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MODELING TIME-TO-CURE FROM COVID-19: A COMPARISON OF VARIOUS PARAMETRIC FRAILTY MODELS:A CASE STUDY AT JIMMA UNIVERSITY AND SHENEN GIBE COVID-19 CARE CENTER, JIMMA ZONE, SOUTH WEST ETHIOPIA

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MODELING TIME-TO-CURE FROM COVID-19 : A COMPARISON OF VARIOUS PARAMETRIC FRAILTY MODELS

MSc Thesis

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Approval Sheet

This certified that the thesis titled "Modeling Time-To-Cure From Covid-19 : A Comparsion of Various Parametric Frailty Models" . The case study at Shenen Gibe and Jimma University Covid Care Center at Jimma zone in partial fulfillment of the requirement for the degree of Master of Science in Biostatistics. Summited to the college of natural science Jimma University. The original thesis was carried out by Meseret Mesfin Bambo. Under my supervision no part of this title has been performed for another research, and therefore, I recommended that would be accepted as fulfilling the thesis requirement.

Geremew Muleta (PhD Scholar) 12/08/2021
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As the members of the board of examiners of M.Sc.thesis open defense examination of Meseret Mesfin Bambo , we certify that we have read and evaluated the thesis and examined the candidate. We recommend that the thesis has been accepted as it fulfills the requirements for the degree of Master of Science in Biostatistics

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ABSTRACT

Novel Corona viruses are a viral family that causes Severe Acute Metabolic Syndrome. The Virus was strictly increasing throughout in the World. From the total cases(91.5%) were cured in the world.In Africa(60%) were cured and In Ethiopia (98.61%) were cured from march 2020 to March 2021. Many scholars conducts prognostic factors of Covid-19 by using coxph,non parametric, and logistic regration model.But loglogistic regration does not account censoring observation and Coxph model and non parametric models were used in the independent and identically distributed covariates.For those model hetrogeneity does not considered. The objective of this thesis was develop various parametric frailty model to detect random effect on time–to-cure of covid-19 in the two treatment care center. Data were collected in Jimma university and Shenen Gibe covid-19 Center. Appropriate model that describes the Covid-19 data were Gamma and Inverse Gaussian frailty with exponential, log-logistic, log-normal, and Weibull baseline function were compared. Based on Akaike information criterion criteria all models were compared.Data were analyzed by using R version 4.0.5 software.298 covid-19 patients 246(82.65%)were cured with the median curing time of 19 days.The log-logstic model with Gamma frailty distribution has the smallest Akaike information criterion(1609.625) value compared with the others. Clustering effect is significant on the modeling time to cure from covid-19 with in test of unobserved hetr0geneity in all models. From this finding, age group, severity ,co morbidity , diabetics, lung-cancer, and oxygen are prognostic (significant) factors for time to cure of covid-19. From this thesis almost of patient were cured in two treatment care center around Jimma zone.log-logistic Gamma frailty model was best fit of Covid-19 dataset.There is heterogeneity between the two treatment center for time to cure of covid-19. Researcher recommend that there is some limitation of parametric frailty model.For further study who have interest to compare parametric model the simulation is appropriate.

Key words: ***AIC,Frailty,Heterogeneity,Parametric Model,Time to cure***

Contents

List of Abrevation and Acronyms

AFT:	Acceleration Failure Time
AIC:	Akaike Information Criterion
BIC:	Bayesian Information Criterion
COVID:	corona virus-19
JUCCC:	Jimma University covid care center
ICU	Intensive cure unite
MLE:	Maximum Likelihood Method
PCR:	polymerase chain reaction
PH:	Proportional Hazards
QQ:	Quantile - Quantile
RT:	Real Time
USA:	United State of America

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1 INTRODUCTION

1.1 Background of the Study

Novel Coronaviruses are a viral family that causes Severe Acute Metabolic Syndrome (SAMS) [1]. The Covid-19 was discovered for the first time in December 2019 in Wuhan, China. It was officially dubbed Covid-19 Pandemic by the world, and it has spread to 213 countries first time and posing a threat to human life [2].

The population affected by Covid-19 in the world was $184,573,435$ from those $168,921,778(91.5\%)$ were cured from december 2020 to march 2020 [3].

Countries like Asia has 56,430,654 total cases from those 53,737,073(95.2%) were cuved,Europe hase 48,257,002 total cases from those 45,579,857(94.4%) were cured ,USA has 34,647,083 total cases from those 29,168,315(84.18%) were cored,India has 30,709,557 total cases from those 29,843,825 (97.1%) were cured,Brazil has 18,909,037 total cases from those 17,352,670(91.7%)were cured,France has 5,794,665 total cases from those 5,638,432(97.3%) were cured,Russia has 5,707,452 total cases from those 5,143,255(90.11) were cured until 5 July 2021 [4].

Africa is one of the continent highly affected by Covid-19 started on April 7/ 2020 Total of 874,036 cases ,524,557(60%) were cured from April 7/ 2020 to March 2021 [5]. Also Africa locked down every activity with serious condition until march 2021 by worries landmarks for public health experts. The virus has been spread in 53 of Africa's except Lesotho [6].

Distribution of Covid-19 in Ethiopia By March 31, 2021 total case=206,589 total cure =203,721 total death=2868 Percentage of cure was 98.61% [7].

The primary cause was a 48 years Japanese man who arrived in Ethiopia from Burkina Faso. The second report was three cases from those two Japanese and one Ethiopian who had direct contact with the primary Japanese person. Before it transmeted to the community, cases were largely imported and sourced from mandatory quarantines. Most of the cases were Ethiopian's and this cases was all nine Regional States and two city Administrations of the country through the bulk of cases, 3822 (71.6%), were reported from Adis-Abeba, the capital city of Ethiopia [8]. Jimma zone is one of Oromia region which is affected by covid 19 May 17/ 2020 (patient card).

1.2 Statement of the problem

Corona virus (Covid-19) is caused by an RNA virus that is renamed severe acute respiratory syndrome(SARS-CoV-2) which started in December 2019 in Wuhan, in China [9]. Covid-19 was

highly distributed in the world, Africa, Ethiopia, and every zone, woreda and kebel [10]. In our country the distribution of Covid-19 was highly concentrated. From the total of 202,545 cases, 151,172(76.6%) was cured until March 2021.

The major aim of this thesis was to perform modeling time to cure from covid -19 by using various frailty model was new research in Ethiopia and to know curing time of covid-19 Jimma zone and to use sustainable resource management to the patients and todetermine gaps from further scholars.

Scholars have conducted to determine prognostic covariates on covid 19 by using the logistic regression and semi-parametric proportional hazard models. But the logistic regression doesn't account for the censoring of observations and doesn't hold for time-to-event data [11]. Nonparametric and semi-parametric models do not Considered about random effect the models. Those parametric and semi-parametric models were preformed when independent and identically distributed covariates exist. In such applications it is assumed that all heterogeneity is captured by theoretically relevant covariates [12].

In many situations ,there are many reasons to suspect omitted or unmeasured factors, that some individuals have more at risk of experiencing the event. It is unlikely the underlying reasons for this variability makes fully captured by the observed covariates. If there is unmeasured frailty, the hazard will not only be a function of the covariates but also of the frailty [13]. To assess the true effects of the observed covariates under this circumstance, some have stressed the need to explicitly account for unobserved heterogeneity [14].

Cox PH model is a frequently used model in the analysis of survival data. Inference based on Cox's models needs identically and independently distributed samples. Even if the concept of this model allows for modeling different levels of risk for different subgroups doesn't control risk levels for some relevant covariates that are often unavailable to the researcher or even unknown. The CoxPH has no distributional assumption for baseline and distribution of survival time [15]. Therefore, this study argued that clustering (frailty) has an effect on modeling time to cure of covid -19 due to the heterogeneity in the covid-19 care center. As a result, the shared frailty model approach is relatively better to determine covariates related to time to cure of covid-19. For these cases, alternatives to the gamma and inverse gaussian frailty model have been proposed. The gamma and inverse Gaussian frailty distribution was proposed for their special cases.

However, different dependence structures result from different frailty distributions. In particular, Gamma frailties typically generate very strong dependence at late times and Inverse gamma frailties lead to stronger dependence at mid-time [16, 17]. For the above situation initiates to argued that clustering (frailty) has an effect on modeling to cure of covid -19 due heterogeneity and various

frailty model approach is relatively better to determine covariates related to time to cure of covid -19 and aimed at addressing the following research questions:

1. Which baseline distributional assumption among the exponential, Weibull and log-logistic, log-normal; as well as frailty distributions, the gamma and inverse Gaussian frailty distributions Fit the data ?
2. What is the estimated median curing time and cure rate of patients with Covid-19 ?
3. What are the determinant prognostic factors related to time to cure of covid 19 datasets?

1.3 Objectives of the study

General Objective of study:-

•Model time–to-cure from covid 19 using various parametric frailty models

Specific objectives were

•To estimate the median curing time of the covid-19 .

•To identify the determinant prognostic factors for time to cure from covid- 19.

•To compare various parametric frailty models.

