heart diseases, asthma, Down syndrome, diabetes mellitus, hyperactive airway disease, SAM, anemia, and rickets) Danger signs during admission (Head nodding, abnormal body movement, severe chest in drawing, grunting, and vomiting) Duration before seeking care (1-3 days, 4-7 days, and more than 7 days) and Others variables (Vaccination status and sunlight exposure).

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#### **Operational Definition**

**Severe pneumonia:** defined as having a cough or difficulty in breathing with oxygen saturation < 90% or central cyanosis, severe respiratory distress, and signs of pneumonia with a general danger sign. The admission criteria for severe pneumonia in children under the age of five at Asella Referral and Teaching Hospital include the following symptoms: difficulty in breathing or fast breathing (respiratory rate of 60 breaths per minute or more in children aged 2-11 months, or 50 breaths per minute or more in children aged 1-5 years), cyanosis, severe chest in drawing, inability to breastfeed or drink, signs of respiratory distress (e.g. nasal flaring, grunting, stridor), history of high fever (39°C or higher), signs of poor general condition or severe illness, a child is unable to stay awake or alert, comorbidities such as HIV infection, severe anemia, or other underlying medical conditions, and history of not improving after initial treatment at home or in outpatient settings.

**Treatment Protocol:** Ceftriaxone is the preferred treatment for suspected community-acquired Methicillin-resistant Staphylococcus aureus (CA-MRSA), with vancomycin or clindamycin for added coverage. For uncomplicated bacterial pneumonia, ampicillin or penicillin G is used. Cefotaxime and ceftriaxone are used for children with incomplete Hib or Streptococcus pneumoniae immunization, or in areas with high penicillin-resistant strains. In severe pneumonia requiring ICU admission, a combination of vancomycin and ceftriaxone is preferred. A combination therapy of ceftriaxone, cefotaxime, and azithromycin is used for complicated pneumonia with effusion or empyema. Antiviral treatment is used if the child is hospitalized during influenza season.

**Recovery time:** The period from admission until the child was released from the hospital because of improvement in symptoms was calculated as the number of days.

**The median recovery time:** was defined as the time at which half of the study participants had recovered.

**Censored**: A child admitted with severe pneumonia whose outcome status was either selfdischarged, transferred, unknown, dead, or not yet recovered up to the end of the study.

Event: Recovery from severe pneumonia

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**Recovered**: A child released from the hospital as a result of clinical improvement confirmed by a doctor.

**High-grade fever:** a temperature ranging from 38.5°C to 41°C.

**Low-grade fever:** a temperature ranging from 37.5°C to 38.4°C.

**Danger signs:** If the child has a loss of consciousness, abnormal body movement, vomiting everything, grunting, and severe chest in drawing.

**Co-morbidity:** If the child had any disease condition (acute or chronic) present during admission in addition to severe pneumonia including, HAAD (childhood asthma), anemia, severe acute malnutrition, rickets, RVI, CHF, CHD, acute gastroenteritis, measles, pertussis, bronchitis, meningitis, and others.

**Fully vaccinated:** was defined as children who had completed all forms of vaccinations per the schedule.

Partially vaccinated: children who had taken at least one dose of PCV

Non-vaccinated: children who had never been vaccinated against PCV or other vaccines.

Up to date: children who had completed vaccination up to their age

**Exclusive breastfeeding**: - is the practice of giving an infant breast milk only up to the age of six months, except for oral rehydration solutions and drugs.

## **Data Quality Control**

To ensure the quality of the data, a pre-test was performed on 5% of the total study population at JUMC to ensure agreement with the data abstraction format. The data collectors were trained prior to the data collection. Supervision and verification were performed to ensure completeness and consistency.

#### **Data Analysis Procedure**

The extracted data were checked for completeness, entered into Epi-Data version 4.6, and exported to STATA software Version 17 for further cleaning, management, and statistical analysis. Descriptive statistics were used to summarize categorical variables. The results were summarized as frequency, percentage, mean, median, standard deviation, and IQR. The Kaplan-Meier (KM) survival curve and log-rank test were used to describe the survival function. Univariate Cox proportional hazards regression was performed to screen candidate variables for multivariable analysis. All covariates associated with the time to recovery (TTR) with a p-value of 0.25 or less

were entered into the multivariable model. The independent predictors of TTR were analyzed using a multivariable Cox proportional hazards model to control for confounding effects. Adjusted hazard ratios (HRs) with a 95% Confidence Interval (CI) were estimated, and a p-value less than 0.05 was used to declare the presence of a significant association between time to recovery and covariates. Independent predictors of recovery time were identified using Cox regression analysis. A global test was conducted to verify the proportional hazard assumption. The p-value for the global test of the Schoenfeld residual test for the Cox regression model was 0.908, indicating that the proportionality assumption was valid. The interaction effects of the variables on time to recovery were examined; however, no variable showed a multiplicative effect. Therefore, the final model accounted only for the main effect. In time-to-event analysis, negative outcomes such as death and disease progression are usually evaluated. In our case, recovery was a positive event, and a hazard ratio of less than one implied a lower rate of recovery or a longer recovery time, which is a negative outcome.

## Results

#### **Baseline characteristics**

Of the 424 selected medical charts, 401 were completed, with a response rate of 94.6%. More than half (58.1%) were males, and 284 (70.8%) were urban residents. 164 (40.9%) had co-morbidities. Severe acute malnutrition (28%) was the most common comorbidity, followed by hyperactive airway diseases (22%), acute gastroenteritis (12%), and congenital heart disease (10.4%). Other medical conditions include anemia, rickets, Down syndrome, spinal bifida, tuberculosis, meningitis, congestive heart failure, myelomeningocele, and hydrocephalus (**Table 1**).

Table 1: Baseline characteristics of children with severe pneumonia admitted to ARTH, Asella, Ethiopia, (N = 401)

Variable	Category	Recovered N (%)	Censored N (%)
Age	2-11 month	194 (91.1)	19 (8.9)
	12-35 month	124 (89.9)	14 (10.1)
	36-59 month	42 (84.0)	8 (16.0)
Sex	Male	213 (91.4)	20 (8.6)
	Female	147 (87.5)	21 (12.5)

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	Residence	Urban	106 (90.6)	11 (9.4)
		Rural	254 (89.4)	30 (10.6)
	Weight for age	Normal	276 (91.7)	25 (8.3)
		Underweight	84 (84.0)	16 (16.0)
)	Height for age	Normal	254 (90.7)	26 (9.3)
2		Stunted	106 (87.6)	15 (12.4)
3 4	Weight for height	Normal	280 (89.5)	33 (10.5)
5		Wasted	80 (90.9)	8 (9.1)
7	Exclusively breastfed	Yes	265 (89.8)	30 (10.2)
9		No	95 (89.6)	11 (10.4)
) 1	Sunlight exposure	Yes	327 (90.1)	36 (9.9)
2		No	33 (86.8)	5 (13.2)
4	Vaccination status	Fully vaccinated	129 (89.0)	16 (11.0)
5		Partially vaccinated	27 (81.8)	6 (18.2)
7		Up to date	182 (91.5)	17 (8.5)
9		None vaccinated	22 (91.7)	2 (8.3)
1	Oxygen saturation	>=90	125 (87.4)	18 (12.6)
2 3		<90	235 (91.1)	23 (8.9)
4	Oxygen support	Yes	304 (90.2)	33 (9.8)
5		No	56 (87.5)	8 (12.5)
7 3	Respiratory rate	Normal	29 (96.7)	1 (3.3)
9		Fast breathing	331 (89.2)	40 (10.8)
1	Body temperature	Normal	97 (90.7)	10 (9.3)
2 3		Low-grade fever	136 (88.3)	18 (11.7)
4 5		High-grade fever	127 (90.7)	13 (9.3)
5 7	History of ARTI	Yes	84 (88.4)	11 (11.6)
3		No	276(90.2)	30 (9.8)
)	History of Asthma	Yes	16 (88.9)	2 (11.1)
1 2		No	344 (89.8)	39 (10.2)
3	Danger sign	Yes	220 (88.4)	29 (11.6)
5		No	140 (92.1)	12 (7.9)
5				

