DEBRE BERHAN UNIVERSITY

COLLEGE OF NATURAL AND COMPUTATIONAL SCIENCE

POST GRADUATE STUDIES

DEPARTMENT OF STATISTICS

TIME TO RECOVERY AND ITS ASSOCIATED FACTORS OF UNDER-FIVE PNEUMONIA PATIENTSADMITTED TO PEDIATRIC WARD,DEBRE MARKOS COMPREHENSIVE SPECIALIZED HOSPITAL, ETHIOPIA

By:

HABITAMU WUDU

A THESIS SUBMITTED TO THE SCHOOL OF GRADUATE STUDIES OF DEBRE BERHAN UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF SCIENCE IN STATISTICS (BIOSTATISTICS)

JUNE, 2021

DEBRE BERHAN

ETHIOPIA

DEBRE BERHAN UNIVERSITY

COLLEGE OF NATURAL AND COMPUTATIONAL SCIENCE

POST GRADUATE STUDIES

DEPARTMENT OF STATISTICS

TIME TO RECOVERY AND ITS ASSOCIATED FACTORS OF UNDER-FIVE PNEUMONIA PATIENTSADMITTED TO PEDIATRIC WARD, DEBRE MARKOS COMPREHENSIVE SPECIALIZED HOSPITAL, ETHIOPIA

By:

HABITAMU WUDU

A THESIS SUBMITTED TO THE SCHOOL OF GRADUATE STUDIES OF DEBRE BERHAN UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF SCIENCE IN STATISTICS (BIOSTATISTICS)

ADVISOR: AYELE ADMASU (ASSISTANT PROFESSOR)

JUNE, 2021

DEBRE BERHAN

ETHIOPIA

DECLARATION

I, the undersigned, declare that the thesis is my original work, has not been presented for degrees in any other University and all sources of materials used for the thesis have been duly acknowledged.

Name HabitamuWudu

Signature _____

This thesis has been submitted for examination with my approval as a University advisor

AyeleAdmasu(Assistant Professor) _____ _____

Name of advisorSignature Date

APPROVAL SHEET

We, the undersigned member of the broad examiners of the final open defense by HabitamuWudu have read and evaluated his thesis entitled "**Time to Recovery and Its Associated Factors of Under-Five Pneumonia Patients Admitted to Pediatric Ward, Debre Markos Comprehensive Specialized Hospital, Ethiopia**" and examined the candidate. This is therefore to certify the thesis has been accepted in partial fulfilment of the requirement for the degree of master of sciences in statistics with specialization of biostatistics.

_____ _____ _____

Name of Advisor Signature Date

_____ _____ _____

Name of External examiner Signature Date

_____ _____ _____

Name of Internal examiner Signature Date

_____ _____ _____

Associate Dean, College Res/CS& Postgraduate Signature Date

_____ _____ _____

Dean collage of Graduate Studies Signature Date

Final approval and acceptance of the thesis is contingent up on the submission of the thesis of the final copy of the thesis to the college of graduate studies (CGS) through the department of graduate committee (DGC) of the candidate's

Stamp of CGS Date _____

ACKNOWLEDGMENTS

First and foremost, praises and thanks to the almighty God, for His showers of blessings throughout my life. Also my deepest gratitude goes to AyeleAdmasu (Assistant Professor), my advisor and instructor, for his constructive comments, encouragement, tireless follow-ups that make this work a reality, for his valuable advice, professional guidance, useful comments and suggestions. I am extremely grateful for what he has offered me.

My deepest thanks go to all members of Debre Berhan University, instructors and all individuals in the Department of Statistics for their moral support and positive attitude when I needed them during my course study. I am also thankful for all my friends and colleagues whoever explicitly or implicitly backed my work in whatsoever means.

And finally, I would like to thank heart fully Debre Markos comprehensive specialised hospital for collecting the data precisely with decent.

TABLE OF CONTENTS

CONTENTS **PAGE**

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVAITIONS

AIC	Akaike information Criterion
AIDS	Acquired Immune Deficiency Syndrome
ARTI	Acute Respiratory Tract Infections
BIC	Bayesian information Criterion
CAP	Community acquired pneumonia.
CHERG	Child Health Epidemiology Reference Group
DMCSH	Debre Markos comprehensive specialized hospital
HAP	hospital acquired pneumonia
IQR	Inter Quartile Range
K-M	Kaplan-Meier
LMIC	Low and middle income countries
PH	Proportional hazard
SAM	Severe acute malnutrition
SCAP	Severe Community Acquired Pneumonia
SSNPR	Southern Nations, Nationalities, and Peoples' Region
UNICEF	United Nations Children’s Fund
U5M	Under-five children mortality
WHO	World Health Organization
AHR	adjusted hazard ratio

ABSTRACT

Pneumonia is described as the inflammation of parenchymal structures of the alveoli and the bronchioles (lungs). In Ethiopia, it is a leading single disease killing under-five childrenand it continous a Major *health problem. The study aimed to identify determinant factors that affect time to recovery of under- five pneumonia patients at Debre Markos Comprehensive Specialized Hospital.a hospital based* cross-sectional *study design was employed at Debre Markos comprehensive specialized hospital.The data was collected in patient's chart from September 2018 to September 2020.Data was entered and analyze using STATA version 14.2 and R 3.4.0 statistical software. The Kaplan Meier survival curve and log rank tests were used to compare the survival time. Cox proportional hazard model assumption and model fitness were checked.the parametric AFT models were used to identify factors associated with the recovery time of Pneumonia patients. All the fitted models were compared by using AIC and BIC.The log-logistic AFT model was fitted as a final model. Accelerated factor (γ) with its 95% confidence interval was used and P-value < 0.05 was considered as statistically significant association. The overall median recovery time was 5 days (95% CI (4-6)). Time elapsed to seek care ($\gamma = 1.256$; 95% CI (1.237-1.274)), being insured (γ =0.904; 95% CI (0.845-0.967)) and treatment type taken at the time of diagnosis ceftriaxone, ampicillin and combined (γ =0.833; 95% CI (0.810 - 0.92), $\gamma = 0.842$; 95% CI (0.759-0.933) and $\gamma = 0.912$; 95%CI (0.842- 0.986) respectively) were significant predictors for shorten timing of recovery. Parents or care takers should take their children to health facility immediately when they become ill.*

Key words:-Pediatrics,Unde-Five,Severe Pneumonia, Time to Recovery

1. INTRODUCTION

1.1.Background of the Study

Pneumonia is described as the inflammation of parenchymal structures of the alveoli and the bronchioles (lungs) (Higgins-Steele et al. 2017).Lung infection is classified by the causative organism as lobar pneumonia, bronchial pneumonia and acute interstitial pneumonia. Pneumonia is most commonly classified by where or how it was acquired. Community-acquired pneumonia (CAP) is an infection that begins outside the hospital and/or diagnosed within 48 hours after admission to the hospital. Whereas, hospital-acquired pneumonia occurs in more than 48 hours after admission and without any antecedent signs of infection at the time of hospital admission (Geleta et al, 2016).It can be caused by bacterial, viral, or parasitic infection as well as by non-infectious agents and the most severe cases of pneumonia is caused by bacteria, of which the most important are Streptococcus pneumonia (pneumococcus) (Aboubaker et al. 2015).

The burden of medical response to pneumonia has significant challenges. Also comorbid conditions like Malaria, TB, HIV/AIDS and risk factors like danger sign, insurance status, residence etc. commonly appear in pneumonia patients which leads to define the severity and risk scores of the disease in which used for clinicians to make care self-site decision as in-patients or out-patients(Ramirez and Anzueto, 2011).Optimal management of these comorbidities may increase survival condition and reduce length of hospitalization among hospitalized patients. Then identifying determinants influencing survival of hospitalized pneumonia patients is critical for optimal utilization of scare resources, appropriate management and minimize child mortality (Premnath, Jana et al. 2012).

The mortality rates of children under the age of five years in most developing countries ranges from 60 to 100 per 1000 live births, one fifth of these deaths are due to pneumonia (WHO, 2016). The incidence of pneumonia in children under the age of five years is 0.29 episodes per child year, which equates 151.8 million cases annually in developing countries, a further 4 million cases occur in developed countries. Fifteen countries contribute 74% of the world's annual pneumonia cases (Rudan I, 2008). And also According to estimates from the World Health Organization Pneumonia kills about 2,500 children every day and more than 150 million cases of pneumonia occur in children under-five in each year, of which 20 million cases require hospitalization (Leung, 2016).

Morbidity and mortality from pneumonia is greater in low and middle income countries (LMIC). An estimate from the Child Health Epidemiology Reference Group (CHERG) puts the total number of pneumonia deaths worldwide in children under-five at 935,000 (Liu et al., 2016). Sub-Saharan Africa takes the lead in having half of its under-five deaths resulting from pneumonia compared to other regions. Also, regional disparities exist in the percentage of under-five deaths resulting from pneumonia with 5% of deaths occurring in developed regions and 17% of deaths in Sub-Saharan Africa (Liu et al., 2016).The African Region has, in general, the highest burden of global child mortality. It has about 45% of global under-5 deaths and 50% of worldwide deaths from pneumonia in this age group (World health statistics, 2007). By contrast, less than 2% of these deaths take place in the European Region and less than 3% in the Region of the Americas.

According to 2012 central statistical agency report there is high burden of pneumonia in Ethiopia that is 88 in 1,000 children under age 5 die before their fifth birthday (CSA, 2012). Acute respiratory infection (ARI), and particularly pneumonia, accounts for 18% of death in Ethiopia; improving early care is a key strategy for early diagnosis and treatment (UNICEF, 2014). Integrated management of common childhood illness and community case management are among the program initiatives scaled up nationally to address ARI (Miller et al., 2014)

It is the leading cause of morbidity and mortality among children below five years of age in Ethiopia, with an approximately 3,370,000 children experiencing pneumonia every year that attributes to 18% of all causes of deaths and killing more than 40,000 under five-children annually, making it the number one cause of death during the postnatal period as well (Wardlaw et al., 2014).In Ethiopia, pneumonia continues to be the major infant problem and killer (Andualem et al., 2020).

Several studies were tried to use statistical models like Binary logistic regression model and multilevel logistic regression models to identify the determining factors of the mortality status of pneumonia and about the prevalence of the pneumonia. The studywas use time to recovery as response variable to identify associated factorsof survival time of under-five pneumonia patients;Survival analysis is a statistical method for data analysis where the outcome variable of interest is the time to the occurrence of an event. The semi-parametric and parametric survival models were used to fit the survival time of pneumonia patients.

Kaplan Meier curves and log rank test were used to compare the survival experience of different category of patients, Cox PH model and Accelerating failure time (AFT) models wereused to fit dataset. Parametric survival models are statistically more powerful than nonparametric or semi-parametric models (Klein, 2005). A survival analysis helps us to understand the distribution of failure time which is often described by using Weibull, Log-logistic and lognormal distributions. Therefore, the aims of this studywere to investigate the survival time of under-five children hospitalized due to pneumonia and identify associated factors with under-five children survival time due to pneumoniaobserved at Debre MarkosComprehensive Specialized Hospital.

1.2.Statement of the Problem

Around the world, significant efforts have been made to minimize pneumonia-related morbidity and mortality. However, the main difficulty is the increasing duration of stay in the hospital and the poor response to antibiotic treatments, which has resulted in a decrease in pneumonia patient survival (Opio, 2018).

In 2016 United Nations Children's Fund (UNICEF) reported that there is 1 out of 6 childhood deaths were due to pneumonia globally in 2015 (UNICEF, 2016). In Sub-Saharan Africa, the proportion of deaths due to pneumonia in children younger than five year is 17-26 percent (Black E, et al, 2003). Nearly 50% of pneumonia deaths take place in only six densely populated and poorest countries: India, Nigeria, Democratic republic of Congo, Pakistan, Angola and Ethiopia (UNICEF, 2014).In Ethiopia, pneumonia is a leading single disease killing under five children and it contributes about 18% of all cases (3,370,000) of under five deaths compared to diseases like diarrhea, AIDS, malaria and measles every year (Walker et al., 2013; Peterson et al, 2019).

Many studies on the prevalence and risk factors of pneumonia have been conducted using logistic regression, and some studies have employed the Cox proportional hazards model with death as the outcome. (Tessema, 2018; Andualem et al., 2020 ; Abate and Tadesse, 2019). .However Logistic regression does not account the censoring observations. Despite the fact that semi-parametric estimate provides more flexibility, parametric estimate is more powerful provided the baseline hazard's form is known in advance.(Munda et al., 2012). Recent studies provide insight on the socio-economic and clinical predictors of mortality and survival of pneumonia patients (Mitiku, 2019). However, these studies were conducted by

using semi-parametric model and not including some set of variables like micronutrient deficiency, SAM (sever acute malnutrition), types of pneumonia and season of diagnosis.Time to recovery and its associted factor of under-five children's hospitalization related to severe pneumonia patients is not well known. So, determining associated factors of recovery time of pneumonia patients whose age is under five years are essential. Therefore, this study focus the analysis of time to recovery, which factor is significantly affects the recovery time of under-five pneumonia with appropriate survival model for the dataat Debre Markos Comprehensive Specialized Hospital, Ethiopia by adding additional variables that affects the survival status of under-five pneumonia patient like types of pneumonia, sever acute malnutrition, Micronutrient Deficiency (such as zinc, vitamin D, vitamin A, etc) and seasons of diagnosis.

Generally, this study has attempted to answer the following basic research questions.

1. What is the median recovery time of under-five pneumonia patients?
2. Which variables are significantly associated with time-to- recovery from pneumonia?
3. How do you compare the survival curves of patients' recovery times across different levels of covariates?
4. Which predictor has high survival Experience among different level of factors?

1.3. Objectives of The Study

1.3.1.General Objective of The Study

- ✓ The aim of this study is to identify determinant factors that affecttime to recoveryof under- five pneumonia patients at Debre Markoscomprehensive specialized Hospital.

1.3.2. Specific Objectives

- ✓ To estimate survival median survival time.
- ✓ To assess the effect of predictive factors associated with time to recovery of under-five pneumonia patients in Debre MarkosComprehensive Specialized hospital.
- ✓ To compare the survival probabilities of the under-five pneumonia patients with respect to Different risk factors.

1.4. Significance of The Study

The results of this study will beneficial for determining the determinant factors of the recovery time of under-five pneumonia patients for concerned bodies like pediatrician, patients for taking service, ministery of health and goverments , it also had great contribution for the patient and the heath professionals for follow up to reduce the time to recovery from theirillnes, List out the most predictive factors affecting the recovery time of under-five pneumonia patients and will provide base-line data for detail and further studies in the future, and investigate the median time taken of recovering from pneumonia disease.

1.5. Limitation of The Study

Because the study was based on secondary data and was conducted retrospectively by reviewing patients' charts, some variables, such as parental socio-demographic, socio-economic, and environmental characteristics, as well as other variables that could be potential predictors of the outcome variable, were left out. and there were a lot of patients with insufficient information; limited of published literature on the country related to associated factors on time to recovery of under-five pneumonia patients.

1.6.Operational Definition

Recovery:children discharged/ declared by the clinician as improved from an illness.
Event: recoveryfrom an illness during the study period.
Survival time:defined as the time starting from the date of admission to recovery as a result of improvement due to sever pneumonia determined for each participant.
Censored: children referred, died or discharged for any reason without recovery during the study period.
Paediatric: Children whose age is above 1 months and below 5 years were pediatrics in our study.

2.RELATED LITERATURE REVIEW

2.1.An Overview of Pneumonia

Pneumonia is defined as an inflammation of parenchymal tissues of the lung, such as the alveoli and the bronchioles(Porth, 2011). It's a lung infection caused by an acute respiratory tract infection (ARTI).Small air sacs called alveoli fill up with air during normal breathing. When kids get pneumonia, their alveoli fill up with pus and fluid, making breathing difficult and uncomfortable. (UNICEF and UNICEF, 2016). The patient's normal growth and development are affected by longer hospital stays and a longer time to clinical stability (recover from illness).Additionally,Parents and caregivers waste time caring for their children, and it has become a significant financial burden for families, communities, and governments. The increased financial burden may be borne by the government as majority of the patients come from poor rural families relying on government health care services (Ma, Gunaratnam et al, 2019).