1.4 Significance of the study

The results of this study might provide information to government and other concerned bodies in setting policies, strategies and further investigation for reducing heterogeneity between covid-19 care center. Finding variation of survival time in two treatment care center with underling unobserved factors that could assist stackholders for decision making process to patients required attention. For academicians, it will direct to give clustering effect and genuine interest on the subject matter for further scholars especially covid-19. Study would have added literature on determinants of time-to Cure from covid-19

2 LITERATUR REVIEW

2.1 Novel Corona viruses

Corona viruses are one of the viruses that affect Severe Acute Respiratory Syndrome [18]. The Covid-19 virus was determined and posted for the primary time in December 2019 in the city of Wuhan, China [20]. It was named Covid-19 disease by the World Health Organization and the disease is distributed through 213 countries and affects human life. Viruses are strictly increasing every day until March 2021 with affecting the numerous numbers of people in the world and the millions of people also cured of Covid-19 in the world. Covid-19 was declared a pandemic as 27 May 2020 by the World Health Organization (WHO) [21].

Novel corona virus (Coved-19) is caused by an RNA virus which is renamed by severe acute respiratory syndrome (SARS-CoV-2) [19].

Novel Covid-19 started in December 2019 in Wuhan, China. Now it distributed in Africa, Ethiopia, as well as every Region, zone, woreda, in every world. Currently, the distribution of Covid-19 in Ethiopia is highly concentrated. From the total of 194,524 cases, 151,172(76.6%) was cured until March 2021 in Ethiopia and their distribution is rapidly increasing through every region a sho in the short period of time. So Covid-19 has no treatment, and it is the worst disease in the world. So many researchers had conducted to determine prognostic covariates on Covid-19 patients by using the logistic regression and Semi-parametric proportional hazard models [22].

From previous findings risk factors related to time to cure of Covid-19 by using different models. Considered for the Studies have been conducted to identify covariates of under time to cure of Covid-19 in Wuhan country from January 23, 2020, to March 13, 2020, a total of 187 patients 96 (51.34%) were cured by using Semi-parametric proportional hazard models 56.76% were a significant relation with age [23]. In China, June 14, 2020, a total of 7,690,708 confirmed cases 84,729 samples taken and analyzed to determine risk factors related to cure of Covid-19 by using multiple logistic registration 14% have significant relation with the oxygen, 51.2% significant relation with the status of smoking, 2.4% has significant with lung cancer, 1.05% diabetics (1.6).% have a significant relation [24].

Based on a study of factor to time to cure Covid-19 the total of 187 patients were diagnosed from January 23 until March 13 in Wuhan countries from those 96 (51.34%) were cured and the mean $\pm$(standard deviation) survival time was 9.40$\pm$7.17 days curing time in Wuhan by using survival analysis. Based on BIC, the exponential regression model was the weakest and the Weibull model was the best for fitting to data [25].

Ethiopia has registered Covid-19 cases since the 13th of March 2020. In Ethiopia, several cases were reported. Currently, more than $202,545$ cases , $155,190(77.71\%)$ cured of Covid-19 until March 30,2021.) [26].

The infection of Covid-19 is affected human Respiratory system associate principally transmitted by the metabolic process by droplets and shut contact with an infected person and most common symptoms of an infected person with Covid-19 are, fever, dry cough, tiredness, and slightly(Less common symptoms) aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, a rash on the skin, or discoloration of fingers or toes [27, 28].

Almost all these important world health containment measures the outbreak still has the potential effect and for a large amount loss of life in the world including Ethiopia. The seriousness of the Covid-19 distribution highly distributed urban areas and on population distribution extent of Covid-19 can cause rises shortage food, political crises, healthy disturbance, famine in Ethiopia, highly risked depression and economical crises were cases and consequences of novel coronaviruses [29].

2.2 Time to Cure from covid-19

The term **Time-to-cure** means the patient takes time from admission day to discharge day that the medical condition of Covid-19 patients cured of the Covid-19 care center and the patient have no longer has that particular condition anymore for that disease [30, 31].

2.3 Severity with covid-19

According to the severity of the disease, Tim to cure of Covid-19 patients varies from patient to patient and country to country. The median cure time ranged from 4 to 53 days within China and 4 to 21 days outside of China [32].

The severe disease takes three to six weeks and mild disease takes two weeks. The severity of Covid-19 has different curing times with the strength of severity. Depending on the severity of Covid-19, mild severe have the shortest time length to cure Covid-19 compared with other severity. The servere has the prolonging time to cure Covid-19 than mild and moderate severity. According to the comorbidity of patients, has different time lengths to cure Covid-19. The patient comorbid has to prolong time to recover(Cure) from Covid-19 compared with non-comorbid patients. The comorbid patients consume a time length of three to six weeks to cure Covid-19 in India [33].

Age crucial factor for time to cure of Covid-19. An aged person with the presence of multiple

comorbid patients has less probability to cure Covid-19. The aged patient takes a prolonged time to cure Covid-19 related to adults. From the previous finding,221 individuals found positive with Covid-19 from March 1, 2020, to 31st March 2021. The male preponderance within the sample with 66% of the Covid-19 patients being male and about 34% being female. The median curing time of Covid-19 patients was 25 days in India [34, 35, 36].

2.4 Median Curing Time of Covid-19

The median curing time of covid 19 were 3 days in newyork with in 95%C.I[1,6] by using Coxph regression. The elder patients cured from covid-19 with median curing time of 62 days with in 95% C.I were [51,72].The adjusted hazard ratio for elder person were 1.31 with C.I [1.09,1.57].The patients who take oxygen have the median curing time were 18 days with C.I[9,28] [37]. From the previous finding in Italy the median curing time of Covid 19 were 8 days with 95%C.I[5,11] [39]. In the Swiss medical hospital there were 196 patients diagnosis and discharged with the median curing time of 7days with 95%C.I[4,10] [40].

2.5 Comorbidity with covid-19

Depending on severity covid 19 patients having co morbidity have different time lengths to cure of covid care center The severity of mild patent with co morbidity patient takes 7-21 days and severity of moderate co morbid patients take 25-41 days and having the severity of severe and critical takes 50-80 days [41, 42].

2.6 hyphertension and covid-19

Scholars suggested that,hyphertension was significant prognostic factor for Covid-19. The hypertensive patients have a low chance of cure of Covid-19. The median curing time a hypertensive patient has prolonged time compared to the non-hypertensive patient in Covid-19. Result in patients with Covid-19. The evaluation of hypertensive patients' treatment of those co morbidities at baseline and through Covid-19 is scarce, and therefore the results are conflicting. Many researchers find out the association between hypertension and Covid-19, their influence on the result, and therefore the effect of treatment of hypertension patients [43]

2.7 Diabetics and covid-19

From the previous research in China, total of 258 patients 63 were diabetics. The median of patents discharged with 23 with the confidence interval [23, 91] by using Coxph model. Diabetic is one prognostic factor to increase severity of Covid-19 and higher risk for mortality. The median time length the patient from admission to discharges in the hospital were 12 days with in 95% C.I(7–15) with P value 0.022 in Chin [44]. Diabetes is one of the diseases of hyperglycemia with devastating complications. If the patient having diabetics don't have a lot of probability of curing Covid19. The patient who diabetic disease includes a high quantitative relation of odds to death and fewer, likelihood with cure of Covid-19. Diabetics are one of the prognostic factors that cause the prolonged time to cure Covid19. There are many sorts of diabetics from that ketoacidosis (DKA) is a degree acute and worst stage of congenital disease.

Diabetic patient with Covid-19 includes an important relation with decelerates the time to cure. The diabetic patient in Covid-19 patients had a better odd of severity and deaths compared to patients while not an inherited disease. From the previous analysis of 244 patients with Diabetics started for Covid-19, one hundred ninety were male, and fifty-five were feminine diabetic patients. Out of 244 collected data, 20 had DKA. The hazard rate of DKA was 8%. From the general twenty recorded DKA of Covid-19, five out of twenty died throughout admission Day.

From the study, a better hazard of DKA is extremely serious in a similar way to two inherited disorders with Covid-19. From this finding conclude twenty % of patients WHO have genetic defect patients with COVID19. From the general quantity place the time to death was 25% and time to cure was 75% within the study of USA. DKA one all told the worst diabetic kind that includes a lot of complications within the treatment of Covid19, and it became an extremely arduous condition once associated with Covid-19. The hazard of DKA and time to cure associated with Covid-19 enlarged once DKA increase [45].

2.8 Lung cancer and covid-19

There are four types of lung ancer [47].These are lung nodels,non small cell lung cancer,small cell lungcancer and mesothelioma. Lung cancer has one prognostic factor that affects the leading time length of Covid-19.From previous finding patient with lung cancer has a higher odds ratio of severity compared to a patient without lung cancer in Covid-19 outcomes. Lung cancer is one of the diseases that cause the tissue of the lung. It causes the cells that line the air passages. Lung cancer causes human life to death.