DPSC	1-3 days	176 (90.7)	18 (9.3)
	4-7 days	162 (90)	18 (10.0)
	>7 days	22 (81.5)	5 (18.5)
Presence of	Yes	141(86.0)	23(14.0)
comorbidities	No	219(92.4)	18(7.6)

Abbreviations: ARTI: Acute respiratory tract infection, DPSC: Duration prior to seeking care

#### The median Recovery Time

Of the 401 study participants, 360 (89.78%) were recovered and the remaining, 41 (10.22%), were censored. The minimum and maximum length of hospital stay was 1 and 29 days, respectively. The time to recovery of children with severe pneumonia was estimated using the Kaplan-Meier survival curve and as shown in the overall Kaplan-Meier curve at the crossing broken lines, the median recovery time was 5 days with an IQR of 3-7. The graph tends to decline rapidly within the first ten days, implying that most children recovered from their illness within this time frame **(Figure 1).** 

## **Comparison of Recovery Status among Categorical Predictors**

The median recovery time for children with comorbidities was 7 days (IQR: 5–11), whereas for children without comorbidities was 4 days (IQR: 3-5). The median recovery time of children with danger signs during admission was 6 days (IQR: 5–9), and that of children without danger signs was 3 days (IQR: 2-4) (Figures 2 and 3).

## Predictors of Time to Recovery from Severe Pneumonia

The variables age, sex, residence, vaccination status, exclusive breastfeeding, weight for age, height for age, weight for height, duration before seeking care, history of asthma, history of acute respiratory tract infection, drug regimen, presence of danger signs during admission, presence of comorbidity and oxygen saturation during admission were associated with recovery time in a Univariable Cox regression analysis. Stepwise variable selection techniques were used to determine which variables should be included or excluded in the model. The decision was based on a p-value of 0.05 in the multivariable Cox regression model. Finally, in this multivariable Cox regression model, age category, residence, weight for age, presence of danger signs during

admission, and presence of comorbidities were significant predictors of time to recovery in children aged 2–59 months.

Being a rural resident (AHR: 0.68, 95% CI: 0.57-0.82), aged 36-59 months (AHR: 0.70, 95% CI: 0.50-0.98), being underweight (AHR: 0.75, 95% CI: 0.59-0.95), the presence of danger signs (AHR: 0.31, 95% CI: 0.24-0.39), and having comorbidities at the time of admission (AHR: 0.38, 95% CI: 0.30-0.48) were significant predictors of recovery time (**Table 2**).

Table 2: Predictors of recovery time in children with severe pneumonia admitted to Asella Referral and Teaching Hospital, Asella, Ethiopia, (N=401)

Variable	Recovered	Censored	CHR[95%CI]	AHR[95%CI]	P-valu
Age categories		5			
2-11 months	194	19	1	1	
12-35 months	124	14	0.83[0.68-1.02]	0.93[0.76-1.13]	0.458
36-59 months	42	8	0.60[0.43-0.85]	0.70[0.50-0.98]	0.038*
Residence					
Urban	106	11	1		
Rural	254	30	0.73[0.59-0.91]	0.68 (0.57-0.82)	0.000*
Weight for age					
Normal	276	25	1	1	
Underweight	84	16	0.61[0.49-0.75]	0.75[0.59-0.95]	0.019*
Danger sign					
No	140	12	1		
Yes	220	29	0.27[0.22-0.34]	0.31 (0.25-0.39)	0.000*
Comorbidity					
No	219	18	1		
Yes	141	23	0.31[0.25-0.39]	0.38 (0.30-0.48)	0.000*
Abbreviations: A	HR: adjusted	hazard ratio:	CI: confidence interv	val; CHR: crude haza	rd ratio: *

## Schoenfeld residual test and Cox-Snell residual plot

The Schoenfeld residual chi-square test was 2.74 with a corresponding p-value of 0.908, greater than 0.05, indicating that the proportional hazard assumption was satisfied.

The Cox-Snell Residual plot showed that the overall goodness of fit of the multivariable coxregression model for time to recovery from severe pneumonia was a good fit for the data (Supplementary Figure 1).

## Discussion

This study aimed to determine the recovery time from severe pneumonia and its predictors in children aged 2-59 months admitted to ARTH. The study analyzed the medical records of 401 children. The study revealed that the overall recovery rate from severe pneumonia was 16 per 100-person day observation with a median recovery time of 5 days. Rural residency, aged 36-59 months, being underweight, the presence of danger signs, and comorbidity were found to be significant predictors of recovery time.

The overall recovery was 16 per 100 person-days. This finding is fairly identical to the finding of the study in Debre Markos, in which the rate of recovery was 16.25 per 100 person-days, <sup>18</sup>and lower than the findings of the studies conducted in Gondar, Hossana, and Central and North Gondar Zones, in which the incidence of recovery was 21.3, 24.6, and 26.7 per 100 person-days, respectively. <sup>19,23,24</sup> Differences in sociodemographic and clinical characteristics of the study participants may explain the discrepancy among studies or it may be due to differences in treatment regimens and availability of quality healthcare services.

The overall median time to recovery from severe pneumonia was 5 days. The findings of this study are almost identical to those of the study carried out in the rural health center of the Gambia and Benshangul-Gumuz, which revealed that the average recovery time was 4.5 and 5 days, respectively.<sup>14,25</sup> This finding is lower than the study findings in Poland, which reported 8.2-10.1 days, and the study conducted in Tanzania, which reported 10 days.<sup>26,27</sup> This disparity could be due to the time difference between studies and the type of analysis employed by both studies, which does not consider subject censoring. In contrast to studies conducted in Nepal, Britain, Gondar, Hossana, Bahirdar, the Central and North Gondar Zones, and Jimma where the median recovery time was 2-4 days, the median recovery time was longer. <sup>10,16,18,19,28,29</sup> This variation

could be brought about by socioeconomic differences between research areas, variations in study times, variations in treatment and care practices, and variations in clinical characteristics of the study population, as this study included a larger number of children who had danger signs and comorbidities.

This study showed that residency significantly predicted the recovery time of children admitted with severe pneumonia; children residing in rural areas had a longer recovery time than their counterparts. The result of the current study is supported by a study carried out in Central and North Gondar Zones .<sup>19</sup> This finding contradicts a study done in Bahirdar, Ethiopia, which found that rural residency increases the chance of early recovery.<sup>17</sup> This could be explained by the fact that children who are rural residents often face economic poverty, limiting access to care and quality healthcare services and causing delayed child care. Malnutrition is more prevalent in rural areas, which has a substantial negative impact on children's immunity, which in turn affects recovery time.<sup>30-32</sup>

Children's age was another important socio-demographic predictor that had a significant impact on recovery time. The recovery time of the children aged 36-59 months was longer than that of the children aged 2-11 months. This finding is supported by similar studies.<sup>16,18</sup> The current findings are in contrast to other findings. For instance, older age was associated with early recovery in a study conducted in Hossana and Nepal.<sup>10,20</sup> The observed variation could be attributed to the differences in age groups among the studies. A study conducted in Nepal focused solely on children aged 2-35 months. Additionally, the inconsistency could also be due to the differences in the baseline clinical conditions and treatment protocols across the study areas. Being underweight was a significant predictor of recovery time. The recovery time of underweight children was longer than that of their counterparts. These findings are consistent with those of similar studies. <sup>14,16,20</sup> This is because the nutritional status of a child plays a crucial role in their overall health, encompassing their growth and development, physical activity, and capacity to combat severe illnesses. Undernutrition can impair T-cell function, cytokine production, and the lymphocytes' ability to respond adequately to cytokines, thereby affecting both acquired immunity and innate host defense mechanisms.<sup>33</sup>

The presence of comorbidities was another significant predictor of recovery time. The recovery time of children admitted with comorbidities was longer than that of their healthy counterparts.