Pneumonias can be classified based on the type of agent causing the infection, distribution of the infection and setting in which it occurs (Porth, 2011). The etiologic agents of pneumonia could be infectious or non-infectious agents. Commonly pneumonias classified as community-acquired and hospital-acquired (nosocomial) pneumonia. Community-acquired pneumonia (CAP) is an infection that begins outside the hospital or is diagnosed within 48 hours after admission to the hospital in a person who has not resided in a long term care facility for 14 days or more before admission(Geleta et al., 2016). Hospital-acquired pneumonia is pneumonia that occurs more than 48 hours after admission and without any antecedent signs of infection at the time of hospital admission (Kieninger and Lipsett, 2009).It is also known as a nosocomial infection (from the Greek nosos, meaning disease, andkomide, care), is an infection that is acquired in a hospital or other health care facility.It refers to any pneumonia contracted by a patient in a hospital at least 48–72 hours after being admitted. In related to pneumonia type,HAP can have negative consequences for patients, including prolonged hospital stay, decreased quality of life and high mortality(Torres et al., 2017).Despite improvements in prevention, antimicrobial therapy and supportive care (Kalil et al., 2016).HAP(nosocomial) remains an important cause of morbidity and mortality and the mortality rate for HAP ranges from 38% than 70% than community acquired pneumonia (Laessig, 2010).

2.2. Survival Time of Under-Five Pneumonia Patients From Related Litertures.

According to the results of a study conducted at Bushulo Major Health Center, 75.5 percent of patients recovered from their illnesses(Zinabu et al., 2014).The global, regional, and national causes of child mortality reports that 73.3 percent of pneumonia patients were recovered (Li Liu, 2012).In a previous research of hospitalized young Nepalese children with acute severe pneumonia, the median duration to recovery was reported to be two days.(Basnet, Sharma et al. 2015).Also, in Taiwan, the mean time to recovery after admission for patients with pneumonia was 6.4 days (median = 5 days; range = 0 to18 days)(Huang, Chang et al. 2015).In three university teaching hospitals in Boston-USA, a study on length of time until a patient hospitalized with pneumonia becomes clinically stable(recover) estimated the median hospital length of stay at 6 days (C.I, 4-10 days)(Mueller, Zheng et al. 2019),the study conducted by(Assfaw et al., 2021) shows that the the average time to recovery was 3 days.In 2013, researchers conducted a study in Mulago hospital to compare clinical outcomes in children suffering from Asthma and Pneumonia, the average duration of hospital stay was 4 days (SD 4.3 days). Children with pneumonia had the longest duration of hospital stay compared to those with Asthma (Nantanda, Ostergaard et al. 2014).According to a study conducted in South West part of Ethiopia at Jimma the median duration of hospital stay was less than 3 days(Bekele, Sinaga et al. 2017),Other study conducted at south west Ethiopia shows that the median recovery time was 4 days(Abate and Tadesse, 2019). The study conducted in rural health centre of Gambia reported that the median time of recovery was 4.5 days(Kuti, Adegoke et al. 2014). According to (Wolf, Edwards et al. 2016) and (Gajewska et al., 2016) the median recovery time from pneumonia was 2.3 days and 10.1 to 8.2 days respectively.

This shows that the treatment response to pneumonia is still low and patients' survival remains a challenge to health and development in Ethiopia and worldwide.

2.3.Determinant Factors of The Survival Status of Pneumonia Patients

2.3.1.Socio Demographic and Socio-Economic Factor

As we saw different studies, there are several socio-demographic & socio economic factors that affect the prevalence, mortality status and survival status of under-five pneumonia

patients. Such as age of the patient (Opio 2018), ,Breastfeeding status of the patient (Wolf, Edwards et al. 2015, Opio 2018),Education level of mothers, Smoking habit of parents(Abdel Mohsen, Amin et al. 2019),sex, residence, sever acute malnutrition (SAM) and seasons of diagnosis ,health insurance and duration.

Accordingly Age of patients, a birth cohort study in Cape Town, South Africa, indicated that the majority of the pneumonia burden among children is within the first 2 years of life (Campbell and Nair, 2015). And the results of their study indicated that severe pneumonia accounts for the most pneumonia deaths in the first 6 months of life. Similarly, other scholars around the globe have found that children less than 59 months are most at risk age-group (Opio 2018).Based on these findings; age remains subject to further assessment to confirm whether it matters as far as survival time of patients are concerned. This relationship of increased pneumonia cases in younger ages has also been long-established by the study in South West Ethiopia, children in the age group 1-11 months were more exposed to pneumonia than other age groups, Considering age groups included in this study 49.82%, of patients were from age group 1-11 months, and the death proportion for this age group were 44.68% (Abate, 2018)if patients are postnatal and child age than those patients in neonatal age group. Accordingly, the risk of dying from pneumonia for postnatal age group and child age Group patients was less by 91 and 92% respectively.The rate of recovery early from pneumonia decreased by 6% (AHR; 0.94, 95% CI (0.90-0.98)).Another study also indicated younger children recover sooner than older ones (Mitiku, 2019), age (2–3-years) (AHR, 1.4, (95% CI: 1.31–2.22)), and ≥4-years (AHR, 1.32, (95% CI: 1.3–2.32)) as compared to age of ≤1 year were important factors ofrecovery time (Assfaw et al., 2021).This study considered age as categorical predictor to find its effect on the recovery time of patients.

The survival of sex differences has been inconsistent according to various studies (Ley, Collard et al. 2011). (Demographic, 2012) found sex has no significant difference Whereas some studies show sex differences in pneumonia patients found that female sex to confer a significant survival advantage, other studies have consistently agreed that female patients have greater risk of dying from pneumonia than male patients (Huang, Chang et al. 2015).It is therefore debatable whether sex of a patient influences survival time of pneumonia patients or not in a substantial manner.The estimated acceleration factor for male patient is estimated to be 0.878 with (95% CI: 0.782, 0.987). This indicates that male patients have less survival time (time to death) than female patients or in the other way female patients survived 12.2%

longer than male patients (Abate and Tadesse, 2019).This study used sex as predictor variable to find its significant effect on the survival time.

Related to residence, some scholars suggested that both urban and rural residence has its own impact on survival time of under-five pneumonia (Azab, Sherief et al. 2014).The acceleration factorsfor patients whose residence was urban were estimated to be 1.158 with (95% CI: 1.010, 1.328).This indicates that patients whose residence was urban had prolonged death timing than patients from rural residence at 5% level of significance (Abate and Tadesse, 2019).Also Study conducted at Jimma University specialised Hospital reported that among the children males accounted for 54.2% of the children and children suffering from severe pneumonia in rural area accounted for 79.4% compared to children in urban area (20.6%) (Firaol B, 2017).

Exclusive breastfeeding is considered both a preventive and curative strategy among children younger than two years. WHO, public and private health workers, have consistently advocated for exclusive breastfeeding at least for the first 6 months of a child's life. The general consensus of many scholars is that, lack of exclusive breastfeeding increases the risk of both upper and lower respiratory tract illness, increasing risk of development of severe pneumonia by 1.5 to 2.6 times. Concerning breastfeeding, many scholars agree that exclusive breastfeeding for the first 6 months of life increases child survival by reducing the length of hospital stay and also reducing risk of treatment failure (Wolf, Edwards et al. 2015).

Related to age of mothers, (Azab, Sherief et al. 2014, Aftab, Ejaz et al. 2016) show that age of mothers have significant effect on child pneumonia. Children with teenage mothers were more likely to have severe CAP compared to those born to older women ($P < 0.01$). Based on smoking habit of parents, previous studies have shown that children whose parents smoke have a higher risk of contracting severe pneumonia and being hospitalized (Perlroth and Branco 2017).

Related to season of diagnosis, Patients admitted throughout the summer and spring seasons had a higher risk of dying from CAP than those admitted during other seasons, according to a study conducted in Hawassa City on under-five-year-old mortality(Tariku T., 2017). According to study conducted in ten district Hospitals in Malawi classified the season in to Quarters as July-September, October-Dec, Jan-March and April-June Generally the pattern of pneumonia cases does not vary between the seasons in Malawi except in January through

March and slightly peaks up again in the cool/dry season June and July. January through March coincides with the rainy season where there is a peak for both malaria and malnutrition (Ellubey R., 2004). Altitude, annual rainfall, number and nature of the seasons and average monthly temperatures are the factors listed by CHERG as factors of under-five pneumonia (Fischer W., 2013). And also other study conducted at southern Israel Hospital reported that the prevalence of the CAP and nosocomial pneumonia were higher in the spring and summer season compared to that of winter and autumn (Lieberman D and PorathA, 2005). Seasonality is another possible risk factor identified by (Rudan I, 2008), likely related to seasonal viruses including influenza. Season of diagnosis, are a predictive (a statistical significant) predictors for the mortality status (dead/alive) of patient's due to pneumonia (Tessema, 2018). It shows that, the odds of being at risk to death during spring season were 7.54 times more likely than patient's diagnosed in winter season.There is less likely to die from pneumonia,Patients diagnosed at spring season and summer season acceleration factor were 0.845 and 0.813 with (95% CI: 0.720, 0.991 and 0.683, 0.966) respectively. And p-values were small (p=0.003 and 0.001) respectively. Patients who were diagnosed at spring and summer season had less survival time (time to death)than patients who was diagnosed at autumn season (Tadesse, 2019)and related to SAM Patients who were not suffered severe acute malnutrition (SAM) had longersurvival time than patients who were suffered severe acute malnutrition (SAM). (Abate et al 2019, Miller, 2014). the presence of severe acute malnutrition can increase mortality from pneumonia 15-fold (Mishra Pet al,2016).

Related to time elapsed to seek care (duration), Duration prior to seeking care is an independent significant predictor for recovery time of pneumonia. Children who presented to the hospital early (before five days of an illness) recovered sooner than those children presented lately (Mitiku, 2019).This finding is consistence with a prospective study conducted in Gambia (Kuti et al., 2014). Andother study shows that, it was found that Patients who late diagnosis has high probability of being at risk than those admitted before 3 days. The odds of being at risk for patients who diagnosed after a week is 8.71 times than those patients diagnosed before three days. The odds of being at risk for patients who diagnosed with 4 to 7 days was also 4.74, which means the risk of dying from pneumonia if patients diagnosed between these days was 4.74 times than those diagnosed before three days(Tessema, 2018).In related to health insurance, Previous studies generally show that lack of health insurance is associated with an increased risk of death in the intensive care unit (ICU) (Lyon et al., 2011).National health insurance membership is associated with increased

access to and utilization of health care (Sarpong et al., 2010) and children were not member of social health insurance were more exposed than children's were member of social health insurance (Mitiku, 2019).

2.3.2.Clinical (Treatment) Factor

The clinical characteristics associated with survival time of hospitalized pneumonia patients were; respiratory rate (Basnet, Sharma et al. 2015),baseline condition at admission (Opio 2018), danger signs such as head nodding, abnormal body movement, breathless(Huang, Chang et al. 2015),baseline comorbidity (like measles, malaria, etc), treatment type among others,Past history of ARTI(Onyango D et al,.2012).

Inrelated to danger sign on survival time of pneumonia patients, many studies have been carried out, some of which explains mortality and some are explained length of hospital stay. For example, studies by (Opio, 2018). Shows that patients with danger sign had short survival times at all times,generally many scholars agree that danger sign at baseline reduce survival time which then increases the risk of mortality among pneumonia patients (Wolf, Edwardset al. 2015). The recovery rate of children who were admitted with danger sign reduced by 39% than those admitted without danger sign (AHR; 0.61, 95% CI ((0.40-0.94)). (Mitiku, 2019)an d in related to past history of ART patients many studies have been carried out the effects of past history of ARTI on the mortality status and prevalence of pneumonia. The study condacted in western kenia shows that children who had past history of ARTI were 2.77 times more likely to devlop pneumonia compaired to those who had no ARTI(Onyango D et al,.2012).An other study conducted by(Fentahun A,2019) also indicates children who had past history of ARTI were 4.11 times more likely to devlop pneumonia compaired to those who had no ARTI

In related to micronutrient deficiency, In Iran, 43 percent of the 200 children were admitted to Children's Medical Centre that were diagnosed with radiologic rickets, were also suffering from bronchopneumonia. Therefore, vitamin D deficiency may be an important factor predicts pneumonia in children less than 5 years in developing countries.(El Basha, Noussa Mohsen et al,2014) The role of vitamin A in the growth and development of cells and tissues (especially in respiratory epithelial cells and lung tissue) is essential. Vitamin Adeficiency is associated with inflammation and infection in children and the severity of the infection (Roomaney RA et al, 2016). Zinc deficiency to be associated with increased risk of infection,

particularly pneumonia. Similarly, Studies conducted in US & Pakistan reported the reduction of pneumonia incidence and prevalence among children who received zincsupplementation (Lassi ZS, Haider BA et al, 2010).astudy conducted by (Fentahun A,2019) indicates children who had Microneutriant deficiency were 3 times more likely to devlop pneumonia than children who had no microneutriant deficiency.

On the manner of comorbidity, many scholars have identified significant relationship between increased mortality and any underlying illness. The common identified comorbidities are malaria, diarrhea, HIV/AIDs, and TB (Reed, 2015).Comorbidity has significant effect on the survival status of pneumonia patients. The acceleration factor for patients suffered comorbidity was estimated to be 0.881 with (95% CI: 0.640, 0.916). This implies that patients who were not suffered co-morbidity had longer survival time than patients who were suffered co-morbidity(Abate and Tadesse, 2019, Miller, 2014).but this study use time to death not time to recovery.Co-morbidity was an independent predictor of recovery time from sever pneumonia among paediatrics and the rate of recovery among children admitted with co-morbidity decreased by 55% as compared to those children who had not co-morbidity at admission (AHR; 0.45, 95% CI ((0.45(0.35-0.58)) (Mitiku, 2019). And this study did not quantify the impact of Types of pneumonia, Sever Acute malnutrition, micro nutrient deficiency and season of diagnosis on time to recovery of under-five pneumonia patients. Therefore, by inserting those variables a survival model were conducted, which study about the time to recovery of under-five pneumonia patients in Debre Markos Comprehensive specialized hospital, Ethiopia.

In case of Treatment type, Study conducted at Mozambican reported that children with severe pneumonia or suspected bacteraemia/sepsis, empirical antimicrobial therapy with parenteral chloramphenicol or a combination of penicillin plus gentamicin was given. Studies example (Mitiku, 2019).Shows that, all children who were treated as an inpatient, more than half (59.66%) received Crystalline penicillin followed by ceftriaxon (33.24%) and only (7.1%) of children treated by ampicilin withgentamicin. Majority of children (89%) recovered from their illness and 11% were died. But, Study conducted at Wondo Genet district, Sidama zone using multivariable logistics regression reported that treatment types taken by pneumonia patients at hospital levels has not significantly associated with mortality status under-five children (Teshome A., 2017).There are multiple antibiotics indicated and effective in the treatment of pneumonia. Administration of the most appropriate antibiotic as a first-line

medicine may improve the outcome of pneumonia. In order to effectively treat the disease while minimizing antimicrobial resistance and virulence, it is important to know which antibiotics work best for children depending on the severity of the illness (UNICEF, 2014). According to Recommendations for management of common childhood conditions: Newborn conditions, pneumonia.there are four types of antibiotics suggested for treatment of pneumonia are ceftriaxone, ampicillin, crystalline penicillin, and combined of one or more (WHO, 2012).Thetype of treatment given for sever pneumonia patients had significant effect on the recovery time of the disease (Don et al., 2010).Of all children who were treated as an inpatient, more than half (59.66%) received Crystalline penicillin followed by ceftriaxon (33.24%) and only (7.1%) of children treated by combined. Majority of children (89%) recovered from their illness and 2.27% were died.