Lung cancer patients with Covid-19 in the diagnosis of Covid-19 at the center from 12 March 2020 to 6 May 2020. From their lung cancer (62% Covid-19 was severe from those 25% were died). From the total of Covid-19 patients with lung cancer who died were (11%). Determinants of Covid-19 severity were highly given to the smoking status, lung cancer, Diabetics and other co morbid conditions of patients. Depending on scholar's research lung cancer have [odds ratio for Covid-19 2.9, with respective 95% confidence interval 1.07, 9.44 and the median time to cure (23.5). Most patients were cured of Covid-19, including 25% patients initially requiring intubation. Among hospitalized patients, hydroxyl chloroquine did not improve Covid-19 outcomes. Covid-19 is associated with a high burden of severity in patients with lung cancer [46].

2.9 Age and covid-19

Further study in Italy were analysis by using loglogstic regration .The Covariate Age have odds ratio were 1.05 with p-value 0.016.The age of patient were significant covariate Prognostic factor for covid-19 [48]. Age of the patient is one of all the leading prognostic factors in time to cure Covid-19. When age increased the time length of your time to cure Covid-19 also increases contrariwise. When the elder patient has lowered accelerated time to cure of Covid-19. When age increases the metabolic activity also decreased and various amounts of co morbidity increase, for such cases the variation of patients' quality is additionally decreasing. Survival time to cure adult age has low prolonged time than the older age. When the researcher performed analysis for Covid-19 from the admitted from March 1 to April 8, 2020, were considered. The researcher was analyzed the socio-demographic and clinical factors related to time to cure and prolonged time to cure for acute respiratory failure Covid-19 infection. The full 486 cases were included in the study. The median curing time of older age was 59 years and from the overall 271 (55.8%) were male; the median curing time of body mass index was 30.6. From the previous analysis by using multiple logistic regression, age, sex, rate, oxygen saturation, history of diabetes, are significant relations. Age contains a great potential factor that causes time to cure Covid-19. Older age of Covid-19 patient consumes longer to cure of Covid- 19 .China, Italy, Japan, Singapore, Canada, and the Republic of Korea, The estimated that age categories of 20 years were approximately half that of adults aged over 20 years, Accordingly, there finding the kids might need a comparatively small impact on reducing. Covid-19 [49].

2.10 Oxygen and covid-19

The scholars conducted on the prevalence of oxygen with covid-19.By using multiple logistic regration model to analysize prevalence of oxygen with Covid-19 and conclude that oxygen treatment was highly required in Covid-19 patients. Scholars conducted on the prevalence of Oxygen therapy was required in 63.1% for patients, the oxygen therapy patients (odds ratio [OR] 2.072, 95% confidence interval CI[1.312-3.271] [50].

2.11 Consequence of ignoring Frailties

Ignoring the existence of heterogeneity will produce incorrect estimation of parameters and their standard errors in survival analysis. Ignoring heterogeneity overestimates life expectancy based on their study on estimating life expectancy in a heterogeneous population. When heterogeneity is ignored, it caused underestimation of covariate effects in his study of time to cure rates. When unobserved or unmeasured effects are ignored, the estimates of survival may be misleading. Showed that ignoring frailty leads to regression coefficient estimates biased towards zero by an amount depending on the distribution and the variability of the frailty terms [60].

3 METHODOLOGY

3.1 Description of Study Area

Jimma zone is one of Oromia region located in south west of Ethiopia. The Jimma zone was widest and beautiful topography surrounded by green area. It has 21 words recently with two referral covid-19 care centers. The study area was around Jimma town which the capital and administrative center of the Zone and is located at a distance of 350 km away from the capital of Ethiopia-Addis Ababa.

The study area is situated between 1689 and 3018(meter above sea level) and receives an average rainfall between 1200 and 2400 mm per year. Data was collected from the patients follow up in Jimma University and Shenen Gibe care center. Jimma University and Shenen Gibe hospital were one of the public hospitals in Ethiopia and it belongs to the Jimma administrative region. Jimma university covid care center has more bedrooms and treatment facilities with many specialized doctors and Shenen Gibe hospital one of medium hospital with not enough bedrooms and no specialized doctors.Jimma and Shenen Gibe hospitals were one of the oldest and recent hospitals in Jimma zone respectively. Currently both hospitals deliver Covid-19 centers.

3.2 Study design

A retrospective cohort study design carry out to retrieve relevant information from the medical records of covid -19 to address the objectives of the study.

3.3 Inclusion and Exclusion Criteria

In this study all covid-19 patients who are registered under follow up in Shenen Gibe hospitals and Jimma Covid Care center from march 17/ 2020 to march30/ 2021(1year) in Jimma zone were included in the study other wise excluded. The Covid-19 datasets in this thesis extracted from the patient's cards and regard patients admitted from March 17 2020 to March 2021(1year). The total number of patients in this study where 298 which come from 21 woreda around Jimma zone.

3.4 Variable Description

3.4.1 Dependent variable

The response variable in this study was time to cure of Covid -19 in the day that the patient starts diagnosis.

Starting time The entry of the survival data was considered from the day that the patient starts diagnosis after admission. The patients fulfill any of the criteria in the following principles of discharging and admission criterion of Covid-19.

Discharge criteria for asymptomatic cases from the outset, Completed 21 days for the time of first positive test result of mandatory isolation at a dedicated center. Discharge criteria for recovering Covid-19 patients are Completed forty-two days (from the time of first positive test result) of mandatory isolation, No symptom or sign of active disease and significant chest CT improvement and Capable of home isolation [62, 63].

Cure: The patient with positve covid-19 can be cure if evidenced by two negative RT-PCR tests done at least 24 hours apart [64].

3.4.2 Independent Variable

The study considers the following explanatory variables that are may be factors of time to cure of covid-19

Table 3.1: Independent Variable coding

Covariate Variable	Discription	Category and coding
Sex	Sex of Patient	Female =0 , Male =1
Agegroup	age group of patients	< 1=0 , $1-4$ =1
		$5-14$=2 , > 15 =3
Comrbidity	comorbidity of patient	No=0, Yes=2
Lungcancer	lungcancer of patients	No=0, Yes=1
Severity	Severity of Disease	mild=0 ,moderate=1,
		sever=2 , critical=
Hypertention	patient having hyphertension	No=0, Yes=1
Oxygen	oxygen given to the patients	No=0, Yes=1
Diabetics	patient having diabetics	No=0 ,Yes =1
Residence	patients residence	urban=0, Semi -urban=1 , Rural =2
Smoking	smoking status of patients	No=0, Yes =1

3.5 Survival analysis

Survival analysis is a collection of statistical procedures for data analysis for which the outcome variable of interest is time until an event occurs. it measures time to event in which time measured by years, months, weeks, or days from the beginning of follow-up of an individual until an event occurs. alternatively, time canrefer to the cure of an individual patients from covid 19 diseasis is an event of interest. in survival analysis our interst of event is time to cure time to death, in various period of time from starting time of diagnosis and ,relapse from remission, recovery interest that may happen to an individual. The problem of analyzing time-to-event data arises in several applied fields such as medicine, biology, public health, epidemiology, engineering,economics, sociology, demography and etc. The terms lifetime analysis, duration analysis, failure-time analysis, reliability analysis, and transition analysis refer essentiallyto the same group of techniques although the emphases in certain modeling aspects could differ across disciplines [51].

The use of survival analysis, as opposed to the use of other statistical method, is most important when some subjects are lost to follow up or when the period of observation is finite certain patients may not experience the event of interest over the study period. In this latter case one cannot have complete information for such individuals. These incomplete observations are referred to as being censored. Most survival analyses consider a key analytical problem of censoring. In essence, censoring occurs when we have some information about individual survival time, but we do not know the survival time exactly.In reality such event can occur due to the following reasons,A person does not experience the event before the study ,A person is lost to follow-up during the study period and person withdraws from the study for unknown/known reasons

There are three categories of censoring 1. **Right censoring**: Survival time is said to be right censored when it is recorded from its beginning to a defined time before its end time. This type of censoring is commonly recognized survival analysis and also considered in this study. Let C denote the censoring time, that is, the time beyond which the study subject cannot be observed. The observed survival time is also referred to as follow up time. It starts at time 0 and continues until the event T or a censoring time C, whichever comes first. Let $C_1, C_2...C_n$ be a sample of censoring times. And $T_1, T_2...T_n$ be event times. We observe a sample of couples, $(y_1, \delta_1), (y_2, \delta_2), ...(y_n, \delta_n)$, where for i=1,2,. . . .n [65].

$$y_i = min(T_i, C_i) = \begin{cases} T_1, if T_i \leq C_i \\ C_i, if T_i \geq c_i \end{cases}$$

$$\delta_i = I(T_i \leq C_i) = \begin{cases} 1, if T_i \leq C_i \\ 0, if T_i \geq c_i \end{cases}$$

2. Left censoring: Survival time is said to be left censored if an individual develops an event of interest prior to the beginning of the study. 3.Interval censoring: Survival time is said to be interval censored when it is only known that the event of interest occurs within an interval of time but the exact time of its occurrence is not known.

3.Interval censoring: Survival time is said to be interval censored when it is only known that the event of interest occurs within an interval of time but the exact time of itsoccurrence is not known. The presence of censoring complicates research design and statistical analysis. Thus, censoring creates some unusual problem in the analysis of data because such data cannot be handled properly by standard statistical methods. Researchers used different techniques to respond to the complication due to censoring unsatisfactorily.