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This may be because children with comorbid diseases may already experience complications from the underlying condition or may have a compromised immune system, which places additional stress on their bodies and makes them vulnerable to delayed recovery. The current finding is supported by a study carried out in Debre Markos, Central and North Gondar Zones, and Gambia.<sup>18,19,34</sup> Danger signs during admission were also predictors of recovery time. The recovery time was shorter in patients with no danger signs during admission. This finding is supported by similar studies.<sup>18,19,34</sup> This could be explained by the fact that children with danger signs have more severe disease, and the time needed to recover from it is longer. Furthermore, the presence of danger signs may indicate complications that further delay treatment and recovery. This finding contradicts a study conducted in Gondar, which stated that the recovery time of children who had severe signs and symptoms of pneumonia was shorter than their counterparts.<sup>24</sup>

The findings of this study can be considered generalizable due to the representative nature of the sample. It was selected using computer-generated simple random sampling. Furthermore, the sample size was adequate, determined using appropriate parameters, and the study achieved a response rate of 94%. However, due to the retrospective nature of the investigation and the use of secondary data, the study was unable to explore potential predictors of time to recovery, such as parental, sociodemographic, and environmental factors. Reliance on secondary data in this study presented significant limitations in exploring the full spectrum of factors influencing time to recovery. Parental factors, including family dynamics, income, education, and healthcare access, may affect recovery times. Additionally, community support, school environment, and exposure to stressors may affect recovery time. The inability to analyze these multifaceted elements leaves a gap in our understanding of the complex interplay between various factors and recovery outcomes.

## CONCLUSION

The findings of this study revealed that the median recovery time was longer than that reported in similar studies. The variables children aged 36–59 months, rural residence, underweight in weight for age, presence of danger signs, and presence of comorbidity were statistically significant predictors of time to recovery in children aged 2–59 months. Therefore, families of children with identified predictors need counseling to prepare for the likelihood of slow recovery. Further

prospective studies need to be conducted to incorporate other potential predictors such as parental factors, environmental and other clinical factors.

# **Consent for Publication**

All authors declared that they have agreed to publication.

# **Competing Interests**

The Authors have declared no conflicts of interest in this work.

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There is no funding to report.

## Availability of data and material

The datasets used for this study are available from the corresponding author upon reasonable request.

# **Ethical Considerations**

Ethical approval was obtained from the Ethical Review Board (IRB) of Jimma University a Ref. No. JUIH/IRB/367/23 and official permission were secured from the Health Department at Asella Referral and Teaching Hospital. As we stated in the methods section, we used secondary data retrieved from the patient cards/databases that had already been collected for the patients' registration cards in the Hospital. The names of the study participants were not recorded to maintain confidentiality, instead, their medical registration numbers were used to distinguish the study participants' information, and all data collected were kept confidential. The hospital database management department had consented to each study participant or caregiver to use the data for research purposes in a confidential way at the time of initiation.

# Authors' contributions

**T.M.:** Conceptualizations, Data curation, Formal analysis, Investigations, Methodology, Supervision, Validation, Visualization, Writing an original draft, and Writing Review and editing the manuscript. He is guarantor.

**A.L.:** Formal analysis, Investigations, Methodology, Supervision, Visualization, Writing Review, and editing the manuscript.

**A.K.:** Formal analysis, Investigations, Methodology, Supervision, Visualization, Writing Review, and editing the manuscript.

#### Acronyms and abbreviations

ACSH: Ayder Comprehensive Specialized Hospital, AGE: Acute gastroenteritis, AHR: Adjusted Hazard ratio, ARTH: Asella Referral and Teaching Hospital, ARTI: Acute respiratory tract infection, CHD: Congenital heart disease, CHR: Crud Hazard ratio, CI: Confidence interval, DM: Diabetes mellitus, DS: Down syndrome, HAAD: Hyperactive airway disease, HHRI: Health and health-related indicators, Hib: Hepatitis B vaccine, HIV: Human immune virus, JUMC: Jimma University Medical Center, PCV: Pneumococcal vaccine, PIV1: Parainfluenza type-1, NEMMCSH: Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital, RVI: Retroviral infection, SAM: Severe acute malnutrition, SCAP: Severe community-acquired pneumonia, SRS: Simple random sampling, TB: Tuberculosis, TTR: Time to recovery, UGCSH: University of Gondar Comprehensive Specialized Hospital, UNICEF: United Nations Children's Fund, and WHO: World Health Organization

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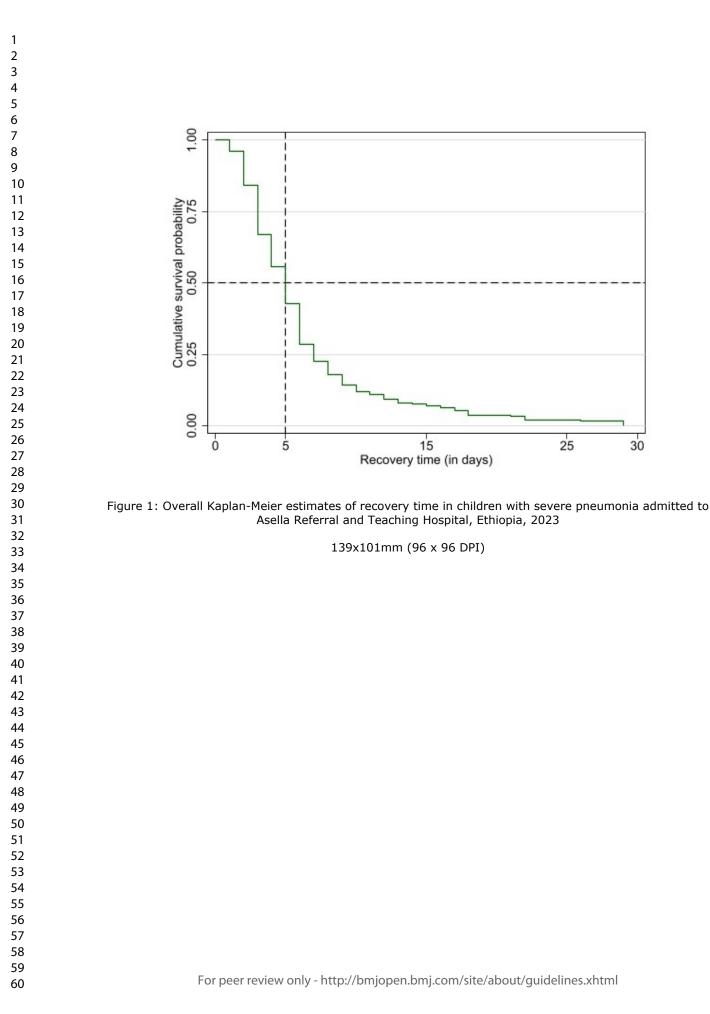
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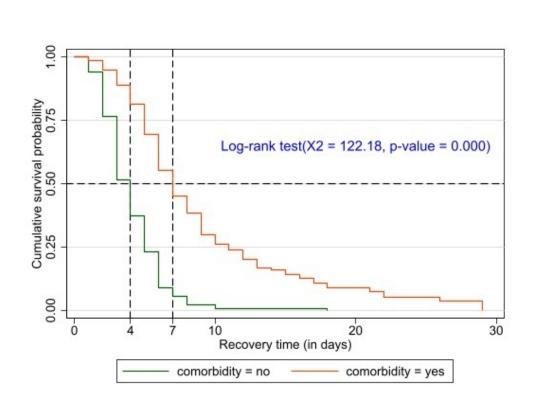
Figure 1: Overall Kaplan-Meier estimates of recovery time in children with severe pneumonia admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023