The other associated clinical factors for survival status of pneumonia patients were Nurse-to-patient ratio (NPRs), it are typically expressed in two ways: the number of nurses working per shift or over a 24 hour period divided by the number of beds occupied by a patient over the same time period; or the number of nursing hours per patient bed days (RCN, 2010). A higher level of nursing staff indicates more nurses for assigned patients. Lower nurse staffing is defined as fewer nurses (or lower proportion) for the number of assigned patients (Penyoyer D., 2010). NPRs are easily and cheaply measured but it is a relatively blunt instrument that can function as one indicator, and can be triangulated with other measurement approaches to establish safe nurse staffing levels. According to the study conducted at Europe, the effect of nurse-to-patient ratios on nurse sensitive patient outcomes in acute specialist units found that a higher level of nurse staffing was associated with a decrease in the risk of in hospital mortality (Andrea D., 2017). For every increase of one nurse, patients were 14% less likely to experience in hospital mortality. In addition to nurse patient ratios, it is also important to incorporate skill mix within a critical care unit particularly when planning workforce shifts (Penyoyer D., 2010). These studies highlight the need for some agreement, at an international level, about the most appropriate way to measure nurse staffing levels (Andrea D., 2017). A study shows that,Acceleration factor for patient nurse ratio was estimated to be 1.095 with (95% CI: 1.018, 1.177). P-value is small (p=0.015) (Abate and Tadesse, 2019).Most of the studies listed in the literature used death as their event and the survival time determined based on the time to death of patients. While this study was used recovery as theevent and the survival time determined based on the time from date of admission to hospital discharge.

3. DATA AND METHODOLOGY

3.1. Study Area and Period

This study was conducted at Debre MarkosComprehensive Specialised hospital which is the only Comprehensive Specialised Hospital that is located in the capital city of East Gojam zone, Debre Markos.It is located in Northwest of Ethiopia 299 kilo meters far from Addis Ababa. The hospital provides service for children less than 15 years inseparate ward of paediatrics. In this hospital, children with severe pneumonia wereadmitted in paediatric ward and further diagnose and treatment provided by paediatricians, generalpractitioners and nurses. The study was conducted from September 11, 2018 to September 11,2020among children who were admitted with sever pneumonia.

3.2.Study Design

A hospital based cross-sectional study design was conducted from retrospectively records.that reviews or visits all under-five aged children cards hospitalized due to Pneumonia in Debre MarkosComprehensiveSpecialized hospital during study period. The source of population of this study was all children admitted at thehospital by severe pneumonia during the studyperiod andthe study population wasall children admitted at the hospital by severe pneumonia whose charts were available during data collecting.

3.3. Source of Data and Data Collection Procedure

The data was retrospective survival data and itwassecondary data that was recorded on pediatric registration chart and cards via nurses, laboratory technicians, medical doctors and clinicians. The hospital's registry is used to extract data of under-five pneumonia patients' initial date of admission up to date of discharge of patients during the study period, the pediatric registration chart and the patient's identification cards were used to select the variables in the study by trained clinicians. The completed data collection forms are examined for completeness and consistency during data management, storage and analysis. The cards were prepared by Federal Ministry of Health to be uniformly used by clinicians to early identify and document clinical and laboratory variables. Thus, the data were collected from patient follow up records based on the variable in the study.

3.4. Inclusion and Exclusion Criteria

The inclusion criteria were children whose age were from 1month to 5 years and admitted at paediatric ward by severe pneumonia during the study period with full information including in the registration log book or in the patients' identification card were considered to be eligible for the study and Exclusion criteria are children who are admitted at the hospital with incomplete medical records which are required as predictor.

3.5.Study Variables

Depending on the reviewed literature reviews the variables included in this study are listed as follows.

3.5.1.Response Variables

The response variable is time to recovery of under-five pneumonia patients in days. The survival time of outcome of interest (recovery in this study) is the duration of time considered from the day that the children admitted in the Hospital until recovery occurs.i.e. becoming normal condition of pneumonia or censored, measured in days.

3.5.2.Independent Variables

Predicting whether an event occurred or not and identifying the variables in making the prediction is an important step in carrying out the study. The independent variables that are used in the study are classified as demographic, clinical (treatment), and other variables. Variables such as age, sex, etc. are considered as demographic variables, Moreover, as some studies revealed, most independent variables which are included in this study are expected to show marked differential in the survival time of the under-five pneumonia patients

Table 3.1: variable description & coding for explanatory variables

No	Variable name	Values of the variable and their code	Type
1	Place of residence (residence)	0= Rural &1=Urban	Categorical
2	Sex of patients (sex)	0=male & 1=female	Categorical
3	Age of under-five pneumonia patients in Month (age).	1-11=0,12-23=1,24-59=2	Categorical
4	Types of pneumonia disease at diagnosed (ptype)	0=CAP ,1=nosocomial (HAP)	Categorical
5	Presence of concomitant disease(Comorbidity)	0=no &1= yes	Categorical
6	Sever acute malnutrition.(SAM)	0=no &1= yes	Categorical
7	Time elapsed to seek care (duration)	in days	Continuous
8	Past history of ARTI (history ARTI)	0= no 1= yes	categorical
9	Treatment types taken at time of Diagnosis (treatmenttype)	Crystalline penicillin=0, Ceftriaxone=1, Ampicillin =2 and 3= combined	Categorical
10	Clinical presentation during admission(danger sign)	0=no & 1= yes	Categorical
11	Seasons of diagnosis (season)	0=Atumun,1=Winter,2=Spring & 3= Summer	Categorical
12	Insurance status (insurance)	0= not insured and 1= insured	Categorical
13	Micronutrient deficiency like zinc, vitamin D, vitamin A etc. (Mdeficiency)	0= no and 1= yes	Categorical

3.6. Method of Data Analysis

A statistical analysis is consists of descriptive data analysis and survival model fitting to make inference by non-parametric Model, semi parametric Cox proportional hazard models and parametric survival (AFT) accelerated failure time models. All inferences were conducted at 5% significance level using R version 3.4.0 &STATA 14.2 are statistical software package uses for analysis.

3.7.Survival Data Analysis

Several multivariable statistical models can be used to predict a dependent variable from a set of independent variables. Since survival time of under -five pneumoniapatients is time to event data, for this reason the Statistical Model to predict a dependent variable from a set of independent variables used is Survival analysis.

Survival analysis is a statistical method for data analysis where the outcome variable of interest is the time to the occurrence of an event(Lemeshow and May, 2008). Survival analysis is also referred to as "time to event analysis", “durational analysis”, “transition data analysis” or “event history analysis”. It is the analysis of the duration for the occurrence or non-occurrence of an event during the risk period and an individual can only be eligible to experience an event if there is a period during which they are at ‘risk’ of experiencing the event e.g. for an individual to be at risk of getting divorced they have to be married. In this regression analysis, the dependent variable measures the time to the occurrence of an event of interest and examines how covariates affect the length of time between consecutive events (Lemeshow and May, 2008).

Censoring is common in survival analysis and it is considered as an important feature of survival data. Survival analysis was well suited to for such data which were very common in medical research. Since studies in medical areas have a special feature that follow up studies could start at a certain observation time and could end before all experimental units had experienced an event. Three additional points should be mentioned in connection with the choice of the model.

Censoring occurs mainly for the following reasons (Kleinbaum and Klein, 2012):

- ✓ When an individual survives beyond the study period or the individual does not experience theevent.
- ✓ Lost to follow-up, that is, an individual may drop out, transfer to other places,etc.
- ✓ Deaths due to other causes different from that/those specified in thestudy.

The term “censoring”, will use in this study to mean in all instance right censoring.

3.7.1. Survival Function

T is a failure time (survival time, lifetime) non-negative-valued random variable. The value of T for this study will be the time from the start of treatment up to an event (i.e. recovery or censored) that occurs.

Let T be a continuous random variable for time to event with probability density function (pdf) f(t)and cumulative distribution function (Cdf)$F(t) = P(T \leq t)$. Then the survival function S(t) is defined as the probability that the event occurs after time (Pintilie, 2006).

$$S(t) = p(T > t) \rightarrow \text{The probability that an individual survives beyond time t.}$$

$$S(t) = P(T > t) = 1 - P(T \leq t) = 1 - F(t) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

3.7.2. Hazard Function

The hazard function describes the instantaneous event rate for an individual who survives uptotime without having an event. The hazard function is also known as the conditional failure rate or simply hazard rate and is defined as the probability that an individual fails at time t, conditional on the fact that he or she has survived to that time(Pintilie, 2006). The hazard function is denoted by h(t).

$$h(t) = \lim_{h \to \infty} \{ \frac{p(t < T \leq t + h | T > t)}{h}$$

$$\mathrm{h(t)} = \frac{\mathrm{f(t)}}{\mathrm{S(t)}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Here, f (t) indicates the density function of the random variable T for time to the event. The cumulative hazard function H (t) is defined as the cumulative hazard up to time (Rizopoulos, 2012)

$$H(t) = \int_0^t h(t)dt \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

3.7.3. Median Survival Time

The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that half of the patients in a group of patients diagnosed with the disease are still alive.i.e $S(T > t) = 0.5$, the values of t is the median survival time.
The median survival time is given as:

$$S(t_{med}) = 0.5 \; and t_{med} = S^{-1}(0.5) \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

3.8. Nonparametric Survival Methods

Nonparametric analyses are more widely used in situations where there is doubt about the exact form of distribution orabout how the covariates affect the hazard function. The hazard and survival functions were instead estimated based on the empirical data, showing change over time. The estimation of the survival distribution provides estimates of descriptive statistics such as the median survival time. These methods are said to be non-parametric methods since they require no assumptions about the distribution of survival time. Preliminary analysis of the data using nonparametric methods provides insight into the shape of the survival function for each group and get an idea of whether or not the groups are proportional, i.e., if the estimated survival functions for two groups are approximately parallel (do not cross).Nonparametric methods are neither able to handle continuous data nor multivariable analysis and control for other explanatory variables. Kaplan-Meier survival analysis is the primary example of the nonparametric approach to event history analysis(Kaplan and Meier,1958) and the study use long rank test to compare the survival difference between two or more groups (Collett, 2015).

3.9. Semi-Parametric Cox Proportional Hazard Model

The non-parametric methods like Kaplan-Meier and log-rank tests are useful in the analysis of a single sample of survival data or in comparing one or more groups of survival time. However, these methods do not control for covariates. In clinical analysis several prognostic (explanatory) variables usually influence the survival experience of the patients. The non-parametric models are unable to estimate the survival experience of the patients controlling for the explanatory variables and hence, the need to use semi-parametric proportional hazard models when carrying of survival analysis in the presence of covariates.

Cox proportional hazards (PH) model is one of the mathematical models designed for the analysis of time until an event. It shows the hazard at time t of an individual given the covariates. The hazard at the time is a product of baseline hazard function h0(t) which is only a function of time and exponential to the linear sum of βixi which is a function of time-independent covariates (David and Hosmer, 1999; Marubini and Valsecchi, 2004). The Cox Proportional Hazard model is given by;

$$h(t, X, \beta) = h_0(t) \exp\left(\sum_{i=1}^{n} \beta_i X_i\right) = h_0(t) \exp\left(\dot{\beta} X_i\right) \ldots\ldots\ldots\ldots\ldots\ldots (5)$$

where $h(t, X, \beta)$is the hazard function at a time for a subject with covariate values x_1, x_2,… x_n and the estimated coefficients of the covariates of β_1,β_2,… β_n.h_0(t)is the baseline hazard function, which is the hazard function for an individual for whom all the variables included in the model are zero, $X = (x1, x2, \ldots xn)$ is the value of the vectors of the explanatory/predictor variables for a particular individual, $\beta(\beta 1, \beta 2, \ldots \beta p)$ is a vector of the estimated coefficients of explanatory/predictor variables .

Although Cox regression is semi-parametric, it is a "robust" model, hence its results always closely approximate the results for the correct parametric model (Kleinbaum and Klein 2005). The Cox PH model is therefore preferred over parametric event history analysis models when there is no clear theoretical reason for positing a particular baseline hazard ratio (David and Hosmer, 1999; Kleinbaum and Klein 2005). The exponential part of the Cox PH model ensures that the fitted model will always give a non-negative hazard and by definition, a hazard function is between zero and plus infinity i.e. $0 \leq h(t, X, \beta) \leq \infty$, then the hazard ratio for the two groups is defined as:

$$HR = \frac{h(t/x = 1)}{h(t/x = 0)} = e^{\beta} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (6)$$

When HR = 1, it implies that the individuals in the two categories are at the same risk of getting the event, when HR > 1, it implies that the individuals in the first category (X = 1) are at a high risk of getting the event and if HR < 1, the individuals in the second category (X = 0) are at a high risk of getting the event.

Assumption of cox proportional model

i. The baseline hazard, h0 (t)depends on *t*, but not on covariates x_1,...,x_p.
ii. The hazard ratio depends on the covariates, but not on time.
iii. The covariates do not depend on time t.
iv. Proportional hazard which means the hazard ratio is constant over time.

Parameter estimation in cox-PH model

Maximum likelihood estimates of the Cox model parameters are derived by maximizing a likelihood function usually denoted as L. The likelihood function is a mathematical

expression that describes the joint probability of obtaining the data observed on the subjects in the study as a function of the unknown parameters (the β's) in the model being considered. L is sometimes written notational as L(β) where β denotes the collection of unknown parameters.

The formula for the Cox model likelihood function is called a "partial" likelihood function rather than a (complete) likelihood function. The term "partial" likelihood is used because the likelihood formula considers probabilities only for those subjects who fail, and does not explicitly consider probabilities for those subjects who are censored. Thus the likelihood for the Cox model does not consider probabilities for all subjects, and so it is called a "partial" likelihood.

Suppose the survival data is represented by (ti, δi, xi) for i=1, 2…, n where ti the length of time a subject is observed (survival time), δi an indicator of censoring for the ith individual and xi a vector of covariates for the i^{th} individual. The likelihood for right-censored data includes both the survival and hazard functions is given as:

$$L(\beta) = \prod_{i=1}^{m} [h(t, x_i, \beta))^{\delta i}] \, S(t, x, \beta) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (7)$$

The proposed partial likelihood function suggested by (Cox ,1972) avoids the specification of the baseline hazard function, treating it as a nuisance parameter and removing it from the estimating equation.

It assumes that there are no tied values among the observed survival times. Suppose we have m distinct failure times and let X (i) is the vector of covariates at ordered failure time t (i). We define the Partial Likelihood as

$$L_p(\beta) = \prod_{i=1}^{m} [\frac{e^{xi\beta}}{\sum j \in Rt(i) e^{xi\beta}}] d_i \dots\dots\dots\dots\dots\dots\dots\dots (8)$$

Where d_i is the number of deaths, $d_i = 1$ we assume there are no tied so excluded for di=0. And, „ $Rt(i)$ is the set of subjects at risk at a time just before ti (ti=0). And the summation in the denominator is over all subjects in the risk set at time ti denoted by $Rt(i)$.

Interpretation of a fitted proportional hazard regression model is based on the hazard function i.e.$e^{\hat{\beta}}$. $\hat{\beta}$ Is the maximum partial likelihood estimator of β.

The (1-α) 100% confidence interval for the estimated parameter is given as:

$$\hat{\beta} \pm z_{\frac{\alpha}{2}} * S.e(\hat{\beta}) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (9)$$

And, for the hazard ratio is obtained as: $exp\left(\hat{\beta} \pm z_{\frac{\alpha}{2}} * S.e(\hat{\beta})\right)$

We use the partial likelihood ratio test for comparing two models and to test the overall goodness of fit of the model.

The test statistic is given by:

$$G = \left[L_p(\hat{\beta}) - L_p(0)\right] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (10)$$

Where $L_p(\hat{\beta}) and L_p(0)$is log-likelihood of the model with and without covariates respectively

G has a Chi-square distribution with p degrees of freedom. If the value of G is greater than the Chi-square value with p degrees of freedom, then the null hypothesis will be rejected. The formulation of the null and alternative hypothesis depends upon the problem of the study. There are also other tests such as Wald and Score tests which we usually use to test the significance of individual parameters.

A $100(1-\alpha)$%CI for the parameter β is the interval with limits $\hat{\beta} \pm \mathrm{Z}\frac{\alpha}{2} \cdot \mathrm{SE}(\hat{\beta})$. If this interval does not included zero, this is evidence that the value of β is non zero. More specifically the hypothesis $H_0: \beta = 0$ can be tested by calculating the statistic $z = \frac{\hat{\beta}}{SE(\bar{\beta})}$ which a standard normal distribution. Equivalently $\chi^2 = Z^2 = \frac{\hat{\beta}2}{\mathrm{var}(\bar{\beta})}$ may be calculated and compared to a chi-square distribution with one degree of freedom. This procedure is called the Wald test.