New developments in statistical theory accompanied by new development in statistical computing have changed how researchers can study such data.An important assumption for methods presented in survival analysis studies for the analysis ofcensored survival data is that the individuals who are censored are at the same risk of subsequentfailure as those who are still alive and uncensored. i.e. a subject whose survival time is censored at time C must be representative of all other individuals who have survived to that time. If this is the case, the censoring process is called non-informative. Statistically, if the censoring process isindependent of the survival time, there will be non-informative censoring. In this study,we assumed that the censoring is non-informative right censoring.

The response variable in survival analysis is survival time and is no longer limited to only time tocure of covid 19. It is a non-negative random variable used loosely for the time period from a starting time point to the occurrence of any event. In this study context, survival time is the length of time ofcure of covid 19 which is measured in months.

3.6 Survival Functions

The survivor function is defined to be the probability that the survival time of a randomly selected subject is greater than or equal to some specified time. Thus, it gives the probability than an individual surviving beyond a specified time. Let T be a continuous random variable associated with the survival times, t be the specified value of the random variable T and $f(t)$ be the underlying

probability density function of the survival time T. The cumulative distribution function $F(t)$, which represents the probability that a subject selected at random will have a survival time less than some stated value$t$ is given by [65, 66].

$S(t) = P(T > t) = \int_t^\infty f(u)du$

$h(t) = \frac{f(t)}{S(t)} = \frac{-dln[S(t)]}{dt}$

3.7 Median Survival Time

Median survival time is the time beyond which 50% of the individuals in the population understudy are expected to survive and is given by that value $t(50)$ which is such that $St(50) = 0.5$. Due to the fact that the non - parametric estimates $S(t)$ step functions, it will not usually be possible to realize an estimated survival time that makes the survival function exactly equal to 0.5. Instead, the estimated median survival time, is defined to be the smallest observed survival timefor which the value of the estimated survival function is less than 0.5. In mathematical terms,

$$(\hat{t})(50) = min\frac{t(i)}{\hat{S}(t_j)} \leq .50$$

where $t_{(i)}$,is the observed survival time for the i^{th} individals $i = 1, 2, \cdots, n$ and $t_{(j)}$ is ordered cur time, $j = 1, 2, \cdots, r$

3.8 The Kaplan-Meier estimate of the survival function

The Kaplan-Meier (KM) estimator is the standard non-parametric estimator of the survival function used for estimating the survival probabilities from observed survival times both censored and uncensored [67]. Suppose that r individuals have failures in a group of individuals, let 0 $\leq$1,$\leq$2...$\leq$ ∞ be the observed Cure time of covid 19 patients.let$j$ be the size of the risk set at j were risk set denoted the collection of individuals to cure and uncensored just before $t(J)$. Let (j) be the number of observed event(j),$J = 1...r$ Then the K-M estimator of $t$is defined by

$S(\hat{t})) = \prod_{j;t(j)}[1 - \frac{d(j)}{r(j)}]$

This estimator is a step function that changes values only at the time of each cure of covid19. The cumulative hazard function of the KM estimator can be estimated

$\hat{H}(t) = -ln[\hat{S}(t)]$ where $\hat{S}t$ is KM estimator

3.9 Modeling Frailty

Frailty models extend Cox proportional hazards model by introducing unobserved frailties to the model. In this case, the hazard rate will not be just a function of covariates, but also a function of frailties. A frailty model is a random effects model which has a multiplicative effect on the hazard rates of all the members of the subgroups. In Univariate survival models, it can be used to model the heterogeneity among individuals, which is the influence of unobserved risk factors in a proportional hazards model. In multivariate survival models, shared frailty model is used to model the dependence between the individuals in the group. In the multivariate case, unobserved frailty is common to a group of individuals [68].

3.9.1 Shared Frailty Model

Many statistical models and methods proposed to model failure time data assume that the observations are statistically independent of each other. However, this does not hold in many applications. Shared frailty model is a conditional model in which frailty is common to all subjects in a cluster. The shared frailty model is responsible for creating dependence between event times. It is also known as a mixture model because the frailties in each cluster are assumed to be random. It assumes that, the given frailty, all event times in a cluster are independent. Shared frailty model was introduced by Clayton without using the notion frailty and extensively studied in [69, 70].
Frailty models are the extensions of the proportional hazards model which is best known as the cox model. The most popular model in survival analysis. Normally, in most clinical application, survival analysis implicitly assumes a homogeneous population of individuals to be studied. This means that all individuals sampled in that study are subject in principle under the same risk (e.g., risk of death, risk of disease recurrence). In many applications, the study population cannot be assumed to be homogeneous, but must be considered as a heterogeneous sample i.e a mixture of individuals with different hazards.Shared frailty model assumes that individuals in a subgroup or pair share the same frailty u, but the frailty from group to group may differ. Conditional on the random term, called the frailty denoted by u_i, the survival times in cluster i($1 \leq$ i $\leq$ n) are assumed to be independent, the proportional hazard frailty model assumes

$$h_{ij}(t/X_{ij}, u_i) = \exp(\beta' X_{ij} + u_i) h_o(t)$$

Where as an alternative if the proportional hazards assumption does not hold is the accelerated failure time frailty model which assumes

$$h_{ij}(t/X_{ij}, u_i) = \exp(\beta' X_{ij} + u_i) h_o(exp(\beta' X_{ij} + u_i)t)$$

Where i indicates the i^{th} cluster and j indicates the j^{th} individual for the i^{th} cluster, $h_0(.)$ is the baseline hazard, u_i the random term of all the subjects in cluster i, X_{ij} the vector of covariates for subject j in cluster i, and β the vector of regression coefficients. If we let Z = $\exp(u_i)$, in thise thesis Z has the gamma or the inverse Gaussian distribution so that the hazard function depends upon this frailty that acts multiplicatively on it. If the number of subjects n_i is 1 for all groups, the univariate frailty model is obtained [71], otherwise the model is called the shared frailty model [72]. Because all subjects in the same cluster share the same frailty value z_i. The main assumption of a shared frailty model is that all individuals in cluster i share the same value of frailty Z_i (i = 1, ..., n), and this is why the model is called the shared frailty model. The lifetimes are assumed to be conditionally independent with respect to the shared (common) frailty. This shared frailty is the cause of dependence between treatment care center within the clusters.

3.9.1.1 Baseline Survivor and Hazard Function

The survival time T is assumed to follow a distribution with density function f (t), then the survival function is given by $S(t) = P(T > t) = \int_t^\infty f(u)du$

The hazard function is a measure of the probability of failure during a very small interval, assuming that the individual has survived at the beginning of the interval. It is defined as:-

$$h(t) = \frac{f(t)}{S(t)} = \frac{d/dtS(t)}{S(t)}$$

The relationship between the survival and the hazard function is given by $S(t) = \exp(-\int_0^\infty h(u)du)$. Under the parametric approach, the baseline hazard function is defined as a parametric function and the vector of its parameters, say ψ, is estimated together with the regression coefficients and the frailty parameter(s). In this research the following distributions are considered. The cumulative hazard function is given by $H_t = \int_0^t h(u)du$ Specifying one functions $f(t), S(t), h(t) or H(t)$ specifies the other three functions. The parameter is reparameterized in terms of predictor variables and the regression parameters. Typically for parametric models and the shape parameter ρ is held fixed

3.9.2 Parameterization

proportional hazards (PH) is said to be the hazard function of a group is proportional to the hazard function of the other group, that means the hazard ratio is constant over the time. The hazard ratio is given by $HR = \exp(\beta' X_{ij})$ is the hazard ratio (HR) Where $\beta' = 1, 2, \cdots, p$ is a vector of

Table 3.2: Parametric distributions for the baseline hazards

Distribution	f(t)	s(t)	h(t)	Parameter Space
Exponential	$\lambda \exp(-\lambda t)$	$\exp(-\lambda t)$	λ	$\lambda > 0$
Weibull	$\rho\lambda t^{\rho-1} \exp(-\lambda t^{\rho})$	$\exp(-\lambda t^{\rho})$	$\rho\lambda t^{\rho-1}$	$\lambda, \rho > 0$
Log-Logistic	$\frac{\lambda\rho t^{\rho-1}}{(1+\lambda t^{\rho})^2}$	$\frac{1}{1+\lambda t^{\rho}}$	$\frac{\lambda\rho t^{\rho-1}}{1+\lambda t^{\rho}}$	$\lambda \in \Re, \lambda > 0$
Log-normal	$\frac{1}{t\sigma\sqrt{2\Pi}\exp(-\frac{\log(x-\mu)^2}{2\sigma})}$	$1 - \Phi(\frac{\log t}{\sigma})$	$\frac{\frac{\Phi(\log t)}{\sigma}}{1-\Phi(\frac{\log t}{\sigma})}$	$\mu\epsilon\Re, \sigma, t > 0$

regression coefficients and Xij is the vector of covariates for subject j in cluster i. the accelerated failure-time (AFT) model describes stretching out or contraction of survival time as a function of predictor variables.The acceleration factor denoted byϕ is $\exp(\alpha^{'} Xij)$ where$\alpha^{'} = (1, 2...p)$ is a vector of regression coefficients in case of AFT model.For the exponential, weibull and log logistic survival model, the relationship between For the exponential, weibull and log logistic survival model, the relationship between and ß is given by

a).For exponential $\beta j = -\alpha j$, the exponential PH and AFT are in fact the same model, except that the parameterization is different, and hence HR=$\exp(-\alpha j)$ is the hazard ratio of the j^{th} group with the reference groups.

b).For weibull $\beta j = -\alpha j\rho$ .whereρ is the shape parameter and hence, HR=$\exp(-\alpha j)$ is the hazard ratio of the j^{th} group with the reference groups

c).For log-logistic, $\beta j = -\alpha j\rho$,where ρ is the shape parameter and OR = $\exp(-\alpha j\rho)$ indicates the failure odds ratio of the j^{th} group with the reference groups. The log-logistic model is a proportional odds model,and it has constant over two groups.