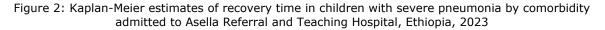
Figure 2: Kaplan-Meier estimates of recovery time in children with severe pneumonia by comorbidity admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023

Figure 3: Kaplan-Meier estimates of recovery time in children with severe pneumonia by danger signs admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023



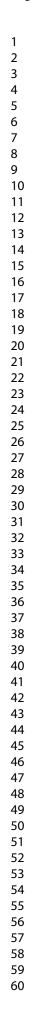






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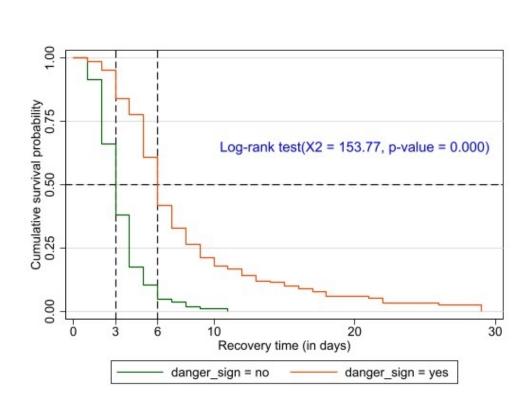


Figure 3: Kaplan-Meier estimates of recovery time in children with severe pneumonia by danger signs admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023

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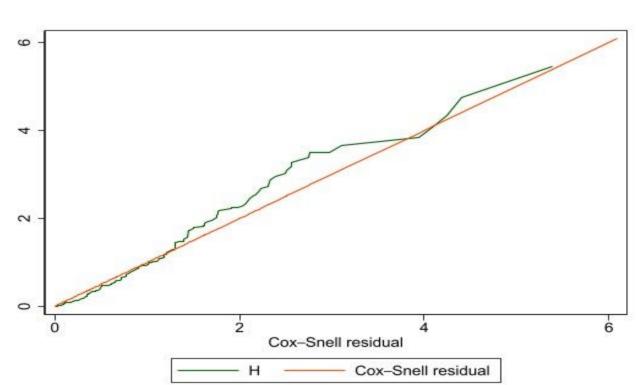


Figure 1: Cox-Snell Residual plot of the multivariable Cox-regression model for time to recovery from severe pneumonia admitted to Asella Referral and Teaching Hospital, Asella, Ethiopia

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## Time to Recovery from Severe Pneumonia and Its Predictors among Children Aged 2-59 Months Admitted To Asella Referral and Teaching Hospital, Asella, Ethiopia, 2023: A Retrospective Cohort Study

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Time to Recovery from Severe Pneumonia and Its Predictors among Children Aged 2-59 Months Admitted To Asella Referral and Teaching Hospital, Asella, Ethiopia, 2023: A Retrospective Cohort Study

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## Abstract

**Objective:** To determine the time to recovery from severe pneumonia and its predictors in children aged 2-59 months admitted to Asella Referral and Teaching Hospital, Ethiopia.

**Design, participants, and setting:** An institution-based retrospective cohort study was conducted on 424 children aged 2–59 months in Asella Town, Ethiopia. Medical records of eligible children were selected using a simple random sampling technique. The Kaplan-Meier curve and log-rank test were used to describe the survival function. Independent predictors of recovery time were identified using Cox regression analysis. The 95% confidence interval of the hazard ratio with a corresponding p-value of 0.05 was used to declare statistical significance.

Primary and secondary outcomes: Recovery time from severe pneumonia and its predictors.

**Results:** The median recovery time was 5 days. The incidence density of recovery was 16 (95% CI: 14.44–17.76) per 100-person-day observation. Being a rural resident (AHR: 0.68, 95% CI: 0.57-0.82), aged 36-59 months (AHR: 0.70, 95% CI: 0.50-0.98), being Underweight (AHR: 0.75, 95% CI: 0.59-0.95), the presence of danger signs (AHR: 0.31, 95% CI: 0.24-0.39), and having comorbidity (AHR: 0.38, 95% CI: 0.30-0.48) were significant predictors of time to recovery in children aged 2–59 months.

**Conclusion**: In this study, the median recovery time was longer than that reported in similar studies. Age, residence, underweight, danger signs, and comorbidities were significant predictors. Therefore, families of children with identified predictors need counseling to prepare for the likelihood of slow recovery.

**Data availability statement:** The datasets used for this study are available from the corresponding author upon reasonable request.

## Strengths and limitations of the study

- A survival model was employed to analyze data that considered censoring of the study participants.
- The study employed five consecutive years of subject records which increased the generalizability of the results.
- However, due to the retrospective nature of the investigation and the use of secondary data, the study was unable to explore potential predictors of time to recovery, such as parental, sociodemographic, and environmental factors.

• Future research should collect primary data or use a prospective study to incorporate potential predictors of recovery time.

## Introduction

Pneumonia is the leading cause of death in children worldwide, more than AIDS, malaria, and measles.<sup>1,2</sup> Pneumonia continues to be a significant cause of death in children worldwide. It claimed the lives of 740180 children under the age of five in 2019 alone. This translates to a staggering 14% of all deaths in children under five and 22% of all deaths in children aged 1 to 5 years. <sup>3</sup> Children under the age of five are particularly vulnerable to this disease. In low- and middle-income countries, approximately 7 million children under the age of five are hospitalized with pneumonia each year. <sup>4</sup> Pneumonia presents a significant challenge for children residing in sub-Saharan Africa and Asia, where the highest numbers of fatalities are concentrated in countries such as the Congo, Nigeria, Ethiopia, India, and Pakistan. These countries account for more than half of all child deaths under the age of five.<sup>5</sup>

It is estimated that 3,370,000 children are diagnosed with pneumonia annually in Ethiopia, contributing to 18% of all causes of death, killing 40,000 under-five children.<sup>6</sup> According to health and health-related indicators (HHRI), pneumonia was the primary cause of death in Ethiopia in 2021, constituting 9.6% of all cases and 4.5% of cases in children under five years of age. Pneumonia has a major impact on Ethiopia's health and economy, especially among children. The medical expenses for pneumonia treatment range from 8 USD for outpatient visits to 64 USD for severe inpatient visits. Non-medical expenses such as transportation costs averaged 2 USD. Severe pneumonia has pushed 7% of households below the extreme poverty threshold, with the Ethiopian government spending 13.9 USD million annually on treatment.<sup>7,8</sup>

Recovery time from severe pneumonia varies worldwide. A median recovery time of 2 days has been reported in Britain and Nepal, while a median recovery of 5 days was reported in India.<sup>9-12</sup> Studies conducted in Africa also reported a median recovery time of 3–10 days.<sup>13,14</sup> In Ethiopia, the recovery time varies between 3 and 4 days. Evidence showed that age, nutritional status, duration before seeking care, danger signs at admission, drug regimens, antibiotic change, severity of signs, and symptoms of pneumonia, mode of infancy feeding, formula feeding, vaccination

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status, and co-morbidity are all factors that influence the rate of recovery of children from severe pneumonia.<sup>15-20</sup>

Some studies conducted in Ethiopia have explored the time to recovery in children with severe pneumonia and its predictors. However, these studies have presented conflicting findings regarding certain predictors. For example, a study conducted in Gondar and Debre Markos found that older age was associated with prolonged recovery, whereas a study in Hossana indicated that older age was associated with early recovery. <sup>16,18,20</sup> Similarly, a study in Gondar found that rural residency prolonged recovery time, whereas a study in Bahirdar reported that rural residency increased the likelihood of early recovery <sup>17,21</sup>. Lastly, a study in Gondar found that the severity of signs and symptoms of pneumonia was associated with early recovery, which contradicts other findings. <sup>16</sup> Without resolving these contradictions, a clear picture of the predictors of time to recovery from severe pneumonia would not be adequately described. This shows the need for further investigation of predictors of recovery time from severe pneumonia. In addition, this problem was not addressed in the study area.