3.10. Accelerated Failure Time Model

Accelerated failure time model is a parametric model that provides an alternative to the commonly used cox-proportional hazard model (PH). Under AFT models, we Measure direct effect of the explanatory variables on the survival time in instead of hazards, as we do in the PH model. This characteristic allows for easier interpretation of the results. For a group of patients with Covariate (X1,X2……Xp) the model is written mathematically as

$$si(t) = S0(t)\left[t/e^{\eta i}\right] \ldots\ldots\ldots\ldots\ldots\ldots (16)$$

Where s0(t) is the baseline survival function and η is an "acceleration factor" that is a ratio of survival times corresponding to any fixed value of S(t).the acceleration factor is given according to the formula.

$$\eta i = e^{\beta 1X1+\cdots.+\beta pXp} \ldots\ldots\ldots\ldots\ldots\ldots (17)$$

Under an AFT model, the covariate effects are assumed to be constant & multiplicative on the time scale, that is, the covariate impacts on survival time by a constant factor (acceleration factor) according to the relation-ship of survival function and hazard function, the hazard function for an individual with the covariate X1,X2,…..Xp is given by

$$h\left(\frac{t}{X}\right) = \left[\frac{1}{\eta(X)}\right] h0\left[\frac{t}{\eta(X)}\right] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (18)$$

The corresponding log linear form of the AFT model with respect to time is given by

$$\log Ti = \mu+\alpha_1 x_{1i}+\alpha_2 x_{2i}+,\ldots,+ \alpha_p x_{pi}+\delta\epsilon_i \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots..(19)$$

Where, μ is intercept, δ is scale parameter and ϵi is the error distribution assumed to have a particular parametric distribution. This form of model is adopted by most software package for AFT model.For each distribution of ϵi, there is a corresponding distribution for T. the most common AFT models are Exponential AFT, Weibull AFT, log logistic AFT, and log normal AFT models (Cox D,1984., lee,et al, 2003, collet, 2003)

Exponential distribution

A useful parametric model employs the exponential distribution. Recall that the exponential Distribution depends on one parameter,λ which in this case represents a constant hazard function. Then, λ(t) = λ>0, over the ranges of T where T is still a random variable representing recovery time, T>0, and t is typical point in the range. The memory less property of the exponential distribution now relates to the instantaneous failure rate being independent of t so that the conditional chance of failure in a time interval of specified length is the same regardless of how long the subject has been observed. A large λ indicates higher risk and decreased probability of survival and a small λ indicates lower risk and increased probability of survival.

Let Tbe the survival time which follows exponentialdistribution with parameter $\boldsymbol{\lambda}$ then the pdf of T.

$$f(t) = \begin{cases} \lambda \exp^{-\lambda t} & t \geq 0, \lambda \geq 0 \\ 0 & \text{Otherwise} \end{cases} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (20)$$

The Cumulative density function is $F(t) = 1 - \exp^{-\lambda t}\ t \geq 0 \ldots\ldots\ldots\ldots\ldots\ldots$ (21)
The survivor function and the hazard function respectively is given by

$$S(t) = \exp^{-\lambda t} \quad t \geq 0; \quad h(t) = \lambda \quad , t \geq 0, \ldots\ldots\ldots (22)$$

Weibull distribution

The assumption of a constant hazard function or equivalently an exponentially distributed survival time is rarely tenable. Amore general form is the Weibull distribution which does not assume a constant hazard rate. The Weibull model was introduced by WaloddiWeibull (1939) and is a popular generalization of the exponential model with two positive parameters ρ and λ. Then The Pdf of Weibull distribution is

$$f(t) = \rho\lambda t^{\rho-1} \exp^{-\lambda t^{\rho}}; \rho, \lambda > 0 \ldots\ldots\ldots\ldots\ldots\ldots (23)$$

The distribution function**,** survivor function and hazard function for Weibull Distribution are $F(t) = 1 - \exp^{-\lambda t^{\rho}}$; $S(t) = \exp^{-\lambda t^{\rho}}$ and $\rho\lambda t^{p-1}$ respectively with ρ(shape of the distribution curve parameter) $and\ \lambda$ (determines its scaling of distribution parameter).

The Log-logistic distribution

A random variable T has the log-logistic distribution with the following hazard, density and survivorship function

$$h(t,\lambda,\rho) = \frac{\lambda\rho t^{\rho-1}}{1+\lambda t^{p}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (24)$$

$$S(t,\lambda,\rho) = \frac{1}{(1+\lambda t^{\rho})}, f(t,\lambda,\rho) = \frac{\lambda\rho t^{\rho-1}}{(1+\lambda t^{p})^2} \ldots\ldots\ldots\ldots\ldots\ldots\ldots (25)$$

Where scale parameter $\lambda > 0$, shape parameter, $\rho > 0$.

Log normal distribution

The lognormal distribution is also defined for random variables that take positive values and so may be used as a model for survival data. Random variables, T, is said to have a lognormal distribution with parameters μ and σ, if LogT has a normal distribution with mean μ and variance σ.The probability density function of T is given by

$$f(t) = \frac{1}{\sigma\sqrt{2\pi}} t^{-1} \exp\left(\frac{(-\log t-\mu)^2}{2\sigma^2}\right) 0 \leq t < \infty, \sigma > 0 \ldots\ldots\ldots\ldots\ldots\ldots (26)$$

The survivor function of lognormal distribution is

$$S(t) = 1 - \Phi\left(\frac{\log t-\mu}{\sigma}\right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (27)$$

Where *Φ(.)*is the standard normal distribution function givenby

$$\Phi(z) = \frac{1}{\sqrt{2\pi}} \int_{-]\infty}^{z} \exp\left(\frac{-u^2}{2}\right) du$$

The hazard function is $h(t) = \frac{f(t)}{S(t)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$ (28)

Parameter estimation in AFT model

Accelerated failure time model (AFT) are fitted using the maximum likelihood method. The likelihood of the n observed survival times t1,t2,……tn is given by

$$L(\beta, \mu, \sigma) = \prod\prod_{i=1}^{n} [fi(ti)]^{\delta i}[si(ti)]^{1-\delta i} \ldots\ldots\ldots\ldots\ldots\ldots (29)$$

Where fi(ti) and Si(ti) are the density and survival function for the i[th] individuals at ti and δi is the event indicator for the i[th] observation. The log likelihood function will be

$$logL(\beta, \mu, \sigma) = \sum_{i=1}^{n} -\delta ilog(\sigma ti + \delta ilogf\epsilon i(zi) + (1 - \delta i)logS\epsilon i)(zi) \ldots\ldots\ldots\ldots (30)$$

Where $zi = (logti - \mu - \beta 1X1i - \cdots - \beta pXpi)/\sigma$

The maximum likelihood estimates of the P+2 unknown parameters $\mu, \sigma, \beta 1, \beta 2, \ldots, \beta p$ are found by maximizing this function using the Newton –Raphaon procedure, which is the same

method used to maximize the partial log likelihood in the cox regression model (cox,1984, Lee et al.,2003 ,collet,2003).

3.11.Method of Variable and Model Selection

3.11.1. Method of Variable Selection

Variable selection is the ways of deciding which covariate to include in the model and it can be done in different ways. According to (HosmerJr and Lemeshow, 1999), similar to classical regression procedure it is recommended to follow the steps. first univariate was performed to screen out potentially significant variables and identified candidate covariate at 25% significance level (Hosmer and Lemeshowrecommendation).on the second step full model was fitted with all significant univariate predictors and using backward selection non-significant variables were eliminated at 10% level of significant, then a model was fitted with non-significant variable at first step(univariate analysis) and significant variable in second step using forward selection with 10% level of significance. Finally the potential variables were identified from all significant variables by stepwise selection.

3.11.2. Method of Model Selection

Model selection and comparison are the most common difficulties of statistical practice, with numerous procedures for selecting among a set of candidate models (Kadane and Lazar, 2004).There are several methods of model selection. Like AIC, BIC and LRT,However in some circumstances, it might be useful to easily obtain AIC value for a series of candidate models (Munda et al., 2012). LRT is best model selection technique, when models are nested. Model with the smallest AIC and BIC is considered a better fit. AIC and BIC can be obtained by

$$AIC= -2LogL+2(k+c+1) \qquad (31)$$

$$BIC=-2LogL+P\ln (n) \qquad (32)$$

Where k is the number of covariates, p is number of parameter, n is sample size, Log L is denoted the fitted log-likelihood and c the number of model specific distributional parameters.

3.12. Model Assessment

3.12.1. Proportional Hazard Assumption Checking

The main assumption of the Cox PH model is proportional hazards. Proportional hazard means that the hazard function of the individuals is proportional to the hazard function of the other individuals; i.e the hazard ratio is constant over time. There are several methods for varying that a model satisfies the assumptions of proportionality.

Graphicalmethod

We can obtain Cox PH survival function by the relation-ship between hazard function and survival function.

$$s(t,X) = s0(t)^{e^{\sum_{i=1}^{p} \beta ixi}} \dots\dots\dots\dots\dots\dots\dots\dots\dots (33)$$

Where x1,x2…….xp are Explanatory variables. When taking the logarithm twice we can easily gate

$$\ln\big(-lns(t,x)\big) = \sum_{i=1}^{p} \beta ixi + ln - lns0(t) \dots\dots\dots\dots\dots (34)$$

By plotting estimated $\ln\big(-lns(t,x)\big)$ versus survival time for two groups we will the parallel curves if the hazards are proportional. This method dose not woke well for continuous predictors or categorical predictors that have many levels. Looking at KM curves and $\ln\big(-lns(t,x)\big)$ is not enough to be certain of proportionality since they are univariable analysis and do not shows whether hazards will still be proportional. When a model includes many other predictors, in this case the following two methods are recommended.

Tests based on schoanfeld residuals

The method of checking the assumption of the Cox proportional hazards model is scatter plots using the Schoenfeld residual (Schoenfeld, 1982). The residuals constructed for each covariate that are included in the model which are expected to predict the recovery time of children's with sever pneumonia. This overcomes the problem that other residuals depend heavily on observed survival time and cumulative hazard function. They are computed for each individual and covariate. It follows that, the Schoenfeld residual for the i^{th} individual and k^{th} covariate is defined as:

$$\hat{S}_{ik} = \delta_i \left[X_{ik} - \frac{\sum_{j \in R(t_i)} X_{ik} \exp^{(\hat{\beta}' x_j)}}{\sum_{j \in R(t_i)} \exp^{(\beta' x_j)}} \right] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (35)$$

Where, X_j is a vector of p fixed covariates for the j^{th} individual, X_{jk} is the value of k^{th} covariate on the j^{th} individual. Because of that, Schoenfeld residuals are defined only for the uncensored observations in which -

$\hat{S}_{ik} = X_{ik} - \frac{\sum j \in R(t_i) X_{ik} \exp^{(\beta' x_j)}}{\sum j \in R(t_i) \exp^{(\beta' x_j)}}$Andfor each covariate it must sum to zero. In addition, they are uncorrelated and with expected value zero (Schoenfeld, 1982).

Under the proportional hazard assumption for the respective covariate, a scatter plot of Schoenfeld residuals against event times is expected to scatter in a nonsystematic way about the zero line, and the polygon (Lowes's curve) connecting the values of the smoothed residuals should have a zero slope and cross the zero line several times (Klein &Moeschberger., 2003). If this plot shows some trend the assumption is violated, where as if the plot demonstrates randomly distributed around the reference line then the assumption is satisfied.

Adding time dependent covariates in the cox model

If we include time dependent covariate to the model & the coefficient for the time dependent variables is significantly different from zero, then the predictor is not [proportional. In the same way can also asses the PH assumption for several predictors simultaneously.

3.12.2.Checking the Adequacy of Parametric Baselines

Graphical approaches (for all distributions listed), as well as Cox-Snell residual plots, are some of the other ways.(Gray and Pierce, 1985). Parametric models are fit to the event times and semi parametric models are fit to the ordered event times respectively. In both the cases we use the AIC to select between parametric models, or to select between semi-parametric models, but not to select from a mixture of the two. The AIC or likelihood tests allow us to assess relative model goodness of fit, but not absolute model goodness of fit. Just because the second model fits better than the first model, it does not mean the second model adequately describes the data. Thus, wewould like a method, at least a graphical one that lets us assess the absolute goodness of fit of a parametric model. The Table 3.2 below provides

informationregarding graphical check for goodness of fit for the identified parametric model for survival data (Aaserud et al., 2013; Limpert et al., 2001)

Table 3.2: Graphical checking for goodness of fit for parametric survival models.

Graph	Behavior	Resulting Distribution
$-logS(t)$ versus t	Straight line through origin	Exponential
log $[-logS(t)]$ versus log$t$	Straight line	Weibull
$\Phi^{-1}(1-S(t))$ versus log$t$	Straight line, where $\Phi(\ )$ is the CDF	Log-normal
log $[\frac{1-S(t)}{S(t)}]$ versus log$t$	Straight line	Log-logistic

3.12.3. Using Residual Plots

There are different types of residuals such as, Cox–Snell residuals, martingale residuals, deviance residuals, e.t.c.

Although the use of residuals vary and depend on the data and user preferences, the suggested uses are the following: Cox–Snell residuals are useful in assessing overall model fit. Martingale residuals are useful in determining the functional form of covariatesto be included in the model and are occasionally useful in identifying outliers. Deviance residuals are useful in examining model accuracy and identifying outliers The residual that is widely used in the analysis of survival data is the Cox-Snell residual, it is a particular example of the general definition of residuals given by (Cox and Snell, 1968). Martingale residuals $\left(r\widehat{M}_i\right)$ are also called modified Cox-Snell residuals and, expressed as

$$r\widehat{M}_i = \delta_i - \widehat{H}_i(t) = \delta_i - rc_i \quad \text{..... (36)}$$

Where $\delta_i = 1$ for uncensored observations and zero otherwise, and r ciare Cox-Snell residuals. These residuals have similar properties to the error components in other models, in addition to the properties that its mean is equal to zero under the correct model. In large samples, the martingale residuals are uncorrelated with one another and have an expected value of zero. However, the martingale residuals are not symmetrically distributed about zero. Plot of these residuals versus explanatory variables is used to indicate whether any particular variable needs to be transformed before incorporating it in the model. In other way round, martingale residuals are useful in determining the functional form of covariate to be included in the model. If after plotting the residuals versus explanatory variables, the plot

does not show an obvious relationship, then the variable is not important in the model to be included. Therefore, if most of the points fall horizontally about zero, in the plots of the martingale residuals versus the values of the independent variables, then the fitted model is taken as satisfactory. The deviance residuals, which were introduced by (Therneau et al., 1990), aremuch more symmetrically distributed about zero. The deviance residuals are martingale residuals that have been transformed to producevalues that are symmetric about zero when the fitted model is appropriate. The deviance is a statistic that is used to summarize the extent to which the fit of a model of currentinterest deviates from the saturated model.

3.13.Ethical Consideration

The Research Ethics Review Board of Debre Brehan University has provided an ethical clearance for the study. The data was brought from Debre Markos Comprehensive Specialized Hospital, and to do so the department of statistics asked to write an official co-operation letter to the Hospital from where data was obtained. The study conducted without individual informed consent because it relied on retrospective data. In this research, the information obtained from log book and patients' card kept secured.

4. STATISTICAL DATA ANALYSIS AND RESULTS

In this section, the researcher presented the results of data analysis, discussion, and interpretation. The first part presents the summary statistics of covariate considered in this study. The second part estimates the survival time and also comparing the survival curve in different groups of variables. The third part was about fitting the model. Finally, the results wereinterpreted and discussed.

4.1. Descriptive Statistics

Descriptive statistics is the beginning of any statistical analysis before proceeding to more complicated models. Of 341 patient medical records, 48 were excluded because of incompleteness, and the remaining 293 were included in the final analysis. Thereforethis study was included a total of 293 under-five pneumonia patients fulfilling the inclusion criteria in Debre Markos Comprehensive Specialized Hospital. Summary results for covariates included in this study are presented in Table 4.1.

As shown in Table 4.1, the total of 293 patients of pneumonia included in the study, 122 (41.64%) of the patients were female and 171(58.36%) were male. Among those patients by considering sex, the recovery proportion for female is 39.61% which is lower than that of male patients which is 60.39%. Seeing age groups included in the study total sample of patients 45.05%, 25.6% and 29.35 of patients were from age group 1-11, 12-23 and 24-59 respectively and the recovery proportion for the age group were 45.89%, 24.15% and 29.95 respectively. Of the total patients 60.07% were from rural area and 39.93% from the urban. Recovery proportions of patients with residences were 39.61% and 60.39% respectively. Out of the total patients, 13.99% were in Autumn, 12.67% were in Winter, 50.51% were in Spring and 22.87% patients were in Summer. The recovery proportions of patients in Autumn, Winter, Spring and Summer patients were 13.04%, 12.08%, 50.72% and 24.15% respectively.