3.10 The Frailty Distributions

The frailty defined and denoted by zi is an unobservable realization of a random variable Z with probability density function $f(.)$ and the frailty distribution. Since zi multiplies the hazard function

and Z has to be non-negative. The mean of Z is typically restricted to unity in order to separate the baseline hazard from the overall level of the random frailties. The main difference between multivariate and univariate frailty models is the assumption of how frailty is distributed in the data. Shared (multivariate) frailty models assume that similar observations share frailty i.e.that means the frailty distribution variability is related to a measure of dependence between clustered subjects, whereas it is rather interpreted as a measure of over dispersion which is caused either by misspecification or omitted covariates in the univariate case. For the study frailty distributions use gamma and the inverse Gaussian wereconsidered. In both cases, as a single heterogeneity parameter repersent indexes the degree of independence.

3.10.1 The Gamma Frailty Distribution

The gamma distribution has been widely applied as a mixture distribution for example [73, 74, 75]. From a computational and analytical point of view, it fits very well to failure data. It is widely used due to mathematical tractability. The density of a gamma-distributed random variable with parameteris given by [76].
$f_Z(zi) = \frac{zi^{\frac{1}{\theta}} \exp(-\frac{zi}{\theta})}{\theta^{\frac{1}{\theta}} \Gamma \frac{1}{\theta}}, \theta \geq 0$ Where$\Gamma(.)$s the gamma function,and its distribution is $\Gamma(\mu, \theta)$ with μ is fied to 1 for identity and the variance θ with laplace transformation

$$L(u) = (1 + \tfrac{u}{\theta})^{-\theta}$$

the conditional survival function of the gamma frailty distribution is given by:

$$S_\theta(t) = [1 - \theta \ln(S(t))]^{-\frac{1}{\theta}}$$

And the conditional hazard function is given by:

$$h_\theta(t) = h(t)[1 - \theta \ln(S(t))]^{-1}$$

Where$S(t)$ and $h(t)$ are the survival and the hazard functions of the baseline distributions. For the Gamma distribution, the Kendall's Tau, which measures the association between any two event times from the same cluster in the multivariate case,

$$\tau = \tfrac{\theta}{\theta+2}, \theta \epsilon (0, 1)$$

3.10.2 Inverse Gaussian frailty distribution

The inverse Gaussian (inverse normal) distribution was introduced as a frailty distribution alternative to the gamma distribution [77, 78]. Similar to the gamma frailty model, simple closedform expressions exist for the unconditional survival and hazard functions, this makes the model attractive. The probability density function of an inverse Gaussian shared distributed random variable with parameter θ ¿ 0 is given by

$$f(z) = \frac{1}{\sqrt{2\pi\theta Zi^3}} \exp\left(-(\frac{1}{2\theta z})(z-1)^2\right)$$

The mean and the variance are 1 and θ, respectively with Laplace transform

$$L(s) = \exp(\tfrac{1}{\theta})(1 - \sqrt{1+2\theta s}), S \geq 0$$

For the inverse Gaussian frailty distribution the conditional survival function is given by:

$$S_\theta(t) = \exp\left(\tfrac{1}{\theta}\right)(1 - [1 - 2\theta \ln S(t)]^{\frac{1}{2}})$$

And the conditional hazard function is given by:

$$h_0(t) = h_{(t)}[1 - 2\theta \ln S(t)]^{\frac{-1}{2}}$$

here $S(t)$ and $h(t)$ are the survival and the hazard functions of the baseline distributions. With multivariate data, an Inverse Gaussian distributed frailty yields τ given

$$\tau = \tfrac{1}{2} - \tfrac{1}{\theta} + 2\frac{\exp\frac{2}{\theta}}{\theta^2} \int_{\frac{2}{\theta}}^{\infty} \frac{\exp(-u)}{u} du \epsilon (0, 1/2)$$

3.11 Method of Parameter Estimation

Estimation of the frailty model can be parametric or semi-parametric. In the former case, a parametric density is assumed for the event times, resulting in a parametric baseline hazard function. Estimation is then conducted by maximizing the marginal log-likelihood [79]. In the second case, the baseline hazard is left unspecified and more complex techniques are available to approach that situation. Even though semi-parametric estimation offers more flexibility, the parametric estimation be more powerful if the form of the baseline hazard is somehow known in advance.Frailty models account for the clustering present in grouped event time data.
For right-censored clustered survival data, the observation for subject $j \in J_i = \{1, ..., \dot{n_i}\}$ from cluster $i \in I = \{1, \dot{...}s\}$ is the couple (y_{ij}, δ_{ij}), where $y_{ij} = min(t_{ij}, c_{ij})$ is the minimum between

the survival time tij and the censoring time c_{ij}, and where $\delta_{ij} = I(t_{ij} \leq c_{ij})$ is the event indicator. When covariate information are been collected the observation will be $(y_{ij}, \delta_{ij}, X_{ij})$, where X_{ij} denote the vector of covariates for the ij-th observation. In the parametric setting, estimation is based on the marginal likelihood in which the frailties have been integrated out by averaging the conditional likelihood with respect to the frailty distribution.Under assumptions of non-informative right-censoring and of independence between the censoring time and the survival time random variables, given the covariate information, the marginal log-likelihood of the observed data can be written as.

$l_{marg}(\psi, \beta, \theta; Z, X) = \sum_{i=1}^{s}\{[\sum_{j=1}^{ni} \delta_{ij}(\log(h_0(y_{ij}))+X_{ij}^T\beta)]+\log[(-1)^{di}L^d([\sum_{j=1}^{ni} H_o(y_{ij})\exp(X_{ij}^T)])]\}$

Where $d_i = \sum_{j=1}^{ni} \delta_{ij}$ is the number of events in the i^{th} cluster, and $L^q(.)$ the q^{th} derivative of the Laplace transform of the frailty distribution defined as

$L(s) = E[\exp(-Zs)] = \int_0^\infty(-Z_i s)f(Z_i)dz_i$, $S \geq 0$, where Ψ represents a vector of parameters of the baseline hazard function, β the vector of regression coefficients and θ the variance of the random effect.

The estimates of h_0, β, θ are obtained by maximizing the marginal log-likelihood of the above. This can be done if one is able to compute higher order derivatives $L^q(.)$ of the Laplace transform up to $q = max\{d_1, d_2, \dot{d}_3, ..., d_s$. Symbolic differentiation is performed in R, but is impractical here; mainly because this is very time consuming [80].

3.12 Prediction of Frailties

Besides parameter estimates, prediction of frailties are sometimes desirable. The frailty term zi can be predicted by $Zi = E(Z/zi, \varphi, \beta, \theta)$, with zi the data of the i^{th} cluster. This conditional expectation can be achieved [81].

$$\hat{zi} = E(Z/zi, \varphi, \beta, \theta) = -\frac{l^{(di+1)(\sum_{j=1}^{ni} H_o(yij)\exp(xij^T\beta))}}{L^{di}(\sum_{j=1}^{ni} H_o\exp(xij^T\beta))}$$

3.13 Comparison of models

Model comparison and selection are among the most common problems of statistical practice, with numerous procedures for choosing among a set of models [82, 83]. There are several methods of model selection. The most commonly used methods include information criteria. One of the most commonly used model selection criteria is Akaike Information Criterion (AIC). A data-driven model selection method such as an adapted version of Akaike's information criterion AIC is used

to find the truncation point of the series. In some circumstances, it might be useful to easily obtain AIC value for a series of candidate models [84, 85]. In this study, we used the AIC criteria to compare various candidates of parametric frailty models. The model with the smallest AIC value is considered a better fit. For comparing models that are non-nested type, the Akaike's information criterion (AIC) which is defined as:

$$AIC = -2\log(L) + 2(k + c + 1)$$

Where k is the number of covariates, c the number of model specific distributional parameters. The preferred model is the one with the lowest values of the AIC. In addition to these criteria, likelihood ratio test (LRT) will be used in order to compare models that are nested type, particularly the effect of the random effects. Manipulation of the comparison was done using the R software with version 4.0.5.