It is essential to study the time to recovery from severe pneumonia and its predictors in children for several reasons. First, understanding the factors that influence recovery time can help healthcare providers optimize treatment strategies and improve outcomes in children with severe pneumonia. Second, identifying predictors of longer recovery times can facilitate resource allocation, ensuring that children receive prompt and appropriate care. In addition, studying recovery time predictors can inform clinical decision-making, allowing healthcare providers to identify children at a higher risk for prolonged illness and intervene accordingly. Moreover, data on recovery times and predictors can inform public health planning efforts, leading to improved health outcomes and reduced healthcare costs. Finally, studying recovery times and predictors can contribute to a growing body of knowledge on severe pneumonia in children, guiding future research efforts to improve treatment and prevention strategies. Therefore, this study aimed to determine the time to recovery from severe pneumonia and its predictors in children aged 2-59 months who were admitted to Asella Referral and Teaching Hospital in Ethiopia.

## **Study Design**

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## Study Setting, Study Design, and Period

An institution-based retrospective cohort study was conducted in ARTH from 2018-2022. ARTH is located in the Oromia Region, Arsi Zone, in Asella Town. Asella Town is located in the Arsi Zone of the Oromia Region, 126 km (78 mi) south of Addis Ababa. The hospital has 297 beds and acts as a medical referral center for a population of 3.5 million inhabitants in the Arsi Zone and its surroundings. It is one of Ethiopia's university teaching hospitals. Asella Teaching and Referral Hospital provides services (inpatient and outpatient) to the community.

# Population

All children with severe pneumonia aged 2-59 months admitted to Asella Referral and Teaching Hospital were the source population. All eligible children with severe pneumonia aged 2 to 59 months admitted to this Hospital pediatric ward from January 2018- December 2022 were the study population.

## **Eligibility Criteria**

All medical charts of children aged 2–59 months with severe pneumonia treated in the pediatric ward were included from January 1, 2018, to December 31, 2022. The criteria for severe pneumonia included the following symptoms: fast breathing (respiratory rate of 60 breaths per minute or more in children aged 2-11 months, or 50 breaths per minute or more in children aged 1-5 years), cyanosis, severe chest in drawing, inability to breastfeed or drink, signs of respiratory distress (e.g., nasal flaring, grunting, stridor), history of high fever (39°C or higher), signs of poor general condition, comorbidities, and history of no improvement after initial treatment at home or in outpatient settings. However, Children were excluded if they had incomplete information regarding the date of admission, discharge, recovery, death, transfer out, refusal, or readmission.

## **Patient and Public involvement**

Patients and the public were not involved in the study design, conduct, choice of outcome measures, recruitment, selection of reporting methods, or dissemination of the study results.

## Sample Size Determination

To estimate sample size, the Schoenfeld DA formula was used.<sup>22</sup> Assuming a 5% level of significance with a 2-sided critical value of 1.96, and 80% power with a table value of 0.84. From a previous similar study done on time to recovery from severe pneumonia, we considered the

probability of recovery rate of 0.93 with the proportion of exposed 93% and the hazard ratio (HR: 0.56) for the underweight variable. <sup>23</sup>

$$E = \frac{(Z_{\alpha/2} + Z_{\beta})^2}{(lnHR)^2 P(1-P)} = \frac{(1.96 + 0.84)^2}{(ln0.56)^2 0.93(1-0.93)} = \frac{7.84}{0.336*0.93*0.07} = 358.22$$
$$n = \frac{E}{\Pr(recovery)} = \frac{358}{0.93} = 385$$

To compensate for the missing/dropout rate, a 10% rate was added and the final sample size was 424.

#### **Sampling Procedures**

A total of 2423 children were recorded in the registration book at ARTH during the study period from January 1, 2018, to December 31, 2022. Patients who did not meet the inclusion criteria were excluded, whereas those who met the criteria were identified and recorded using their unique medical registration numbers. Using computer-generated random numbers, 424 records were randomly selected. Twenty-three randomly selected records were incomplete for nearly all independent variables and were thus excluded from the analysis.

#### **Data Collection Tools and Procedure**

A pre-tested structured data collection checklist was used to extract routinely recorded data from patients with severe pneumonia. Data collection tools and study variables were selected after an extensive review of the literature. The data were gathered by two well-trained BSc pediatric nurses and one supervisor. Height-for-age, weight-for-height, and weight-for-age z-scores were calculated according to the 2006 WHO Child Growth Standards. Subjects were classified as stunted if their height-for-age Z-score fell below -2 compared to the WHO Child Growth Standards median for their respective age and sex. Wasting is a weight-for-height Z-score (WHZ) below -2, indicative of acute undernutrition or rapid weight loss. Furthermore, underweight was defined as a weight-for-age Z-score (WAZ) below -2.

#### **Study Variables**

#### **Dependent Variable**

Time to recovery from severe pneumonia

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Socio-demographic factors: Residence, age, sex, treatment-related factors (medication used, Nutritional status: history of exclusive breastfeeding, wasting, and stunting) Comorbidity status (HIV infection, heart failure, congenital heart diseases, asthma, Down syndrome, diabetes mellitus, hyperactive airway disease, SAM, anemia, and rickets) Danger signs during admission (Head nodding, abnormal body movement, severe chest in drawing, grunting, and vomiting) Duration before seeking care (1-3 days, 4-7 days, and more than 7 days) and Others variables (Vaccination status and sunlight exposure).

#### **Operational Definition**

**Severe pneumonia:** defined as having a cough or difficulty in breathing with oxygen saturation < 90% or central cyanosis, severe respiratory distress, and signs of pneumonia with a general danger sign. The admission criteria for severe pneumonia in children under the age of five at Asella Referral and Teaching Hospital include the following symptoms: difficulty in breathing or fast breathing (respiratory rate of 60 breaths per minute or more in children aged 2-11 months, or 50 breaths per minute or more in children aged 1-5 years), cyanosis, severe chest in drawing, inability to breastfeed or drink, signs of respiratory distress (e.g. nasal flaring, grunting, stridor), history of high fever (39°C or higher), signs of poor general condition or severe illness, a child is unable to stay awake or alert, comorbidities such as HIV infection, severe anemia, or other underlying medical conditions, and history of not improving after initial treatment at home or in outpatient settings.

**Treatment Protocol:** Ceftriaxone is the preferred treatment for suspected community-acquired Methicillin-resistant Staphylococcus aureus (CA-MRSA), with vancomycin or clindamycin for added coverage. For uncomplicated bacterial pneumonia, ampicillin or penicillin G is used. Cefotaxime and ceftriaxone are used for children with incomplete Hib or Streptococcus pneumoniae immunization, or in areas with high penicillin-resistant strains. In severe pneumonia requiring ICU admission, a combination of vancomycin and ceftriaxone is preferred. A combination therapy of ceftriaxone, cefotaxime, and azithromycin is used for complicated pneumonia with effusion or empyema. Antiviral treatment is used if the child is hospitalized during influenza season.

**Recovery time:** The period from admission until the child was released from the hospital because of improvement in symptoms was calculated as the number of days.

**The median recovery time:** was defined as the time at which half of the study participants had recovered.

**Censored**: A child admitted with severe pneumonia whose outcome status was either selfdischarged, transferred, unknown, dead, or not yet recovered up to the end of the study.

Event: Recovery from severe pneumonia

**Recovered**: A child released from the hospital as a result of clinical improvement confirmed by a doctor.

High-grade fever: a temperature ranging from 38.5°C to 41°C.