As shown in Table 4.1 of total patients 40.96% patients were no Presence of concomitant disease or Co-morbidity and 59.04% were Presence of concomitant disease or with Co-morbidity. Recovery proportions among not Presence of concomitant disease or co-morbidity and with comorbidity were 44.93 % and 55.07 % respectively. Similarly in Sever Acute Malnutrition (SAM) case, out of the total patients there were 68.94% patients without Sever

Acute Malnutrition and 31.06% were with Sever Acute Malnutrition. Recovery proportions among without Sever Acute Malnutrition and with Sever Acute Malnutrition were 72.46% and 27.54% respectively. Among under-five aged children included in the study, 30.03% patients took treatment type crystalline Penicillin, 24.57% patients took treatment type Ceftriaxone, 13.31% patients took treatment type Ampicillin and 32.08% patients took the Combination of two and above treatments types. The recovery proportions of patients who took crystalline Penicillin, Ceftriaxone, Ampicillin and Combination of two or above were 23.19%, 29.95%, 15.94%, and 30.92% respectively.

Among the total patients included in the study 66.21% patients was no micronutrient deficiencies and 33.79% patients were with micronutrient deficiencies. The recovery proportion among patients who were no micronutrient deficiencies and patients with micronutrient deficiencies were 64.25% and 35.75% respectively. Based on insurance status of under- five aged patients 67.24 % were not member of social health insurance and 32.76% were member of social health insurance. The recovery proportion of patients who were not member of social health insurance and member of social insurance were 63.29% and 36.7% respectively. The mean of Time elapsed to seek care (Duration) included in the study was 4.43 days with standard deviation of 0.145.

Table 4.1: Descriptive summary of pneumonia patients at DMCSH

Variable	Category (codes)	Event (status)		
		Recovered (%)	Censored (%)	Total
Sex	Male (0)	125 (60.39)	46 (53.49)	171 (58.36)
	Female(1)	82 (39.61)	40 (46.51)	122 (41.64)
Age	1-11 (0)	95 (45.89)	37 (43.02)	132 (45.05)
	12-23 (1)	50 (24.15)	25 (29.07)	75 (25.6)
	24-59 (2)	62(29.95)	24 (27.91)	86 (29.35)
Residence	Rural (0)	125 (39.61)	51 (59.3)	176 (60.07)
	Urban (1)	82 (60.39)	35 (40.7)	117(39.93)
Danger sign	Yes (1)	144 (69.57)	66 (76.74)	210 (71.67)
	No (0)	63 (30.43)	20 (23.26)	83 (28.33)
History of ARTI	No (0)	121 (58.45)	38 (44.19)	159 (54.27)

	Yes (1)	86 (41.55)	48 (55.81)	134 (45.73)
Season	Autumn (0)	27 (13.04)	14 (16.28)	41 (13.99)
	Winter (1)	25 (12.08)	12 (13.95)	37 (12.67)
	Spring (2)	105 (50.72)	43 (50)	148 (50.51)
	Summer (3)	50 (24.15)	17 (19.77)	67 (22.87)
P type	SCAP (0)	147 (71.01)	50 (58.14)	197 (67.24)
	Nosocomial (1)	60 (28.99)	36 (41.86)	96 (32.76)
Comorbidity	No (0)	93 (44.93)	27 (31.4)	120 (40.96)
	Yes (1)	114 (55.07)	59 (68.6)	173 (59.04)
Treatment type	Crystalline penicillin (0)	48 (23.19)	40 (46.51)	88 (30.03)
	Ceftriaxone (1)	62 (29.95)	10 (11.63)	72 (24.57)
	Ampicillin (2)	33 (15.94)	6 (6.98)	39 (13.31)
	Combined (4)	64 (30.92)	30 (34.88)	94 (32.08)
SAM	No (0)	150 (72.46)	52 (60.47)	202 (68.94)
	Yes (1)	57 (27.54)	34 (39.53)	91 (31.06)
Insurance status	Not insured (0)	131 (63.29)	66 (76.74)	197 (67.24)
	Insured (1)	76 (36.71)	20 (23.26)	96 (32.76)
Mdeficiency	No (0)	133 (64.25)	61 (70.93)	194 (66.21)
	Yes (1)	74 (35.75)	25 (29.07)	99 (33.79)
Continuous variable		Mean	Standard deviation	
	Duration	4.426	0.145	

After the medical cards of pediatric were reviewed among those patients of under-five pneumonia 86(29.35%) censored and 207(70.65%) were recovered see figure 4.1.

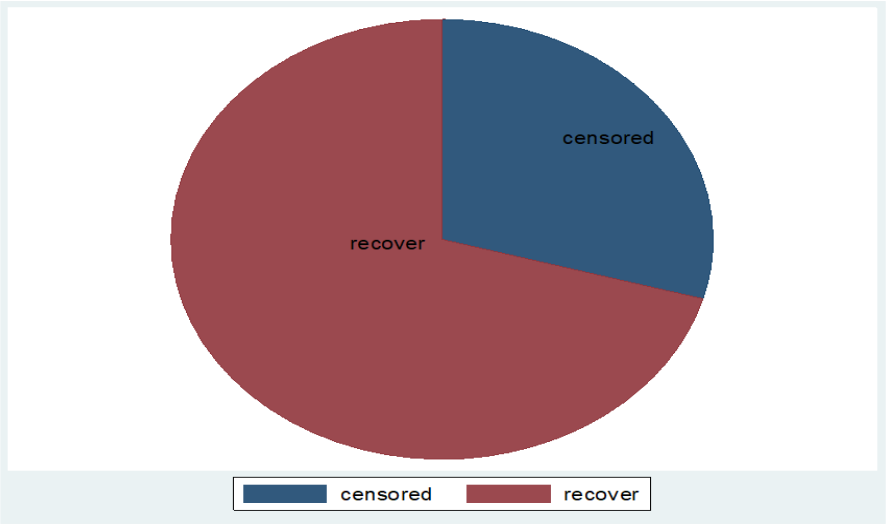


Figure 4.1: discharge status of sever pneumonia patient's data set at DMCSH

4.2. Non parametric survival analysis

4.2.1. Survival Characteristics of Time to Recovery of Pneumonia Data Set

A patients‟ recover from pneumonia disease before the end of the study was called events while children'sdeath due to pneumonia, lost follow up and drop out the study was censored. A plot of the KM curves to the survival experience of time-to-recovery is shown in figure 4.2. The estimated value of the survivor function patients decreases at decreasing rate from the time origin until 10 days, and zero after 23 days and The estimated hazard function illustrated in Figure 4.2 shows that an increase in the hazard rate has direct relation with the increase in time.

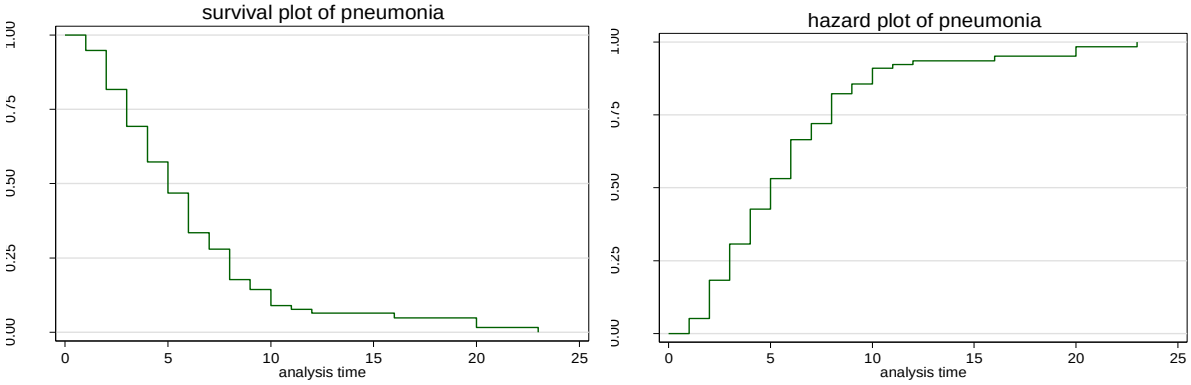


Figure 4.2:The K-M plot of survival and hazard function of pneumonia patient's data set

4.2.2. Survival Time-To-Recovery for Different Groups of Predictors

Descriptive graphs of the survivor function were used for the purpose of comparing the event experiencing times of two or more groups and the survival quantities of predictors to describe the survival experience of an individual at specific times. Separate Kaplan-Meier survivor functions were constructed for different predictors to see for possible existence of differences in survival experience between the indicated categories. In general, the pattern of one survivorship function lying above another means the group defined by the upper curve had a better survival than the group defined by the lower curve. In this case the event is recovery time, group defined by the lower curve attend normal condition of pneumonia faster (have a better recovery time/survival experience).

As shown in figure 4.3 the survival Experience of both sever community acquired and hospital acquired pneumonia patients were similar until 7 days, after this points the survival experience of Sever community acquired pneumonia patients decline with higher rate than hospital acquired Pneumonia patients.As shown in figure 4.3until 12 days under-five pneumonia patients who had not a clinical presentation during admission like impaired consciousness, abnormal body movement, vomiting everything or danger sign has better survival Experience than had danger sign.i.ePatients who had a danger sign had a higher probability of extending their recovery time at a given time than patients who did not have a danger sign.After 12 days both patients with and without danger sign have similar survival Experience and the survival Experience of patients with danger sign became zero after 20 days.

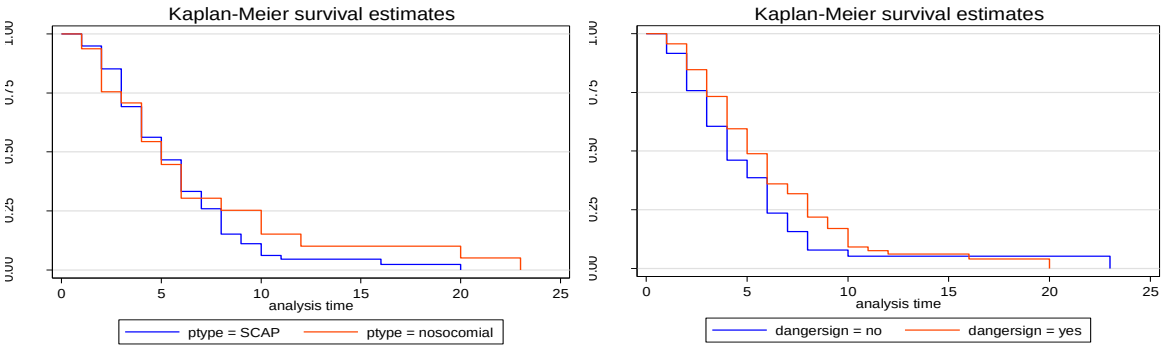


Figure 4.3:K-M survival plot by pneumonia typeand danger signof pneumonia patients

As shown in figure 4.4 similarly, until 9 days under-five pneumonia patients who were insured had better survival Experience than patients who were not insured. And for treatment types, that treatment type taken at the time of diagnosis was ceftriaxone attained good control of pneumonia faster than other treatment type. Patients who take ceftriaxone had a lowerprobability of extending their recovery time at a given time than patients who take other treatment type.and patients who take crystillinpencilline had higher probability of extending their recovery time at a given time than patients who take other treatment type.

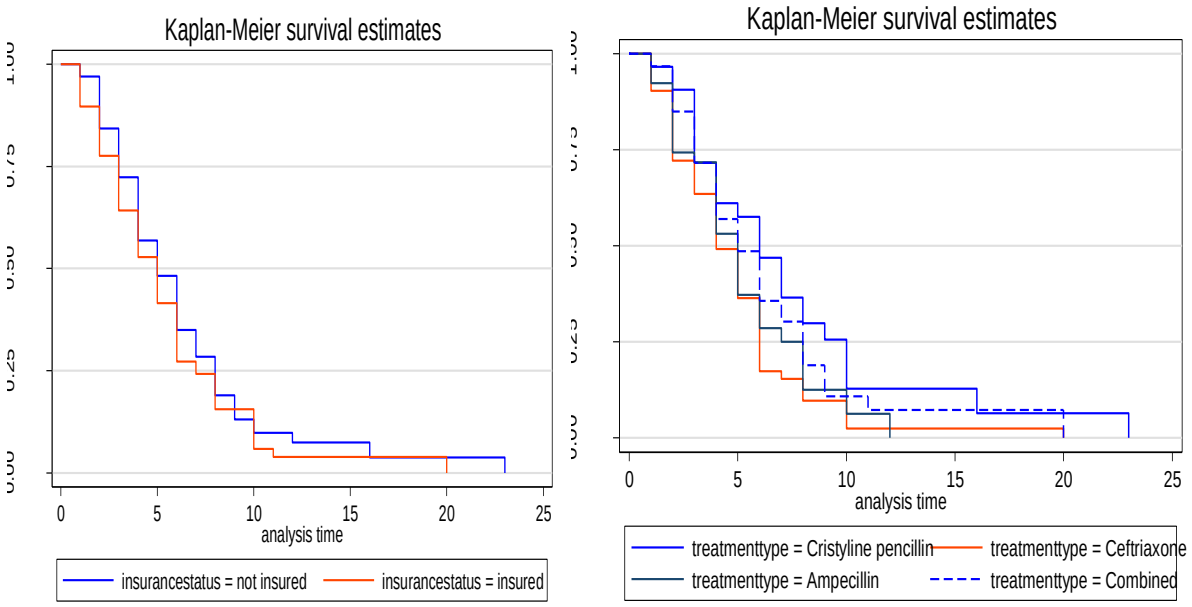


Figure 4. 4:K-M survival plot by insurance status and treatment type of pneumonia patient.

Figure A1 in Appendix shows that, until 12 days from their admission patients who no comorbidity hadbetter survival experience than patients who had comorbidity and the survival time of patients who had no comorbidity became after 20 days. As shown in figure A2 in appendix shows patients without past history of ARTI had better survival experience than patients with past history of ARTI from 3 days until 16 days, from the start of follow up to 3 days and 16-20 days, it had similar survival experience and became 0 after 20 days. The log rank test also revealed that past history of ARTI had significant difference in survival time of pneumonia patients (p=0.0175) at 5% level of significance

4.2.3.Comparison of Survival time (Long Rank Test)

The log-rank test was used to compare the survival functions of two or more groups of under-five pneumonia patients. Log-Rank test was used to compare survival time between

categories of different predictors. Based on this test, survival time among different groups of predictors such as treatment type, danger sign and past history of ARTI were significantly different in survival time at 5% level of significant as presented table 4.2.

From table 4.2, an estimated median time to recovery from sever pneumonia for all observations were 5 days with 95 % CI (4, 6). Median recovery time of children from sever pneumonia varied among various categories of socio-demographic and clinical predictors. For example, the median recovery time of patients who came from rural area was 5 days and patients came from urban area was 4 days. The median recovery times of pneumonia patients with past history of ARTI and without past history of ARTIwere 6 and 5 daysrespectively.As shown in table 4.2 the median recovery time of patients who take treatment type at the time of diagnosis, crystalline penicillin, ceftriaxone, and ampicillin and combined were 6,4,5 and 5 days respectively and median recovery time who had past history of ARTI and had not past history of ARTI were 6 and 5 days respectively.