3.14 Model Diagnostics

3.14.1 Evaluation of the Baseline Parameters

The graphical methods can be used to check if a parametric distribution fits the observed data or not. Appropriateness of assumed distributions baseline hazard function is evaluated as follows: The appropriateness of model with the exponential baseline can graphically be evaluated by plotting

•$(-\log(\hat{S}(t)))$ versus t where S(t) is Kaplan-Meier survival estimate. This plot should be linear , Because for exponential distribution, S(t) = $\exp(-\lambda t)$, and hence, $-\log(S(t)) = \lambda t$ is linear with time.

•Model with the weibull baseline has a property that the $\log(-log(S(t))$ is linear with the $\log$ of time, where $S(t) = \exp(-\lambda t^{\rho})$. Hence, $\log(-\log(S(t))) = \log(\lambda) + \rho\log(t)$. This property allows a graphical evaluation of the appropriateness of a Weibull model by plotting $\log(-\log(\hat{S}(t)))$ versus$\log(t)$ where $\hat{S}(t)$ is Kaplan-Meier survival estimate [86].

•log-normal baseline plot of $\Phi^{-1}\{1 - \exp(-H(t))\} = \Phi^{-1}\{1 - \hat{S}(t)\}$ versus $\log$ time (t) should be linear, if the log-normal distribution is appropriate.

•The log-failure odd versus log time of the log-logistic model is linear. Where the failure odds of log-logistic survival model can be computed as:

$$\frac{1-S(t)}{S(t)} = \frac{\frac{\lambda t^{\rho}}{1+\lambda t^{\rho}}}{\frac{1}{1+\lambda t^{\rho}}} = \lambda t^{\rho}$$

Therefore the log-failure odds can be written as:

$$\frac{\log(1-S(t))}{S(t)} = \log(\lambda t^{\rho}) = \log(\rho) + \rho\log(t)$$

Therefore the appropriateness of model with the log logistic baseline can graphically be evaluated by plotting $\log((1 - (\hat{S}(t)/\hat{S}(t))$ versus $\log$ time where $\hat{S}(t)$

3.14.2 The Cox Snell Residuals

For the parametric regression problem, analogs of the semi parametric residual plots can be made with a redefinition of the various residuals to incorporate the parametric form of the baseline hazard rates [87]. The first such residual is the Cox–Snell residual that provides a check of the overall fit of the model. The Cox–Snell residual, rj, is defined by:
$\hat{H}(\frac{Tj}{Hj})$ where $\hat{H}$is the cumulative hazard function of the fitted model. If the model fits the data, then the rj's should have a standard $(\lambda = 1)$ exponential distribution, sothat a hazard plot of rj versus the Nelson–Aalen estimator of the cumulative hazard of the $rj's$ should be a straight line with slope 1. For the three baseline hazard functions will considered in this thesis.

Table 3.3: table:the Cox–Snell residuals

Exponential	$\hat{\lambda ti}\exp(\hat{\beta}, Xj)$
Weibull	$\hat{\lambda ti^{\rho}}\exp(\hat{\beta}, Xj)$
lognormal	$\ln[1 - \Phi\frac{(\ln t_j - \hat{\mu} - \hat{\gamma}^t z_j)}{\hat{\sigma}})]$
loglogistic	$\ln(\frac{1}{1+\hat{\lambda ti^{\rho}}\exp(\hat{\beta}, Xj)})$

3.14.3 Quantile - Quantile plot

A quantile-quantile or (q-q)plot is used to check if the accelerated failure time model provides an adequate fit to the data. The plot is based on the fact that, for the accelerated failure-time model $S_1(t) = S_o(\phi t)$
Where S_0 and S_1 are the survival functions in the two groups and ϕ is the acceleration factor

Let $t_{(op)}$ and $t_{(1p)}$ be the $p^{(th)}$ percentiles of groups 0 and 1, respectively, that is
$$t_{kp} = s_k^{-1}(1-p), k = 0, 1$$

Using the relation $S_1(t) = S_o(\phi t)$ have $t_{(op)} = 1 - p = S_1(t1p) = S_o(\phi tp1)$ for all t.

accelerated failure time in the model holds, $t_{op} = t_{1p}$.
Determining this assumption we we can compute the Kaplan–Meier estimators of the two groups and estimate the percentilest_{1p}, t_{0p}, for various covarietes of p.
If we plot the estimated percentile in group 0 versus the estimated percentile in group 1 (i.e., plot the points t_{1p}, t_{0p} for various values of p), the graph should be a straight line through the origin, if the accelerated failure time model holds. If the curve is linear, a crude estimate of the acceleration factor q is given by the slope of the line [90].

4 Result And Descution

4.1 Descriptive Summary

In this study 298 patients were follow up Covid-19 treatments in Jimma University and Shenen Gibe covid care center from March 2020 to march 2021(1year). The main objective of this finding was determining the prognostic factors time to cure covid- 19 in both care center. From this result of thesis 246 (82.65%) were cured and the remaining 52 (17.45%) were censored. From the total of 298 patients 194 (65.1%) were males from those 156(80.4%) were cured with median curing time takes 19 days with in 95% C.I[13,31]and 104(34.8%))were females from those 90 (86.53%) were cured with median curing time takes 20 days with in 95% C.I[11,30].

Depend on the severity of disease, mild patients were 139(100%) with a median curing time of 13days with in 95% C.I[10,18], moderate 52(91.2%) were cured with a median curing time of 22 days with in 95% C.I[18,32], sever 50(70.4%)with a median curing time of 24 days with in 95% C.I[21,38] and the critical were 5(16.1%) with a median curing time of 48 days with in 95% C.I[31,56]respectively.

From this result Patients with diabetic 46(51.1%) with a median curing time of 33 days with in 95% C.I[23,42] and non diabetic patients was 200(96.2%) with a median curing time of 15 days with in 95% C.I[11,22].

Depending on the treatment care center 130 patients were diagnosed in the Shenen Gibe center from those 110 (84.6%) were cured with a median curing time of 20 with in 95% C.I[15,32]and 168 patients were in the Jimma university center from those 136 (80.9%) were cured with median curing time of 18 days with in 95% C.I[11,30].

From this result total of 298 patients 4(100%) were age group 1-4 with a median curing time of 2 days with in 95% C.I[2,2] ,23(100%) were age group 5-14 with a median curing time of 9 with in 95% C.I[6,12] ,and 219(80.8%) were age group above 14 with a median curing time of 20 with in 95% C.I[14,32].

Covariate like smoking status of the patients 198 (90%) were nonsmoker with a median curing time of 18 with in 95% C.I[11,23] and 48 (61.5%) were smokers with a median curing time of 31 days with in 95% C.I[23,42].

From this output patients with hypertension were 31 (57.4%) with a median curing time of 32 days with in 95% C.I[21,49] and non hypertensive patients were 215(88.11%) with a median curing time of 17 days with in 95% C.I[17,27].

From this result total patients who has take oxygen 151 (50.7%) from those 119(78.8) were used

with a median curing time of 21 days with in 95% C.I[14,35] where as 127(86.4%) do not take oxygen with median curing time of 19 days with in 95% C.I[11,26].

From the total of 289 Patients, 119 (40%) were co morbid patients from those 69 (57.98%) were cured with a median curing time of 32 days with in 95% C.I[22,42] and 179 (60%) were non co morbid patients from those 177 (98.9%) were cured with a median curing time of 14 days with in 95% C.I[10,20].

From the total of 298 patients 30(10.1%) patient was lung cancer ,from those 5(16.6%) were cued while 268(89.9%) was non lung cancer, from those 241(89.9%) were cured from covid-19 .Source(table 4.1)

Table 4.1: Descriptive summary of covariate variables of of covid 19 patients

		Patients Status				
Covariate Variable	Category	Censored	Cured	Total	Median time	95% C.I
Sex	Female	14(13.5%))	90 (86.5%)	104(34.8%))	20	[11,30]
	Male	38(19.6%)	156(80.4%)	194 (65.2%)	19	[13,31]
Agegroup	$1-4$	0	4(100%)	4(1.4%)	2	[2,2]
	$5-14$	0	23(100%)	23 (7.7%	9	[6,12]
	>15	52(19.2%)	219 (80.8%)	271 (90.9%)	20	[14,32]
Smoking	No	22(10%)	198 (90%)	220(73.8%)	18	[11,23]
	yes	30(38.5%)	48 (61.5%)	78(26.2%)	31	[23,42]
Oxygen	No	20 (13.6%)	127 (86.4%)	147 (49.3%)	19	[11,26]
	Yes	32(21.2%)	119 (78.8%)	151(50.7%)	21	[14,35]
hypertension	No	29(11.89%)	215 (88.11%)	244(81.9%)	17	[11,27]
	Yes	23(42.6%)	31 (57.4%)	54(18.1%)	32	[21,49]
Co morbidity	No	2(0.11%)	177(98.9%)	179(60%)	14	[10,20]
	Yes	50 (42%)	69 (57.98%)	119 (40%)	32	[22,42]
Severity	mild	0	139(100%)	139 (46.64%)	13	[10,18]
	moderate	5(8.8%)	52(91.2%)	57(19.1%)	22	[18,32]
	Sever	21(29.6%)	50(70.4%)	71(23.8%)	24	[21,38]
	critical	26 (83.9%)	5(16.1%)	31 (10.4%)	48	[31,56]
Dibetics	No	8 (3.8%)	200(96.2%)	208 (69.8%)	15	[11,22]
	Yes	44(48.9%)	46(51.1%)	90 (30.2%)	33	[23,42]
Treatment center	Shenengibe	20 (15.4%)	110 (84.6%)	130 (43.62%)	20	[15,32]
	JU center	32 (19.1%)	136 (80.9%)	168 (56.4%)	18	[11,30]
Residence	Urban	31 (16.6%)	155 (83.4%)	186 (62.4%)	19	[13,30]
	Semi-urban	8(22.2%)	28(77.8%)	36 (12%)	17.5	[12,34]
	Rural	13(17.1%)	63 (82.9%)	76(25.6%)	21	[12,32]
Lungcancer	No	27(10.1%)	241 (89.9%)	268(89.9%)	18	[12,27]
	Yes	25 (83.4%)	5 (16.6%)	30 (10.1%)	38	[30,Na]