Low-grade fever: a temperature ranging from 37.5°C to 38.4°C.

**Danger signs:** If the child has a loss of consciousness, abnormal body movement, vomiting everything, grunting, and severe chest in drawing.

**Co-morbidity:** If the child had any disease condition (acute or chronic) present during admission in addition to severe pneumonia including, HAAD (childhood asthma), anemia, severe acute malnutrition, rickets, RVI, CHF, CHD, acute gastroenteritis, measles, pertussis, bronchitis, meningitis, and others.

**Fully vaccinated:** was defined as children who had completed all forms of vaccinations per the schedule.

Partially vaccinated: children who had taken at least one dose of PCV

Non-vaccinated: children who had never been vaccinated against PCV or other vaccines.

Up to date: children who had completed vaccination up to their age

**Exclusive breastfeeding**: - is the practice of giving an infant breast milk only up to the age of six months, except for oral rehydration solutions and drugs.

# **Data Quality Control**

To ensure the quality of the data, a pre-test was performed on 5% of the total study population at JUMC to ensure agreement with the data abstraction format. The data collectors were trained prior

to the data collection. Supervision and verification were performed to ensure completeness and consistency.

## **Data Analysis Procedure**

The extracted data were checked for completeness, entered into Epi-Data version 4.6, and exported to STATA software Version 17 for further cleaning, management, and statistical analysis. Descriptive statistics were used to summarize categorical variables. The results were summarized as frequency, percentage, mean, median, standard deviation, and IQR. The Kaplan-Meier (KM) survival curve and log-rank test were used to describe the survival function. Univariate Cox proportional hazards regression was performed to screen candidate variables for multivariable analysis. All covariates associated with the time to recovery (TTR) with a p-value of 0.25 or less were entered into the multivariable model. The independent predictors of TTR were analyzed using a multivariable Cox proportional hazards model to control for confounding effects. Adjusted hazard ratios (HRs) with a 95% Confidence Interval (CI) were estimated, and a p-value less than 0.05 was used to declare the presence of a significant association between time to recovery and covariates. Independent predictors of recovery time were identified using Cox regression analysis. A global test was conducted to verify the proportional hazard assumption. The p-value for the global test of the Schoenfeld residual test for the Cox regression model was 0.908, indicating that the proportionality assumption was valid. The interaction effects of the variables on time to recovery were examined; however, no variable showed a multiplicative effect. Therefore, the final model accounted only for the main effect. In time-to-event analysis, negative outcomes such as death and disease progression are usually evaluated. In our case, recovery was a positive event, and a hazard ratio of less than one implied a lower rate of recovery or a longer recovery time, which is a negative outcome.

## Results

## **Baseline characteristics**

Of the 424 selected medical charts, 401 were completed, with a response rate of 94.6%. More than half (58.1%) were males, and 284 (70.8%) were urban residents. 164 (40.9%) had co-morbidities. Severe acute malnutrition (28%) was the most common comorbidity, followed by hyperactive airway diseases (22%), acute gastroenteritis (12%), and congenital heart disease (10.4%). Other

medical conditions include anemia, rickets, Down syndrome, spinal bifida, tuberculosis, meningitis, congestive heart failure, myelomeningocele, and hydrocephalus (**Table 1**).

Table 1: Baseline characteristics of children with severe pneumonia admitted to ARTH, Asella, Ethiopia, (N = 401)

Variable	Category	Recovered N (%)	Censored N (%)
Age	2-11 month	194 (91.1)	19 (8.9)
	12-35 month	124 (89.9)	14 (10.1)
	36-59 month	42 (84.0)	8 (16.0)
Sex	Male	213 (91.4)	20 (8.6)
	Female	147 (87.5)	21 (12.5)
Residence	Urban	106 (90.6)	11 (9.4)
	Rural	254 (89.4)	30 (10.6)
Weight for age	Normal	276 (91.7)	25 (8.3)
	Underweight	84 (84.0)	16 (16.0)
Height for age	Normal	254 (90.7)	26 (9.3)
	Stunted	106 (87.6)	15 (12.4)
Weight for height	Normal	280 (89.5)	33 (10.5)
	Wasted	80 (90.9)	8 (9.1)
Exclusively breastfed	Yes	265 (89.8)	30 (10.2)
	No	95 (89.6)	11 (10.4)
Sunlight exposure	Yes	327 (90.1)	36 (9.9)
	No	33 (86.8)	5 (13.2)
Vaccination status	Fully vaccinated	129 (89.0)	16 (11.0)
	Partially vaccinated	27 (81.8)	6 (18.2)
	Up to date	182 (91.5)	17 (8.5)
	None vaccinated	22 (91.7)	2 (8.3)
Oxygen saturation	>=90	125 (87.4)	18 (12.6)
	<90	235 (91.1)	23 (8.9)
Oxygen support	Yes	304 (90.2)	33 (9.8)
	No	56 (87.5)	8 (12.5)

Respiratory rate	Normal	29 (96.7)	1 (3.3)
	Fast breathing	331 (89.2)	40 (10.8)
Body temperature	Normal	97 (90.7)	10 (9.3)
	Low-grade fever	136 (88.3)	18 (11.7)
	High-grade fever	127 (90.7)	13 (9.3)
History of ARTI	Yes	84 (88.4)	11 (11.6)
	No	276(90.2)	30 (9.8)
History of Asthma	Yes	16 (88.9)	2 (11.1)
	No	344 (89.8)	39 (10.2)
Danger sign	Yes	220 (88.4)	29 (11.6)
	No	140 (92.1)	12 (7.9)
DPSC	1-3 days	176 (90.7)	18 (9.3)
	4-7 days	162 (90)	18 (10.0)
	>7 days	22 (81.5)	5 (18.5)
Presence of	Yes	141(86.0)	23(14.0)
comorbidities	No	219(92.4)	18(7.6)

Abbreviations: ARTI: Acute respiratory tract infection, DPSC: Duration prior to seeking care

## The median Recovery Time

Of the 401 study participants, 360 (89.78%) were recovered and the remaining, 41 (10.22%), were censored. The minimum and maximum length of hospital stay was 1 and 29 days, respectively. The time to recovery of children with severe pneumonia was estimated using the Kaplan-Meier survival curve and as shown in the overall Kaplan-Meier curve at the crossing broken lines, the median recovery time was 5 days with an IQR of 3-7. The graph tends to decline rapidly within the first ten days, implying that most children recovered from their illness within this time frame (Figure 1).

## **Comparison of Recovery Status among Categorical Predictors**

The median recovery time for children with comorbidities was 7 days (IQR: 5–11), whereas for children without comorbidities was 4 days (IQR: 3-5). The median recovery time of children with

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danger signs during admission was 6 days (IQR: 5–9), and that of children without danger signs was 3 days (IQR: 2-4) (Figures 2 and 3).

## Predictors of Time to Recovery from Severe Pneumonia

The variables age, sex, residence, vaccination status, exclusive breastfeeding, weight for age, height for age, weight for height, duration before seeking care, history of asthma, history of acute respiratory tract infection, drug regimen, presence of danger signs during admission, presence of comorbidity and oxygen saturation during admission were associated with recovery time in a Univariable Cox regression analysis. Stepwise variable selection techniques were used to determine which variables should be included or excluded in the model. The decision was based on a p-value of 0.05 in the multivariable Cox regression model. Finally, in this multivariable Cox regression model, age category, residence, weight for age, presence of danger signs during admission, and presence of comorbidities were significant predictors of time to recovery in children aged 2–59 months.

Being a rural resident (AHR: 0.68, 95% CI: 0.57-0.82), aged 36-59 months (AHR: 0.70, 95% CI: 0.50-0.98), being underweight (AHR: 0.75, 95% CI: 0.59-0.95), the presence of danger signs (AHR: 0.31, 95% CI: 0.24-0.39), and having comorbidities at the time of admission (AHR: 0.38, 95% CI: 0.30-0.48) were significant predictors of recovery time (**Table 2**).