Table 4.2:Median time to recovery and long-rank test by predictors

Variable	Category	Median recovery time (95%CI)	Long rank X^2 value (df)	p-value
Age	1-11	5 (4-6)	0.99(2)	0.611
	12-23	5 (4-6)		
	24-59	5 (4-6)		
Residence	Rural	5 (4-6)	0.16(1)	0.68
	Urban	4 (4-6)		
danger sign	No	4 (3-5)	6.23(1)	0.0223*
	Yes	5 (4-6)		
historyARTI	No	5 (4-5)	5.4(1)	0.0175*
	Yes	6 (5-6)		
Pneumonia type	SCAP	5 (4-6)	0.34 (1)	0.560
	Nosocomial	5 (4-6)		
SAM	No	5 (4-6)	0.76 (1)	0.3844
	Yes	6 (5-6)		
Insurance status	Not insured	5 (4-6)	1.64 (1)	0.2001
	Insured	5 (4-6)		

Treatment type	Crestline penicillin	6 (4-7)	10.84 (3)	0.0126*
	Ceftriaxone	4 (4-5)		
	Ampicillin	5 (4-6)		
	Combined	5 (4-6)		
Comorbidity	No	5 (4-6)	0.74(1)	0.39
	Yes	5 (5-6)		
Mdeficiency	No	5 (4-6)	0.00(1)	0.9976
	Yes	5(4-6)		
Total observation	293	5 (4-6)		

*indicate that the comparison difference was significance at 5% significance level and df is degree of freedom.

4.3.Cox Proportional Hazard Regression Model

4.3.1. Uni-variable Analysis of Cox proportional Hazards Model

After making a comparison of the survivorship experience among groups of covariates, the next important step is model building.An initial step in the model building process is uni-variable analysis. It was performed in order to see the effect of each covariate on recovery time of pneumonia patients and to select variables to be included in the multivariable analysis. In this research the variable selection was done using the method stated under section 3.11.The relationship between each covariates and survival time of under-five pneumonia patients are presented in table A1in appendix. As shown from this table, survival of the patients is significantly related with comorbidity, past history of ARTI,time elapsed to seek care, clinical presentation during admission and insurance status at 25 % level of significance.

4.3.2. Multi-variable Analysis of Cox proportional Hazards Model

Using Hosmer and Lemesshow recommendation potential covariates were selected as stated in table A1 appendix. As shown in table 4.3, all selected predictors were fitted in the proportional hazard model and candidate predictors at 10% level of significant were choose using the backward selection method. Variables duration, past history of ARTI, insurance

status and clinical presentation during admission were selected as candidate potential variables.

Table 4. 3:candidate covariates using backward selection method

Variable	P value	AIC	BIC
Duration	0.000	1741.3	1756.1
Insurance status	0.000		
Danger sign	0.002		
History ARTI	0.004		

All selected variable at 10% level of significant in second step and the non-significant variable in the univariate analysis at 25% level of significant were modeled together using forward selection method the following predictors were selected at 10% level of significant.

Table 4.4: candidate covariates using forward selection method

Variable	P value	AC	BIC
Duration	0.000	1730.4	1748.8
Pneumonia type	0.003		
Treatment type	0.005		
Danger sign	0.021		
Insurance status	0.000		

Finally all significant predictors were modeled together using step wise selection method. The following potentialpredictors presented in table 4.5 were chosen.

Table 4.5: Final multi-variable Cox Proportional Hazard Modal

Variable	Category	$\hat{\beta}$	SE	Sig	HR	95% CI HR	
Danger sign	No (ref)						
	Yes	0.354	0.175	0.043*	1.425	(1.01	2.01)
Insurance status	Not insured(ref)						
	Insured	0.667	0.157	0.000*	1.948	(1.43	2.65)

Pneumonia type	SCAP(ref)					
	Nosocomial	-0.653	0.173	0.000*	2.475	(0.370 .73)
Treatment type	Crystalline penicillin (ref)					
	Ceftriaxone	0.906	0.208	0.000*	2.475	(1.64 3.72)
	Ampicillin	0.966	0.250	0.000*	2.627	(1.61 4.29)
	Combined	0.657	0.209	0.002*	1.930	(1.28 2.91)
Duration		-0.943	0.071	0.000*	0.520	(0.340.45)
AIC= 1717.4BIC=1743.2						

SE=Standard error,HR= Hazard Ratio, CI=Confidence Interval, ref. Reference and * statistical significant at 5% significance level.

Time of elapsed to seek care (duration), insurance status, types of pneumonia, danger sign , and Treatment type taken at the time of diagnosis were statistically significant at 5% significance level and those predictors were selected as the final model. It is best model compared to the above two models in table 4.3and 4.4since it has the smallest value of AIC.

4.4. Examined Assumptions of Proportional Hazard Model

The adequacy of the model needs to be assessed after the model has been built to the observed survival data. Then proceed to check the proportionality assumption for each covariate included in the final model. The proportionality assumption was examined using global test (Goodness of fit testing approach) by using graphical, Schoenfeld residuals for different predictors, and time varying covariate added in to Cox-PH model.

Using Graphical Method

using graphical method as shown in figure 4.5 the plots of group of predictor's (pneumonia type) were not parallel this is also an indication of violation of PH assumption

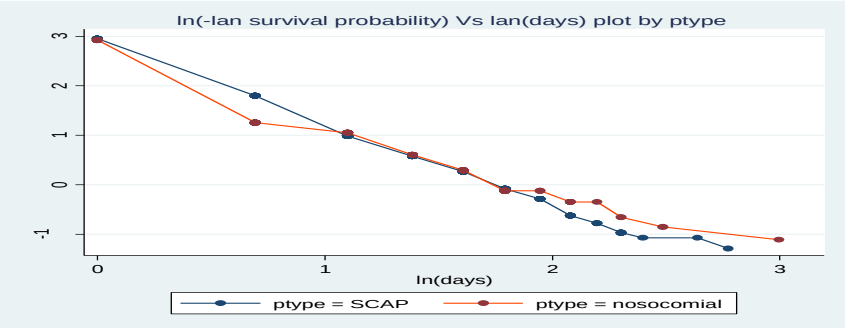


Figure 4.5:graphical method for PH assumption by pneumonia type

Using Schoenfeld Residuals

Goodness of fit testing approach is interesting because it provides a test statistic and p-value for assessing the PH assumption for a given predictor of interest. rho is a relation between survival time and schoenfeldresiduals. The test of correlation (rho) is insignificant that indicates proportional hazards assumption is fulfilled. The P-values given in the Table 4.6 provide goodness-of-fit tests for each variable in the fitted model adjusted for the other variables in the model are quite high for variables insurance status and treatment type, suggesting that these variables satisfy the PH assumption. But variable duration, pneumonia type and clinical presentation during admission were not satisfies the PH assumption. Moreover it is alsopossible to see its global test and if it's p-value is greater than 0.05 the assumption has satisfied by the covariates in the model. In this study the p-value for global test is less than 0.05 the assumptions do not satisfied by the covariate in the model.

Table 4.6: Test of proportional hazards assumption for pneumonia patient dataset

Covariates	Rho	chi-squared	DF	P-value
Duration	0.602	104.34	1	0.000*
Pneumonia type	-0.138	4.98	1	0.0256*
Insurance status	0.092	1.71	1	0.1903
Treatment type	0.045	0.43	1	0.5136
Danger sign	0.143	4.88	1	0.0272*
Global test		164.04	5	0.000*

DF=degree of freedom, * significant at 5% significance level.

The scatter plots of Scaled Schoenfeld residuals in figerA3 in Appendix also used to check PH assumption. If the PH assumption is met, Schoenfeld residuals should look horizontal

since the scaled Schoenfeld residuals would be independent of survival time. The plots of scaled Schoenfeld residuals against survival time for predictor duration and pneumonia type were also slightly upward and downward (not horizontal). These also revealed that there is a violation of the proportional hazard assumption for the predictor duration and pneumonia type. Thus, we doubt the accuracy of the PH assumption and consider the AFT model for this data set

By Adding Time Varying Covariate in Cox-PH Model

Another way to test the proportional hazard assumption is to create time-varying covariates by generating interactions between predictors and a function of survival time. The output in appendix Table A2 indicates that the p-value of the predictors,duration and danger sign was less than 0.05, indicating that the proportional hazard assumption was not satisfied and duration and danger sign were time dependent predictors.

4.5. Accelerated Failure Time (AFT) Model

When PH assumptions were not satisfied, the parametric AFT model should be used instead of the Cox model (Klein J., 2005). Since the p-value of the goodness of predictorswas significant for the variable duration, pneumonia type and danger sign. In this case AFT model is appropriate for the data as discussed in section 3.10. So, the study fitted the data using accelerated failure time model withExponetial,Weibull, Lognormal and Log-logistic as a baseline distribution.

4.5.1.Multivariable Analysis and Model Comparison

As discussed in section 3.10, εi is a random variable assumed to have a particular distribution.Multivariable analysis of exponential, Weibull, log-normal and log-logistic parametric models were done by using all significant predictors in the final multivariable cox PH model at 5% level of significance.In all used models of multivariable analysis pneumonia type, danger sign, duration, insurance status and treatment type were used and model comparison was done using those predictors.

From table 4.7, we see the value of AIC or BIC of the four parametric models, AIC or BIC was used to compare the model. The AIC and BIC value of Log-logistic AFT model were 155.58 and 188.70 respectively and they are smallest. This indicates that the log-logistic

model is the bestmodel to describe the pneumonia patient's dataset among the candidates parametric model.

Table 4.7:AIC, BIC and log likelihood of the candidate parametric models

Distribution	AIC	BIC	Log-likelihood
Exponential	578.10	607.54	-281.049
Weibull	231.58	264.70	-106.79
Log-normal	204.42	237.54	-93.21
Log-logistic	155.58	188.70	-68.79

4.6.Model Diagnosis

after the model has been compared,it is desirable to determine whether the selectedparametric model adequately describes the data or not.

4.6.1.Checking Adequacy of ParametricBaselines Using Graphical Methods

To check the adequacy of our baseline hazard the exponential is plotted by the -log(S (t) with the time of the study; the Weibull is plotted by log (-log(S(t)) with the logarithm of time of the study; the log-logistic is plotted by log $\frac{1-s(t)}{s(t)}$ with the logarithm of time of the study and the log-normal baseline by $\Phi^{-1}(1-s(t))$ against log (t) of time of the study. If the plot is linear, the given baseline distribution is appropriate for the given dataset. Accordingly, the plots in figure 4.6 the plot for the log-logistic baseline distribution makes straight line better than exponential, Weibull and Log-normal baseline distribution. This evidence also strengthens the decision made by AIC value that log- logistic baseline distribution is appropriate for the given dataset.

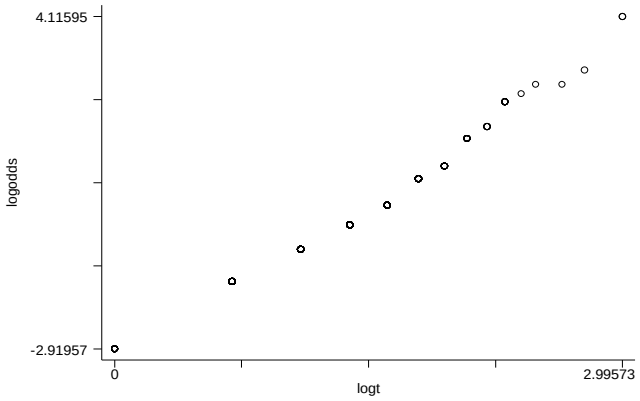


Figure 4.6: Log-logistic baseline distributions plot of pneumonia patient

The likelihood ratio test in Table 4.8 shows that the model is significant and the log likelihood values of the null model and the full model indicates that the model had a significant improvement after the covariates were added in the model.

Table 4.8:the likelihood ratio and significance of the Log- logistic AFT model

Loglik(intercept only)	Loglik(model)	Chisq	DF	Sig
-273.12	-68.79	408.66	7	0.000

4.6.2. Cox-Snell Residual Plot

The Cox-Snell residuals are one way to investigate how well the model fits the data. The plot for fitted model of residuals for log-logistic to our data via maximum likelihood estimation with cumulative hazard functions is given in figure 4.7, If the model fits the data, the plot of cumulative hazard function of residuals (H) against Cox-Snell residuals should be approximately a straight line on the line with the unit slope. It suggested that log-logistic AFT model is appropriate for survival time of under-five pneumonia patient data set as seencox-snell plots of AFT models in figure A4 in Appendix.

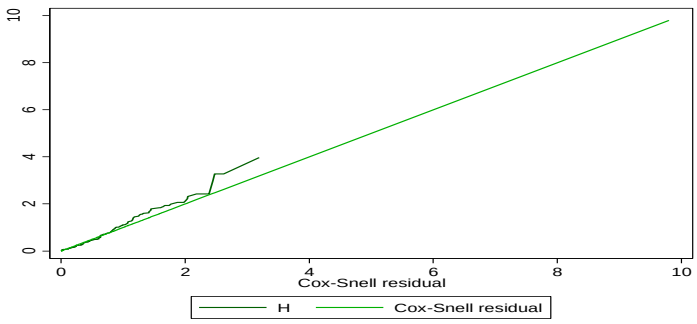


Figure 4.7: Cox- Snell residuals plots of log-logistic baseline distribution

Let's now look at the martingale-like and deviance residuals. We use the term "martingale-like" because, although these residuals do not arise naturally from martingale theory for parametric survival models as they do for the Cox proportional hazards model, they do share similar form. Martingale residuals take values between $-\infty$ and 1 and therefore are difficult to interpret. For this reason, deviance residuals are preferred for examining model accuracy and identifying outliers. The deviance residuals are a rescaling of the martingale-like residuals so that they are symmetric about zero and thus more like residuals obtained from linear regression. Plots of either deviance residuals against the linear predictor (that is, the log relative hazard in PH models) or of deviance residuals against individual predictors can be useful in identifying aberrant observations and in assessing model fit. Continuing with our under-five pneumoniapatient data, we plot the deviance and martingale-like residuals obtained after fitting a log-logistic model: As shown figure A5 in appendix, it shows that the log-logistic AFT model devianceresidualstoberelativelywellbehaved, withafewminorearlyexceptions.

4.7. Results From AFT Model

Model diagnostics were presented in section 4.6 suggested that the Log-logistic AFT model was good fit the under-five pneumonia patient dataset. An acceleration factor greater than one (positive coefficient) indicates extending the recovery time while an acceleration factor less than one (negative coefficient) indicates shortenedrecovery time.Time elapsed to seek care, insurance status and treatment type were significant at 5% significance level.The output of the final log-logistic AFT model is presented in Table 4.9. This output showedchildren's with sever pneumoniapatients with Treatment type taken at the time of diagnosis:ceftriaxone Ampicillin and combined and children who were insured were significantly shortenedsurvival time of children's with sever pneumonia while patients with Time elapsed to seek careprolong the survival time of pneumonia patients in Debre Markos Comprehensive Specialized Hospital.From table 4.9, the estimated acceleration factor for patients with treatment type ceftriaxone is 0.883 with (95% CI: 0.810, 0.962).The confidence interval for the acceleration factor did not include one and P-value is small (p=0.004). This indicates patients who take treatment type ceftriaxone at the time of diagnosis have less survival time than patients with treatment type crystalline penicillin. Similarly acceleration factor for patients with treatment type Ampicillin are estimated to be 0.842 with [95% CI: 0.759, 0.933] the γ CI did not include one and P-value is small (p = 0.001). This implied that children

whotake treatment type Ampicillinshortened the recovery time by a factor of 0.842compared to crystalline penicillin.Likewise acceleration factor for patients who take treatment type combined is estimated to be 0.912 with [95% CI: 0.842, 0.986] the γ CI did not include one and P-value is small (p=0.022). As shown in Table 4.9 the estimated acceleration factor for patients who were insured estimated to be 0.904 with [95% CI (0.845, 0.967)] the confidence interval for the acceleration factor did not include one and P-value is very small. This indicates patients who were member of social health insurance (insured) shortenedthe survival time by factor of 0.904 than patients who were not insured. Similarly the acceleration factor for time elapsed to seek care is 1.256, the p value is small it indicates that duration is significant factor for the recovery time of pneumonia patients.it shows that for a one day increase in time elapsed to seek care (duration) the recovery time of patients from pneumonia were prolonged by 1.256 times in days.