4.2 Survival of Significantly different groups

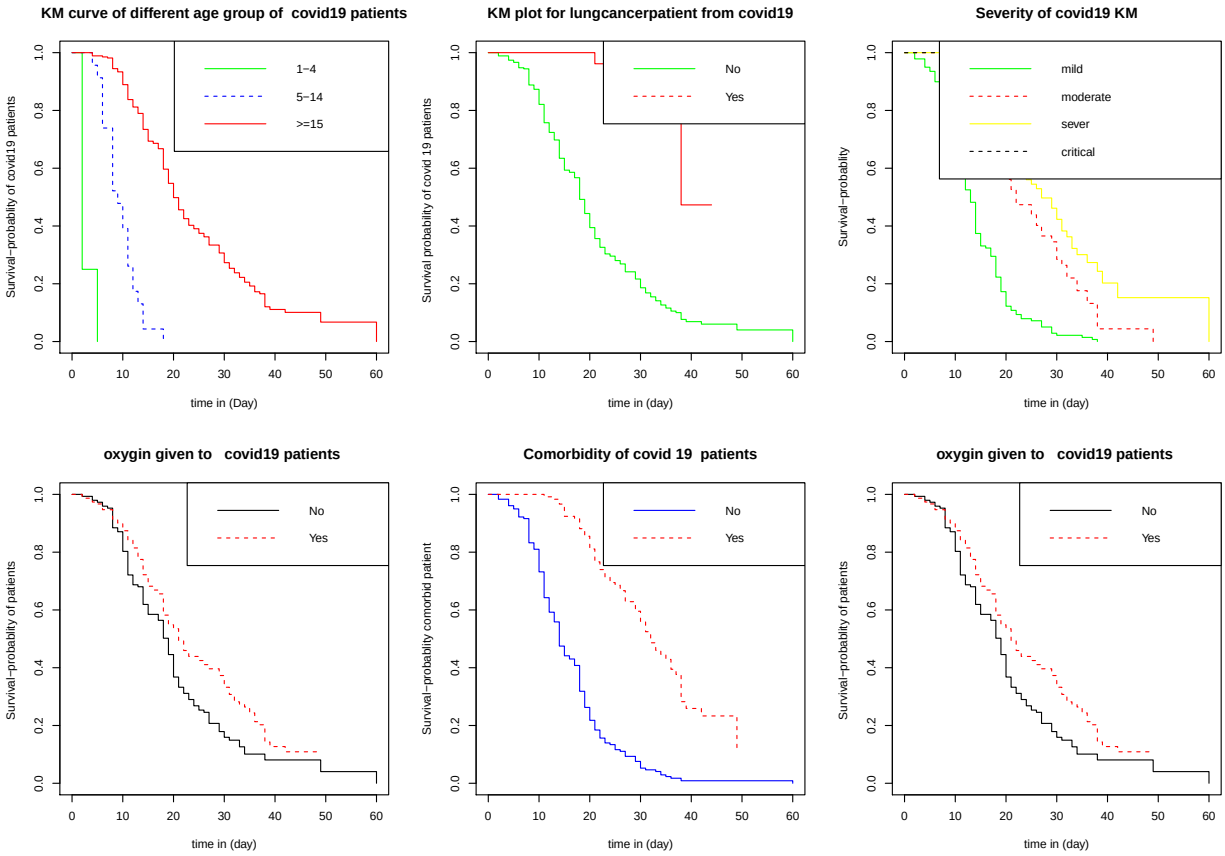

Figure 1: KM curves for significant variables

The Survival time to cure from covid 19 patient whose agegroup greater than or equalto 15 was greater than the patient whose age group1-4.From these result displayed above figure1,The survival time to cure from Covid-19 age group 5-14 has a prolonged time length to cure from Covid-19 compared to reference group (1-4). Also the age group greater or equalto 15 has more prolonged time to cure compared to the reference group (1-4) in fig1.

Now from the result displayed above fig 1, the patient who had lung cancer have a more prolonging time to cure from Covid-19 compared to reference group (non lung cancer) fig 1.

From the results display below in the figure1, it seems that there is an effect on time-to-cure due to the severity of the disease. The moderate has longer time length of time to cure of Covid-19 than reference group(mild), also sever has more prolonged time to cure of Covid 19 compared to reference group(mild) and lastly Critical has the most prolonged time to cure of Covid-19 compared reference groupmild fig 1.

Oxygen is one of covariate displayed in the figure1. It seems that there is an effect on time-to-cure from covid-19 due to the oxygen given to the patients. The patients who take oxygen have more prolonged time to cure compared to the reference group who (do not take oxygen).Because scarcity of oxygen supply,the distribution of covid-19 was not equally .

Co morbidity display below figur1, the patient having co morbidity have a longer time length of Time to Cure of Covid-19 than reference group (not co morbidity) fig 1.

Results display below in the survival of diabetic patients in the figure1, have an effect on time-to-cure from covid-19.The patient having diabetic have a prolonged Time to Cure of Covid-19 than those with not having diabetic patients.

4.3 Univariable Analysis

From the result of log-logistic-Gamma Univariable analysis below the table (4.2), we can observe that the covariate age group, Smoking status, hypertension, co morbidity, diabetics, severity, the residence of patient, Sex, and oxygen are the leading prognostic factors about Time to cure of covid-19. From those output age groups, hypertension, co morbidity, diabetics, severity, and oxygen are significant prognostic factors that affect the Time to cure of covid-19 in the model. These covariates accelerated factor confidence interval do not include 1, at 5%. However, the sex, residence are insignificant factors in the in this model. Because covariates of those covariates accelerated factor confidence interval include 1 at 5%. So candidate covariates for the multivariable analysis are like age group, hypertension, co morbidity, diabetic's severity and oxygen are candidate variables for Multivariable analysis in the parametric frailty distribution with various hazard functions. Source(table 4.2)

Table 4.2: Loglogstic - Gamma Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p value	95% CI(ϕ)
Sex	Coef female(rf)	3.1234	22.723	0.8563	0.000	[21.04,24.40]*
	Male	0.0884	1.0924	0.0696	0.732	[0.95 1.22]
AGe group	Coef Age1-4(rf)	0.872	2.391689	0.257	0.0068	[1.44, 3.95]*
	Age5-14	1.320	3.74342	0.743	0.0002	[2.17, 6.45]*
	Age>=15	2.176	8.810	0.259	0.0042	[5.30, 14.64]*
Co-morbidity	Coef Yes(rf)	2.672	14.4688	0.6296	0.0003	[13.23 ,15.70]*
	No	0.799	2.223	0.0595	0.012	[2.10 2.33]*
Lung cancer	Coef No(rf)	2.90	18.174	0.389	0.036	[17.41,18.93]*
	Yes	1.14	3.1267	0.174	0.0067	[2.78 3.46]*
Hypertension	Coef No(rf)	2.870	17.637	0.2349	0.001	[17.17,18.09]*
	Yes	0.614	1.8478	0.0911	0.019	[1.66 2.02]*
Severity	Coef mild(rf)	2.565	13.000	0.6650	0.167	[11.69,14.30]*
	moderate	0.579	1.7842	0.069	0.001	[1.64 1.91]*
	Sever	0.788	2.1989	0.0636	0.02	[2.07, 2.32]*
	Critical	1.415	4.1164	0.1335	0.002	[3.85 4.37]
Oxygen	Coef No(rf)	2.873	17.690	0.1088	0.0023	[17.47,17.90]*
	Yes	0.223	1.2498	0.0727	0.011	[1.10 1.39]*
Diabetics	Coef No(rf)	2.757	15.7	0.5131	0.016	[14.74, 16.75]*
	yes	0.771	2.161	0.0704	0.001	[2.02 2.29]*

4.4 Multivariable Analysis

The multivariable survival analysis in the study is done again by assuming the exponential, Weibull, log-logistic, and log-normal for the baseline hazard function; and the gamma and the inverse Gaussian frailty distributions using Seven most significant covariates from the Univariable output analysis. From the output log-logistic gamma frailty model is selected model by using AIC. Multivariable frailty models, the covariance age group, Co morbidity, lung cancer, severity, oxygen, and Diabetics are significant prognostic factors for Time to cure of covid -19 datasets. The confidence interval of its acceleration factor does not include 1, that indicates 5% level of significance indicating that prognostic factor for the Time to cure of covid- 19 are age group, co morbidity, lung cancer, severity, oxygen, and diabetics are significant in four models, like weibull- gamma frailty, Weibull- inverse Gaussian frailty, log-logistic- gamma frailty, log logistic-inverse Gaussian frailty, log-normal- gamma frailty, lognormal- inverse Gaussian frailty, exponential- gamma frailty, exponential- inverse Gaussian frailty, whereas Sex of patients, hypertension is not significant in those four models.