 Table 2: Predictors of recovery time in children with severe pneumonia admitted to Asella Referral and Teaching Hospital, Asella, Ethiopia, (N=401)

Variable	Recovered	Censored	CHR[95%CI]	AHR[95%CI]	<b>P-value</b>
Age categories					
2-11 months	194	19	1	1	
12-35 months	124	14	0.83[0.68-1.02]	0.93[0.76-1.13]	0.458
36-59 months	42	8	0.60[0.43-0.85]	0.70[0.50-0.98]	0.038*
Residence					
Urban	106	11	1		
Rural	254	30	0.73[0.59-0.91]	0.68 (0.57-0.82)	0.000**
Weight for age					
	276	25	1	1	

Und	Normal	84	16	0.61[0.49-0.75]	0.75[0.59-0.95]	0.019*
Danger	-					
	No	140	12	1		
	Yes	220	29	0.27[0.22-0.34]	0.31 (0.25-0.39)	0.000**
Comort	oidity					
	No	219	18	1		
	Yes	141	23	0.31[0.25-0.39]	0.38 (0.30-0.48)	0.000**

**Abbreviations:** AHR: adjusted hazard ratio; CI: confidence interval; CHR: crude hazard ratio; \*, \*\* indicates the significance of the variables

## Schoenfeld residual test and Cox-Snell residual plot

The Schoenfeld residual chi-square test was 2.74 with a corresponding p-value of 0.908, greater than 0.05, indicating that the proportional hazard assumption was satisfied.

The Cox-Snell Residual plot showed that the overall goodness of fit of the multivariable coxregression model for time to recovery from severe pneumonia was a good fit for the data (Supplementary Figure 1).

## Discussion

This study aimed to determine the recovery time from severe pneumonia and its predictors in children aged 2-59 months admitted to ARTH. The study analyzed the medical records of 401 children. The study revealed that the overall recovery rate from severe pneumonia was 16 per 100-person day observation with a median recovery time of 5 days. Rural residency, aged 36-59 months, being underweight, the presence of danger signs, and comorbidity were found to be significant predictors of recovery time.

The overall recovery was 16 per 100 person-days. This finding is fairly identical to the finding of the study in Debre Markos, in which the rate of recovery was 16.25 per 100 person-days, <sup>18</sup>and lower than the findings of the studies conducted in Gondar, Hossana, and Central and North Gondar Zones, in which the incidence of recovery was 21.3, 24.6, and 26.7 per 100 person-days, respectively. <sup>19,23,24</sup> Differences in sociodemographic and clinical characteristics of the study

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participants may explain the discrepancy among studies or it may be due to differences in treatment regimens and availability of quality healthcare services.

The overall median time to recovery from severe pneumonia was 5 days. The findings of this study are almost identical to those of the study carried out in the rural health center of the Gambia and Benshangul-Gumuz, which revealed that the average recovery time was 4.5 and 5 days, respectively.<sup>14,25</sup> This finding is lower than the study findings in Poland, which reported 8.2-10.1 days, and the study conducted in Tanzania, which reported 10 days.<sup>26,27</sup> This disparity could be due to the time difference between studies and the type of analysis employed by both studies, which does not consider subject censoring. In contrast to studies conducted in Nepal, Britain, Gondar, Hossana, Bahirdar, the Central and North Gondar Zones, and Jimma where the median recovery time was 2-4 days, the median recovery time was longer. <sup>10,16,18,19,28,29</sup> This variation could be brought about by socioeconomic differences between research areas, variations in study times, variations in treatment and care practices, and variations in clinical characteristics of the study population, as this study included a larger number of children who had danger signs and comorbidities.

This study showed that residency significantly predicted the recovery time of children admitted with severe pneumonia; children residing in rural areas had a longer recovery time than their counterparts. The result of the current study is supported by a study carried out in Central and North Gondar Zones .<sup>19</sup> This finding contradicts a study done in Bahirdar, Ethiopia, which found that rural residency increases the chance of early recovery.<sup>17</sup> This could be explained by the fact that children who are rural residents often face economic poverty, limiting access to care and quality healthcare services and causing delayed child care. Malnutrition is more prevalent in rural areas, which has a substantial negative impact on children's immunity, which in turn affects recovery time.<sup>30-32</sup>

Children's age was another important socio-demographic predictor that had a significant impact on recovery time. The recovery time of the children aged 36-59 months was longer than that of the children aged 2-11 months. This finding is supported by similar studies.<sup>16,18</sup> The current findings are in contrast to other findings. For instance, older age was associated with early recovery in a study conducted in Hossana and Nepal.<sup>10,20</sup> The observed variation could be attributed to the differences in age groups among the studies. A study conducted in Nepal focused solely on

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children aged 2-35 months. Additionally, the inconsistency could also be due to the differences in the baseline clinical conditions and treatment protocols across the study areas. Being underweight was a significant predictor of recovery time. The recovery time of underweight children was longer than that of their counterparts. These findings are consistent with those of similar studies. <sup>14,16,20</sup> This is because the nutritional status of a child plays a crucial role in their overall health, encompassing their growth and development, physical activity, and capacity to combat severe illnesses. Undernutrition can impair T-cell function, cytokine production, and the lymphocytes' ability to respond adequately to cytokines, thereby affecting both acquired immunity and innate host defense mechanisms.<sup>33</sup>

The presence of comorbidities was another significant predictor of recovery time. The recovery time of children admitted with comorbidities was longer than that of their healthy counterparts. This may be because children with comorbid diseases may already experience complications from the underlying condition or may have a compromised immune system, which places additional stress on their bodies and makes them vulnerable to delayed recovery. The current finding is supported by a study carried out in Debre Markos, Central and North Gondar Zones, and Gambia.<sup>18,19,34</sup> Danger signs during admission were also predictors of recovery time. The recovery time was shorter in patients with no danger signs during admission. This finding is supported by similar studies.<sup>18,19,34</sup> This could be explained by the fact that children with danger signs have more severe disease, and the time needed to recover from it is longer. Furthermore, the presence of danger signs may indicate complications that further delay treatment and recovery. This finding contradicts a study conducted in Gondar, which stated that the recovery time of children who had severe signs and symptoms of pneumonia was shorter than their counterparts.<sup>24</sup>

The findings of this study can be considered generalizable due to the representative nature of the sample. It was selected using computer-generated simple random sampling. Furthermore, the sample size was adequate, determined using appropriate parameters, and the study achieved a response rate of 94%. However, due to the retrospective nature of the investigation and the use of secondary data, the study was unable to explore potential predictors of time to recovery, such as parental, sociodemographic, and environmental factors. Reliance on secondary data in this study presented significant limitations in exploring the full spectrum of factors influencing time to recovery. Parental factors, including family dynamics, income, education, and healthcare access,

may affect recovery times. Additionally, community support, school environment, and exposure to stressors may affect recovery time. The inability to analyze these multifaceted elements leaves a gap in our understanding of the complex interplay between various factors and recovery outcomes.

# CONCLUSION

The findings of this study revealed that the median recovery time was longer than that reported in similar studies. The variables children aged 36–59 months, rural residence, underweight in weight for age, presence of danger signs, and presence of comorbidity were statistically significant predictors of time to recovery in children aged 2–59 months. Therefore, families of children with identified predictors need counseling to prepare for the likelihood of slow recovery. Further prospective studies need to be conducted to incorporate other potential predictors such as parental factors, environmental and other clinical factors.

# **Consent for Publication**

All authors declared that they have agreed to publication.

# **Competing Interests**

The Authors have declared no conflicts of interest in this work.

# Funding

There is no funding to report.

# Availability of data and material

The datasets used for this study are available from the corresponding author upon reasonable request.