Table 4.9: Summary result of the final Log-logistic AFT model ofpneumonia patients

Variable	Category	$\hat{\beta}$	SE	Sig	γ	95% CI (γ)
Danger sign	No (ref)					
	Yes	0.005	0.035	0.988	1.001	(0.933 1.072)
Insurance status	Not insured(ref)					
	Insured	-0.101	0.034	0.003*	0.904	(0.8450.967)
Pneumonia type	SCAP(ref)					
	Nosocomial	0.068	0.036	0.056	1.071	(0.998 1.149)
Treatment type	Crystalline penicillin(ref)					
	Ceftriaxone	-0.125	0.044	0.004*	0.883	(0.8100.962)
	Ampicillin	-0.172	0.052	0.001*	0.842	(0.7590.933)
	Combined	-0.092	0.0402	0.022*	0.912	(0.8420.986)
Duration		0.228	0.0075	0.000*	1.256	(1.237 1.274)
Constant		0.534	0.0502	0.000	1.705	(1.545 1.881)
AIC=155.6BIC=188.7gamma =1/p =0.142						

P=Shape parameter,γ Indicates Acceleration factor; 95%CI(γ): 95% confidence interval for acceleration factor, S.E standard error for the coefficient and * indicatessignificant at 5% significance leve.

5.DISCUSSION,CONCLUSIONS AND RECOMMENDATION

5.1. Discussion

Pneumonia in under- five children is a leading cause of morbidity and mortality in Ethiopia and other developing countries. Time to recovery and its determinant factors of under-five pneumonia are important for planning child health care services, for proper management and prevention strategy of under-five pneumonia.The objective of this study was to identify the determinant factors of time to recovery of under-five pneumonia patients in Debre Markos comprehensive specialized hospital. For determining the associated factors of time-to recovery of under-five pneumonia patients; a total of 293 patients were included in the study out of those patients 70.65% were recovered from their illness and this study is agreed with study conducted at Bushulo Major Health Center that is 75.5% by (Zinabu et al., 2014) and with the Global, regional and national causes of child mortality report that is 73.3% by (Li Liu, 2012). The average length of stay in the hospital for children with severe pneumonia was about 4 days. This study agrees with study conducted in Sidama Zone Wondo Genet District by (Teshome, 2017), children were not insured more exposed than children who were insured and patients who were taken ceftriaxone, crystalline penicillin and combined had high proportion of recovery.

In this study nonparametric method, semi-parametric and parametric survival models were applied. None parametric method is used to compare the difference between each categorical covariate based on Kaplan-Meier estimation method. The semi-parametric survival analysis using Cox PH model was fitted and the assumptions cox PH model was checked using graphical method and schoenfeld residuals and assumptions were violated for Cox PH model. Then the researcher introduced an alternative model for Cox PH model which is parametric AFT survival model to fit the pneumonia data in Debre Markos comprehensive specialized hospital. The researcher used different types of the baseline distributions to fit AFT models for pneumonia dataset in Debre Markos comprehensive specialized hospital. The baseline distributions used in this study were Exponential, Weibull, Log-normal and Log-logistic. The log-logistic AFT model was selected as good AFT model thanWeibull, Exponential and log-normal model based on comparison criteria with smaller AIC value. The overall median recovery time from sever pneumonia was 5 days (mean = 5 days; standard deviation=3 days). This study is almost consistent with the Researchers conducted a study in Uganda,

Mulagohospital to compare clinical outcomes in children suffering from Asthma and Pneumonia, the median duration of hospital stay to recover from pneumonia was 4 days (Nantanda et al., 2014) and the study conducted in rural health center of Gambia which reported that the mean time of recovery was 4.5 days(Kuti et al., 2014) and in Taiwan, the median time to stability/recovery after admission for patients with pneumonia was 5 days (mean = 6 days; range = 0 to18 days) (Huang, Chang et al. 2015). The finding of this study is higher than the study done in Vanderbilt (2.3days) and Nepal (2days)(Wolf et al., 2015) and(Basnet et al. 2015) respectively.This variation might be due to socio-economic in the study areas and harshness differences. This finding is lower than the study finding in Poland on trends in hospitalization of children with bacterial pneumonia that reported 10.1 to 8.2 days (Gajewska et al., 2016). This discrepancy might be due to the time difference in which the studies were conducted. As it was conducted from 2010 to 2011, different things such as treatment protocol which could reduce hospitalization period have been done after it. Another possible reason for this inconsistency might be related to differences in treatment and other practices, health care settings and other socioeconomic factors between areas where the studies were conducted.

In this study treatment type taken at the time of diagnosis, patient's insurance status and time elapsed to seek care were statistical significant predictors for the survival status of pneumonia patients. But in different studies for instance study conducted by (Mitiku, 2019) the predictors age, comorbidity, duration and danger sign were significant predictor for the survival time of pneumonia patients and study conducted by (Abate and Tadesse, 2019) in south west Ethiopia the predictors, sex, residence, season of diagnosis and comorbidity were significant predictors for time to death of pneumonia patients. This difference may be due to study area, time and socio economic and demographic status of study populations.

In this study the time elapsed to seek care was Also a predictor that had a significant effect in the time to recovery from Sever pneumonia. Patients who presented to the hospital early (preceding by one day of an illness) recovered sooner than those children presented late. This finding is consistence with study conducted by (Mitiku, 2019).This may due to the fact that as progression of disease increased, the required time to recover from it also increases. it is significant on a prospective study conducted in Gambia (Kuti et al., 2014).The findings of this study also showed that the patient's insurance status was a significant factor. That is patients who were insured had shorter survival time than patients were not insured this study

is not agree with several studies (Abate and Tadesse, 2019) this difference result may be due to socio-economic status of patients family, because health insurance uses for low income country. Since, it protects insured persons from paying high treatment costs in the event of sickness (Conn and Walford, 1998) andNational health insurance membership is associated with increased access to and utilization of health care(Sarpong et al., 2010). The other important predictor which was significantly and strongly associated with recovery time from sever pneumonia is the Treatment type taken during diagnosis. In this study it was found that Patients whose treatment type taken at the time of diagnosis were ceftriaxone, Ampicillin and combined have shorten timing of recovery and had high risk of recovery from pneumonia as compared with crystalline penicillin. This result agrees with study conducted by (Don et al., 2010).This may be due to different reasons like, content of treatment type and efficacy of treatment type. But this variable is not significant in the study conducted by (Mitiku, 2019).

5.2. Conclusion

This study used survival time of under-five pneumonia patients' dataset of those patients who started their pneumonia treatment from 2018-2020 years with the aim of determining thedeterminant factors of time-to-recovery of under-five pneumonia patients in Debre Markos Comprehensive specialized hospital. Out of the total 293 under-five pneumonia patients who started Pneumonia treatments, about 70.65% were recovered at the end of the study. The estimated median survival time of under- five pneumonia patients was 5 days.

To determine the associated factors of survival time of under-five pneumonia patients, Cox PH model was used and the PH assumption was checked by graphical, scheonfeld residual plot and global test. Then AFT model was fitted because the assumption of Cox proportional model was violated. Different AFT models by using different baseline distributions were applied. Among them using AIC, Log-logistic AFT model is better fitted survival time of under-five pneumonia patients' dataset than other AFT base line distributions.

The best model to fit the data to explain survival time of children with severe pneumonia dataset in Debre Markos Comprehensive Specialize Hospital was the Log-logistic AFT model, which was revealed using the graphical technique and Cox-Snell residuals plots.

In Debre Markos Comprehensive Specialized Hospital, the results of a Log-logistic AFT model revealed that time elapsed to seek care, treatment type taken at the time of diagnosis, and insurance status were found to be important predictors of recovery time for under-five

pneumonia patients. Patients' treatment types at the time of diagnosis were ceftriaxone, ampicillin, and combination, and patients who were insured had considerably shorter recovery times (higher survival experience). While a one-day increase in duration (late presenter) lengthened the time it took for a child to recover from pneumonia.

5.2. Recommendation

Based on the finding of the study the following recommendations were made for ministry of health, policy makers, the community at large, Debre Markos comprehensive specialized Hospital and researcher.

- The recovering time from pneumonia was prolonged on children who were not member of social health insurance (not insured) and on Duration prior to seeking care of Children who presented to the hospital lately.Caretakers are expected to train their parents to become members of social health insurance in order to reduce the time it takes for their children to recover from pneumonia and When their children become ill, parents or caregivers should take them to a medical facility right away and.

- Since ceftriaxone, ampicillin and a combination of these therapies were found to reduce the time it took to recover from pneumonia when given at the time of diagnosis, health care professionals should give these therapies at the time of diagnosis.

- Since some determinant factors for pneumonia patients are not included in the study, the Federal Ministry of Health should create well-designed pediatric registration charts for all hospitals and health facilities that cover all risk variables for future research.

REFERENCE

Aaserud, S., Kvaløy, J. T. & Lindqvist, B. H. 2013. Residuals and functional form in accelerated life regression models. Risk Assessment and Evaluation of Predictions. Springer.

Abate, L. & Tadesse, M. 2019. South West Ethiopia". International Journal of Current Research.

Abdel Mohsen, A., et al. (2019). "Acute Respiratory Tract Infection (ARI) in Children Under-five Years; Study of Prevalence, Risk Factors and Outcome in Minia University Children Hospital, Egypt." International Journal of Pediatrics

Akaike, H. (1974) 'A New Look at the Statistical Model Identification', IEEE Transactions on Automatic Control, 19(6), pp. 716–723. doi: 10.1109/TAC.1974.1100705.

Allison, P. D. (2010). Survival analysis using SAS: a practical guide, Sas Institute.

Andualem, Z., Adane, T., Tigabu, A., Yallew, W. W., Wami, S. D., Dagne, H., Azanaw, J., Guyasa, G., Azene, Z. N. & Endalew, M. (2020). Pneumonia among Under-Five Children in Northwest Ethiopia: Prevalence and Predictors—A Community-Based Cross-Sectional Study. International journal of pediatrics, 2020.

Ásbjörnsdóttir, K. H., Slyker, J. A., Weiss, N. S., Mbori-Ngacha, D., Maleche-Obimbo, E., Wamalwa, D. & John-Stewart, G. 2013. Breastfeeding is associated with decreased pneumonia incidence among HIV-exposed, uninfected Kenyan infants. AIDS (London, England), 27, 2809.

assfaw, T., Yenew, C., Alemu, K., Sisay, W. & Geletaw, T. 2021. Time-to-Recovery from Severe Pneumonia and Its Determinants Among Children Under-Five Admitted to University of Gondar Comprehensive Specialized Hospital in Ethiopia: A Retrospective Follow-Up Study; 2015–2020. *Pediatric Health, Medicine and Therapeutics,* 12**,** 189.

Basnet, S., et al. (2015). "Predictors of duration and treatment failure of severe pneumonia inhospitalized young Nepalese children." PLoS One 10(3).

Bekele, F., et al. (2017). "Factors associated with outcomes of severe pneumonia in children aged 2 months to 59 months at jimma university specialized hospital, southwest Ethiopia." Current Pediatric Research.

Bartlett, J. G., O'keefe, P., Tally, F. P., Louie, T. J. & Gorbach, S. L. 2009. Bacteriology of hospital-acquired pneumonia. *Archives of internal medicine,* 146**,** 868-871.

Campbell, H. & Nair, H. 2015. Child pneumonia at a time of epidemiological transition. The Lancet Global Health, 3, e65-e66.

Conn, C. P. & Walford, V. 1998. An introduction to health insurance for low income countries. London: Institute for Health Sector Development.

Collett,D,2003. Modelling survival data in medical research.second. , London: chapman and Hall

Collett, D. (2015). Modelling survival data in medical research, CRC press.

Collett,D,2003. Modelling survival data in medical research.second. , London: chapman and Hall

Cox, D. R. And Snell, E. J. (1968) 'A General Definition of Residuals', Journal of the Royal Statistical Society: Series B (Methodological), 30(2), pp. 248–265. doi: 10.1111/j.2517-6161.1968.tb00724.x.

CSA. (2012). Central Statistical Agency ,Addis Ababa, Ethiopia. Measure DHS, ICF Macro Calverton, Maryland, USA. Ethiopia Demographic and Health Survey.

Crighton, E. J., Elliott, S. J., Moineddin, R., Kanaroglou, P. & Upshur, R. 2007. A spatial analysis of the determinants of pneumonia and influenza hospitalizations in Ontario (1992–2001). Social science & medicine, 64, 1636-1650.

David, W. And L. Hosmer (1999). Applied survival analysis: regression modeling of time to event data, Wiley-Interscience.

Driscoll, A., Grant, M. J., Carroll, D., Dalton, S., Deaton, C., Jones, I., Lehwaldt, D., Mckee, G., Munyombwe, T. & Astin, F. 2018. The effect of nurse-to-patient ratios on nurse-

sensitive patient outcomes in acute specialist units: a systematic review and meta-analysis. European Journal of Cardiovascular Nursing, 17, 6-22.

Geleta, D., et al. (2016). "Determinants of community acquired pneumonia among children in Kersa District, Southwest Ethiopia: facility based case control study." J Pediatr Neonatal Care 5(2): 00179.

Higgins-Steele, A., et al. (2017). "Ending Preventable Child Deaths from Pneumonia and Diarrhoea in Afghanistan: An Analysis of Intervention Coverage Scenarios Using the Lives Saved Tool." Journal of tropical medicine 2017

Hosmer, D. (1999) 'Hosmer D.W., Lemeshow S. Applied Survival Analysis.pdf'.Huang, C.-Y. et al. (2015). "Risk factors of progressive community-acquired pneumonia inhospitalized children: A prospective study." Journal of Microbiology, Immunology and Infection48(1): 36-42.

Kadane, J. B. & Lazar, N. A. 2004. Methods and criteria for model selection. Journal of the American statistical Association, 99, 279-290.

Kieninger, A. N. & Lipsett, P. A. (2009). Hospital-acquired pneumonia: pathophysiology, diagnosis, and treatment. Surgical Clinics of North America, 89, 439-461.

Kleinbaum, D. G. and M. Klein (2005). "Competing risks survival analysis." Survival Analysis: A self-learning text: 391-461.

Kuti, B. P., Adegoke, S. A., Oyelami, O. A. & Ota, M. O. 2014. Predictors of prolonged hospitalisation in childhood pneumonia in a rural health centre. South African Journal of Child Health, 8, 11-15.

Lee, E, Wang, J.(2003). Statistical model for survival analysis. 3rd. ed. Wiley, New York,2003.

Lemeshow, S. And S. May (2008). Applied survival analysis: regression modeling of time-to-event data, Wiley.

Liu, L., Oza, S., Hogan, D., Chu, Y., Perin, J., Zhu, J., Lawn, J. E., Cousens, S., Mathers, C. & Black, R. E. (2016). Global, regional, and national causes of under-5 mortality in

2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet, 388, 3027-3035.

Leung, D. T. (2016) Prevention and Control of Childhood Pneumonia and Diarrhoea. . Paediatric clinics, 63(1), 67-79.

Ma, C., Gunaratnam, L. C., Ericson, A., Conroy, A. L., Namasopo, S., Opoka, R. O. & Hawkes, M. T. 2019. Handheld point-of-care lactate measurement at admission predicts mortality in Ugandan children hospitalized with pneumonia: a prospective cohort study. The American journal of tropical medicine and hygiene, 100, 37-42.

Mcallister, D. A., Liu, L., Shi, T., Chu, Y., Reed, C., Burrows, J., Adeloye, D., Rudan, I., Black, R. E. & Campbell, H. (2019). Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. The Lancet Global Health, 7, e47-e57.

Mengist, B., Tesfa, M. & Kassie, B. (2020). Time to recovery and predictors of severe community-acquired pneumonia among pediatric patients in Debre Markos referral hospital, North West Ethiopia: A retrospective follow-up study. PloS one, 15, e0239655.

Miller, N., Amouzou, A., Tafesse, M. Amd Hazel E. (2014) Integrated Community Case management of common childhood illness in Ethiopia: implementation strength and quality of care. The American journal of tropical medicine and hygiene, 91(2), 424-434.

Mitiku, B. M. (2019). Time To Recovery And Its Predictors Among Severe Community Acquired Pneumonia Patients Admitted To Pediatric Ward, Debre-markos Referral Hospital, North West Ethiopia, Retrospective Follow-up Study, 2019.

Musa, U. K. (2018). Assessment of House to House Inspection Manual in the Control of Sanitation

Nantanda, R., Ostergaard, M. S., Ndeezi, G. & Tumwine, J. K. 2014. Clinical Outcomes Of Children With Acute Asthma And Pneumonia In Mulago Hospital, Uganda: A Prospective Study. Bmc Pediatrics, 14, 1-10.

Nuru, A. N. (2019). Endocervical Microbial Pattern, Antibiotic Sensitivity and Complications Seen With Septic Abortion at Kenyatta National Hospital in 2018. University of Nairobi.