# **Ethical Considerations**

Ethical approval was obtained from the Ethical Review Board (IRB) of Jimma University a Ref. No. JUIH/IRB/367/23 and official permission were secured from the Health Department at Asella Referral and Teaching Hospital. As we stated in the methods section, we used secondary data

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retrieved from the patient cards/databases that had already been collected for the patients' registration cards in the Hospital. The names of the study participants were not recorded to maintain confidentiality, instead, their medical registration numbers were used to distinguish the study participants' information, and all data collected were kept confidential. The hospital database management department had consented to each study participant or caregiver to use the data for research purposes in a confidential way at the time of initiation.

## Authors' contributions

**T.M.:** Conceptualizations, Data curation, Formal analysis, Investigations, Methodology, Supervision, Validation, Visualization, Writing an original draft, and Writing Review and editing the manuscript. He is guarantor.

A.L.: Formal analysis, Investigations, Methodology, Supervision, Visualization, Writing Review, and editing the manuscript.

**A.K.:** Formal analysis, Investigations, Methodology, Supervision, Visualization, Writing Review, and editing the manuscript.

## Acronyms and abbreviations

ACSH: Ayder Comprehensive Specialized Hospital, AGE: Acute gastroenteritis, AHR: Adjusted Hazard ratio, ARTH: Asella Referral and Teaching Hospital, ARTI: Acute respiratory tract infection, CHD: Congenital heart disease, CHR: Crud Hazard ratio, CI: Confidence interval, DM: Diabetes mellitus, DS: Down syndrome, HAAD: Hyperactive airway disease, HHRI: Health and health-related indicators, Hib: Hepatitis B vaccine, HIV: Human immune virus, JUMC: Jimma University Medical Center, PCV: Pneumococcal vaccine, PIV1: Parainfluenza type-1, NEMMCSH: Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital, RVI: Retroviral infection, SAM: Severe acute malnutrition, SCAP: Severe community-acquired pneumonia, SRS: Simple random sampling, TB: Tuberculosis, TTR: Time to recovery, UGCSH: University of Gondar Comprehensive Specialized Hospital, UNICEF: United Nations Children's Fund, and WHO: World Health Organization

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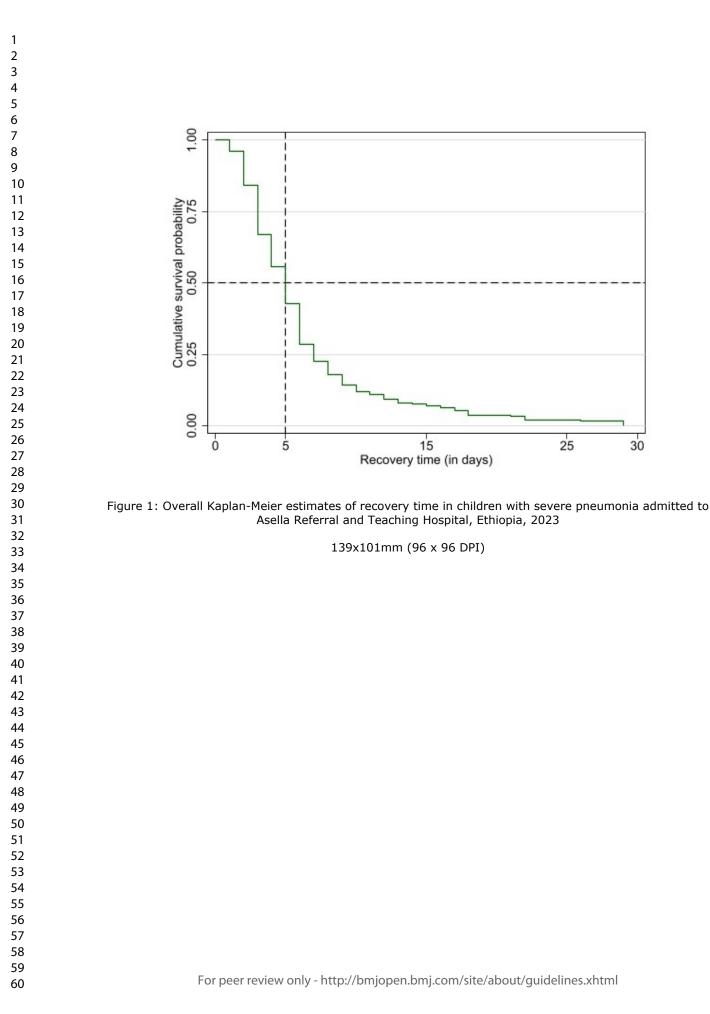
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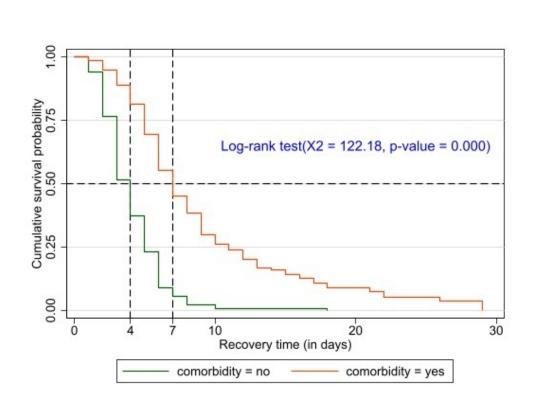
Figure 1: Overall Kaplan-Meier estimates of recovery time in children with severe pneumonia admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023

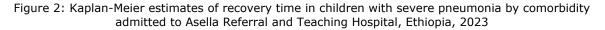
Figure 2: Kaplan-Meier estimates of recovery time in children with severe pneumonia by comorbidity admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023

Figure 3: Kaplan-Meier estimates of recovery time in children with severe pneumonia by danger signs admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023



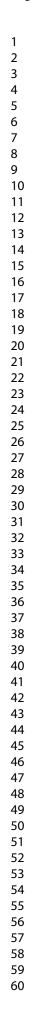






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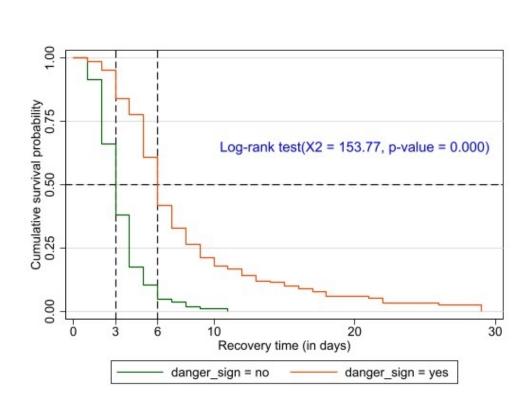


Figure 3: Kaplan-Meier estimates of recovery time in children with severe pneumonia by danger signs admitted to Asella Referral and Teaching Hospital, Ethiopia, 2023

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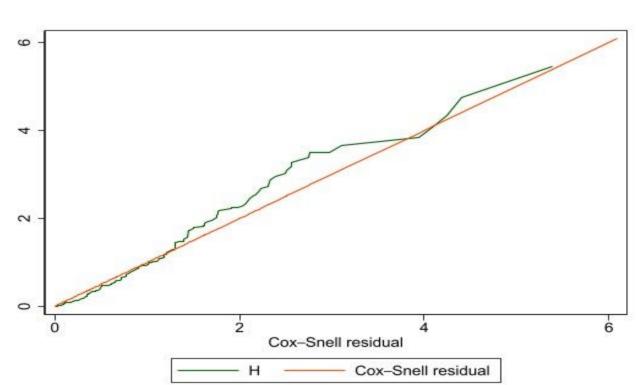


Figure 1: Cox-Snell Residual plot of the multivariable Cox-regression model for time to recovery from severe pneumonia admitted to Asella Referral and Teaching Hospital, Asella, Ethiopia

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