Opio, J. H. (2018). Survival of Children Aged Less Than Two Years with Pneumonia in Mulago Hospital Kampala, Uganda, Makerere University.

Pires, S. M., Fischer-Walker, C. L., Lanata, C. F., Devleesschauwer, B., Hall, A. J., Kirk, M. D., Duarte, A. S., Black, R. E. & Angulo, F. J. (2015). Aetiology-specific estimates of the global and regional incidence and mortality of diarrhoeal diseases commonly transmitted through food. PloS one, 10, e0142927.

Porth, C. (2011). Essentials of pathophysiology: concepts of altered health states, Lippincott Williams & Wilkins.

Pradhan, S. M., Rao, A. P., Pattanshetty, S. M. & Nilima, A. (2016). Knowledge and perception regarding childhood pneumonia among mothers of under-five children in rural areas of Udupi Taluk, Karnataka: A cross-sectional study. Indian Journal of Health Sciences and Biomedical Research (Kleu), 9, 35.

Reed, R. A. (2015). An investigation into the role of HIV exposure status in infectious disease mortality in children in Western Cape, University of Cape Town.

Requejo, J. H., Bryce, J., Barros, A. J., Berman, P., Bhutta, Z., Chopra, M., Daelmans, B., De Francisco, A., Lawn, J. & Maliqi, B. (2015). Countdown to 2015 and beyond: fulfilling the health agenda for women and children. The Lancet, 385, 466-476.

Rizopoulos, D. (2012). Joint models for longitudinal and time-to-event data: With applications in R, CRC press.

Rudan, I., Boschi-Pinto, C., Biloglav, Z., Mulholland, K. & Campbell, H.(2008). Epidemiology and etiology of childhood pneumonia. Bulletin of the world health organization, 86, 408-416B.

Schoenfeld, D. (1982). "Partial residuals for the proportional hazards regression model." Biometrika 69(1): 239-241.

Shibre, G. (2015). Assessment of the prevalence and associated factors of pneumonia in children 2 to 59 months old, Debreberhan district, North East Ethiopia. M. Sc. Dissertation. Addis Ababa University, Ethiopia.

Teshome A. (2017). Prevalence of pneumonia and factors associated among children 2-59 months old in Wondo Genet district, SNNPR, Ethiopia . Curr Pediatr Res , 21 (1): 19-25.

Tessema, T. (2018). Modelling Under-Five Mortality among Hospitalized Pneumonia Patients in Hawassa City, Ethiopia: A Cross-Classified Multilevel Analysis. Annals of Data Science, 5, 111-132.

Therneau, T. M., et al. (1990). "Martingale-based residuals for survival models." Biometrika 77(1): 147-160.

UNICEF (2014). Pneumonia and Diarrhea Progress Report. International Vaccine Access

UNICEF. (2016) United Nations Children's Fund United Nations Children's Fund.

UNICEF & UNICEF, W. (2016). Ending child deaths from pneumonia and diarrhoea. World Health Organization Press.

Walker, C. L. F., Rudan, I., Liu, L., Nair, H., Theodoratou, E., Bhutta, Z. A., O'brien, K. L., Campbell, H. & Black, R. E. (2013). Global burden of childhood pneumonia and diarrhoea. The Lancet, 381, 1405-1416.

Wardlaw, T., You, D., Hug, L., Amouzou, A. & Newby, H.(2014). UNICEF Report: enormous progress in child survival but greater focus on newborns urgently needed. Reproductive health, 11, 1-4.

WHO. (2016). Pneumonia. http://www.who.int/ mediacentre/ factsheets/fs331/en/.

Wolf, R. B., Edwards, K., Grijalva, C. G., Self, W. H., Zhu, Y., Chappell, J., Bramley, A. M., Jain, S. & Williams, D. J.(2015). Time to clinical stability among children hospitalized with pneumonia. Journal of hospital medicine, 10, 380-383.

APPENDIXES

Kaplan Meier survival time plot of under-five pneumonia Patients atDebre Markos comprehensive specialized hospitalby Different Covariates

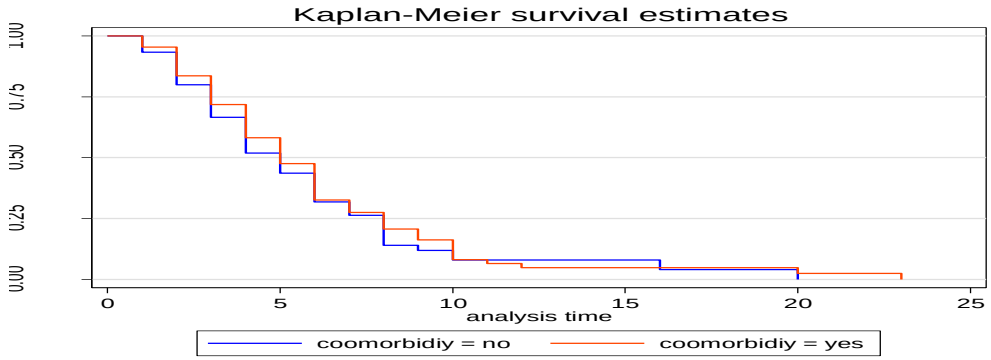
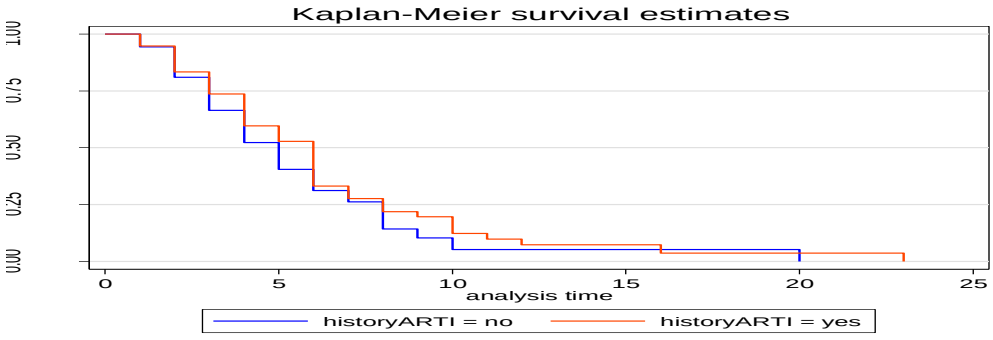


Figure A1: KM survival plots of under-five pneumonia patients by comorbidity



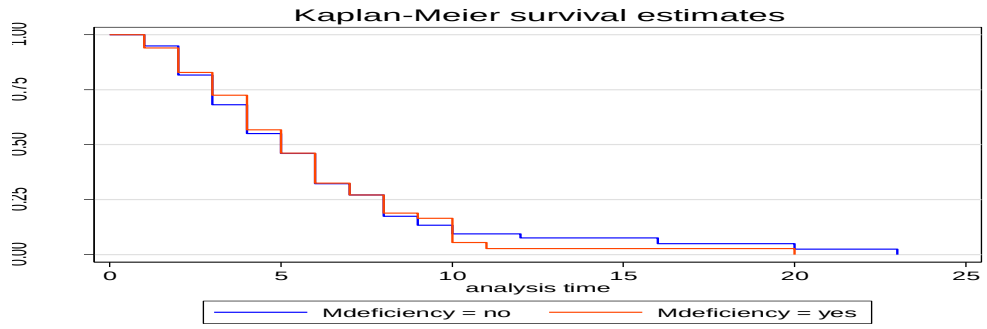


Figure A2:KM survival plots for historyARTI and Mdeficiencyof pneumonia patients

Table A1: Univariate Analysis of Cox Proportional Hazards model

Variables	Category	$\hat{\beta}$	SE	Sig	HR	95% CI for HR
Danger sign	No(ref)					
	Yes	-0.27	0.15	0.076*	0.760	(0.565 1.029)
Insurance status	No(ref)					
	Yes	0.178	0.145	0.218*	1.195	(0.899 1.589)
pneumonia type	SCAP(ref)					
	Nosocomial	-0.100	0.154	0.517	0.904	(0.667 1.244)
Treatment type	Crystalline penicillin(ref)					
	Ceftriaxone	0.524	0.226	0.260	1.690	(0.999 2.46)
	Ampicillin	0.402	0.250	0.620	1.490	(.958 2.332)
	Combined	0.208	0.189	0.307	1.231	(.848 1.786)
Age	1-11(ref)					
	12-23	-0.13	0.175	0.607	0.878	(0.624 1.237)
	24-59	0.0397	0.163	0.619	1.04	(0.756 1.431)
Season	Autumn(ref)					
	Winter	-0.302	0.270	0.264	0.712	(0.434 1.256)
	Spring	-0.125	0.214	0.751	0.933	(0.579 1.341)
	Summer	-0.095	0.234	0.611	0.885	(0.573 1.439)
historyARTI	No (ref)					
	Yes	-0.192	0.140	0.125*	0.804	(0.609 1.062)
Comorbidity	No (ref)					
	Yes	-0.108	0.139	0.118*	0.803	(0.610 1.057)
Residence	Rural (ref)					
	Urban	0.0521	0.142	0.471	1.108	(0.837 1.467)
SAM	No (ref)					
	Yes	-0.120	0.153	0.367	0.868	(0.639 1.179)
Micro-neutral deficiency	No (ref)					
	Yes	0.013	0.145	0.927	1.013	(0.762 1.347)
Sex	Male (ref)					
	Female	-0.0137	0.142	0.467	0.901	(0.682 0.192)
Duration		-0.762	0.061	0.000*	0.466	(0.414 0.525)

* indicates statistical significant at 25% level of significance, ref if reference, SE is standard error

Test of proportional hazards assumption by Scaled Schoenfeld residuals

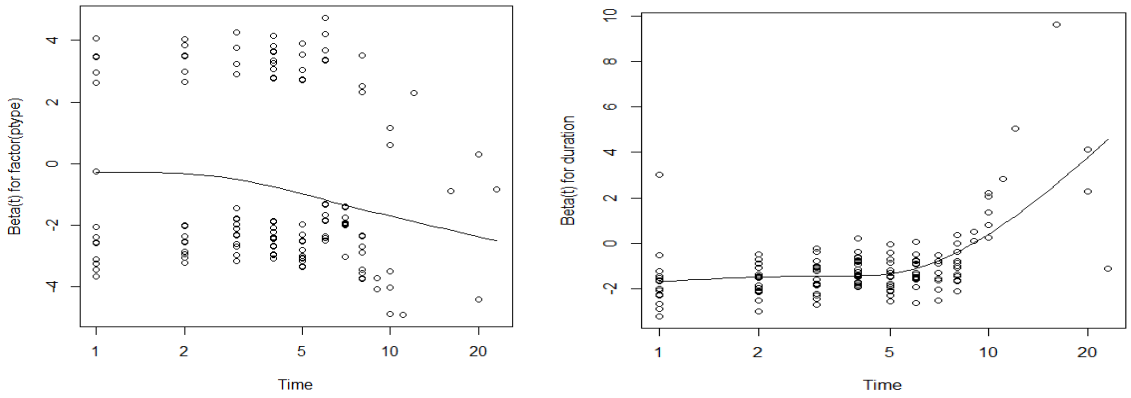
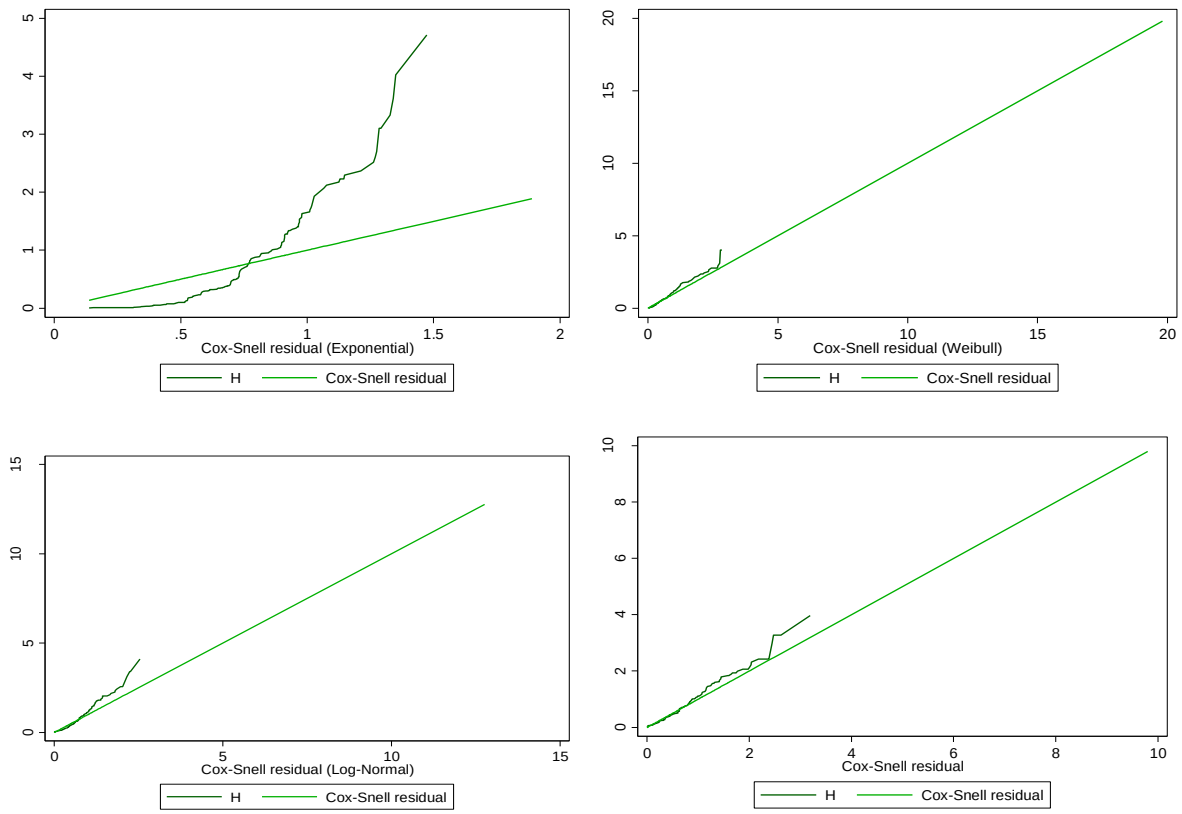


Figure A3:the scaled Schoenfeld residuals plot by duration and pneumonia type

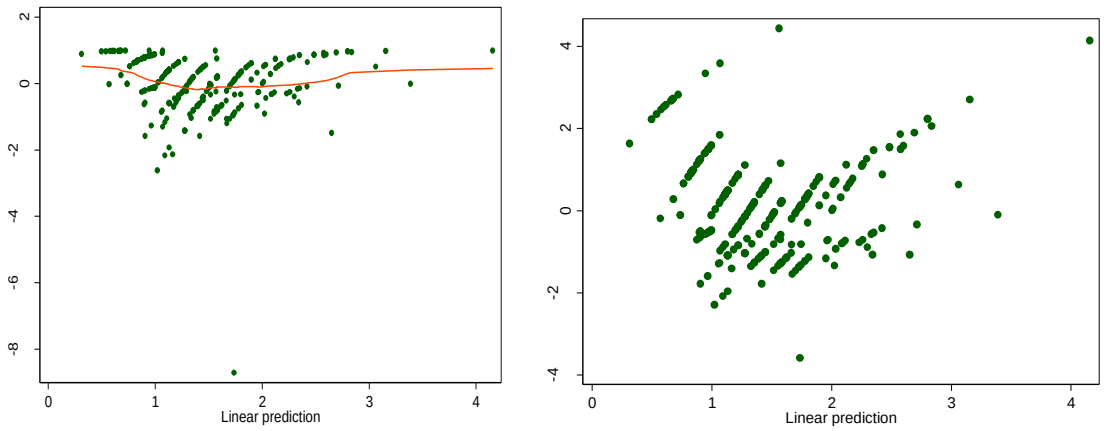
Table A2: time dependent predictors for examining PH assumption

Parameter	Level	P value
time*duration	Continuous	0.000
time*danger sign	No	
	Yes	0.011

Assessing over all goodness of model fit for the four AFT modelsusing cumulative hazard Vs cox snell residual plot



FigureA4: Cox Snell residual plots for four AFT models of pneumonia patient'sdata set



FigureA5: Deviance and martingale-like residualsof log-logistic AFT model