The AIC value of the log-logistic- Gamma model is **1609.6** is the minimum from all the other AIC values of the models which indicates that it is the most efficient model to fit with various parametric frailty models in the covid-19 dataset. Analysis based on log-logistic- Gamma frailty model shows that the age group, co morbidity, lung cancer, Severity, oxygen, and Diabetics were significant at a 5% level of significance. This indicates that they were the contributing factor for the Time to cure of Covid-19.

However, according to this model Sex of patients; hypertension has no significant effect on the time to cure of covid-19. co morbidity of the covid-19 patient (Yes) had a significantly different Time to cure of Covid-19 than the reference groups (No) with an acceleration factor of 1.376 when the effect of other factor kept fixed. The respective 95% confidence interval was [1.200, 1.577]. Therefore, the Co morbidity of covid19patient had a longer Curing time from covid-19 by a factor of 1.376 than the reference group (no).

The result of this study suggested that the age of covid-19 patients had a significant effect on the time to cure of the covid-19 dataset. Patient with age $(5-14, >= 15)$ had significantly different Curing time than the reference age group (1-4) with acceleration factor (Θ= 3.68,5.842). Therefore, Patients with age $(5-14, >= 15)$ years had prolonged time to cure of covid-19 by a factor of (3.68, 5.842) than reference age group (1-4)) respectively when the effect of other factors kept fixed. The Severity of Covid-19 (moderate, severe, and critical) had a significantly different Time

to cure of covid-19 than the reference groups (mild) with an acceleration factor of [1.399, 1.5896 and 2.532] respectively. Their respective 95% confidence interval was [1.238, 1.580], [1.400, 1.804] and [1.995, 3.214]. Therefore, with severity 0f covid-19 moderate, sever and critical had longer time to cure of covid-19 by a factor of 1.399, 1.5896 and 2.532 respectively than the reference group (mild). From we can understand the severity of covid-19 increase the time required for curing of covid-19 also increases. Depending on the result, diabetics of covid-19 patients (yes) had a significantly different Time to cure Covid-19 than the reference groups (no) with an acceleration factor of 2.162 when the effect of other factors kept fixed. The respective 95% confidence interval was [1.011, 3.31368]. Therefore, covid-19 patient having diabetics had prolonged curing time of covid-19 by a factor of 2.162. Source(4.3)

Table 4.3: Results of Loglogstic-Gamma multivariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Intercept	Coef	0.84413	2.325	0.9967	0.067	[0.329, 4.27]
Age group	1-4(rf)					
	5-14	1.30483	3.687	0.1856	0.032	[2.56 ,5.30]*
	>=15	1.76514	5.842	0.1743	0.034	[4.151 ,8.222]*
Comrbidity	No(rf)					
	Yes	0.31927	1.376	0.0695	0.003	[1.20 ,1.57]*
Lungcancer	No(rf)					
	Yes	0.28741	1.3329	0.1245	.001	[1.04 ,1.70]*
Severity	Mild(rf)					
	moderate	0.33581	1.3990	0.0622	.001	[1.23, 1.58]*
	severe	0.46349	1.5896	0.0646	0.016	[1.40, 1.80]*
	critical	0.92920	2.532	0.1217	.0034	[1.99 ,3.21]*
Oxygin	No(rf)					
	Yes	0.8912	2.4380	0.0440	0.050	[1.34, 3.52]*
Diabetics	No(rf)					
	Yes	0 .771209	2.162	.0718	0.004	[1.01, 3.31]*
$\tau = 0.995$	θ= 0.959 λ=0.179	ρ= 3.774		AIC=1609.625		

Data sours=JUCC and SHGCC in 2021 $\hat{\beta}$= coefficents,St.err =standard erro, ϕ = accelareted factor, τ=kendel's tau, θ=variance of random effect, λ =scale, ρ =shape

4.4.1 Model Comparison

Table 4.4: Model Compared with AIC

Model			
Baseline hazard function	frailty distribution	AIC	BIC
Exponential	Gamma	2030.071	645.0501
	Inversgausian	2029.364	645.0509
Loglogstic	Gamma	**1609.625**	**393.9638**
	Inversgausian	1610.186	394.0478
Lognormal	Gamma	1625.238	406.6858
	Inversgausian	1625.720	407.5847
Weibull	Gamma	1625.720	412.0174
	Inversgausian	1622.609	412.0041

From the above table 4.4 summarizes all the results of the four baseline hazard function with two frailty models. Among those models, the Gamma frailty model with log-logistic baseline hazard function has the smallest AIC (1609.625) fit the model well.

4.4.2 Tests of unobserved heterogeneity

Table 4.5: test of unobserved hetrogeneity

	Model				
Baseline	Frailty	θ	LRT	τ	p value
Exponential	Gamma	0.00615	145	0.003	0.006
	Inversgausian	0.0314	146	0.001	0.0007
Loglogstic	Gamma	**0.959**	445	0.995	0.002
	Inversgausian	0.0506	444	0.788	0.000
Lognormal	Gamma	0.954	434	0.005	0.002
	Inversgausian	0.0563	434	0.948	0.0009
Weibull	Gamma	0.942	443	0.05	0.0003
	Inversgausian	0.0378	443	0.078	0.0005

θ=variance of random effect,τ=kendel's tau,LRT=likelihood ratio

From result various frailty models to predicted random effect of θ to get an idea on heterogeneity among clusters. When θ is large and significant it has heterogeneity among clusters and a strong correlation among individuals in the same cluster. On the other hand, when θ is equal to zero, there is no frailties which implies that the cluster effects are not present and events are in-

dependent within and across clusters [14] .Likelihood ratio is used for comparing the models with and without frailties .Likelihood test shows at null hypothesis there is no random effect versus alternative hypothesis says there is a random effect. Heterogeneity among parameter θ from the frailty models was estimated using the mariginal Likelihood technique.

From the above table(4.5) test of unobserved heterogeneity ,There is unobserved heterogeneity in Multivariable analysis in the exponential, log-logistic, log-normal and Weibull baseline hazard functions with gamma and Inverse-Gaussian frailty models shows that the likelihood ratio tests of variance of random term θ for exponential-gamma(145) with p-value(0.006), exponential-Inverse-Gaussian(146)with p-value(0.007), loglogstic-gamma(445)with p-value(0.002), loglogstic-Inverse-Gaussian(444) with p-value(0.000),lognormal-gamma(434)
with p-value(0.002).
lognormal-Inverse-Gaussian(434)with p-value(0.009),Weibull-gamma(443)with p-value(0.003), an d Weibull-Inverse-Gaussian(443)with p-value(0.005) ,frailty models with p value are statistically significant .Thus, from this results we can conclude that unobservable heterogeneity is significant in all models at 5% level of significance .From those thesis heterogeneity (variance of random term) is highest for loglogstic-gamma frailty model (θ= 95.9%) followed by loglogstic-Inverse-Gaussian frailty model (θ =5.06%),Next model log-normal-gamma frailty model (θ =95.4%) followed by lognormal-Inverse-Gaussian frailty model (θ =5.63%),third model , Weibull-gamma frailty model (θ =94.2%) followed by Weibull-Inverse-Gaussian frailty model (θ =3.78%) and last model were exponential-gamma frailty model (θ =0.615%) followed by exponential-Inverse-Gaussian frailty model (θ =3.14%) .

Kendall's tau is used to measure the dependence within the clusters (treatment center) and it is higher for the higher variance of random effect for θ values. Kendall's tau $\tau$for the loglogstic -gamma(0.995),loglogstic-inverse Gaussian(0.788), Lognormal-gamma(0.005),Lognormal-inverse Gaussian(0.948),Weibull-gamma(0.05),Weibull-Gaussian(0.078),exponential-gamma(0.003),exponential-inverse Gaussian(0.001) respectively .

From result we can conclude that, on average, there is a correlation between times -to cure of covid-19 within the clusters (treatment center) and highest variance of random effect have highest corrolation in the selected model.

4.5 Checking for overall goodness of fit

4.5.1 Diagnostic Plots of the Parametric Baselines

The model assessment is to be determined by the overall goodness of fit. Therefore, it is desirable to determine whether a fitted parametric model adequately describes the data or not. Check the adequacy of the baseline hazards, from the four parametric baseline plots that log-logistic is linear than others. This indicates that log-logistic is a more appropriate baseline hazard in the Covid-19.

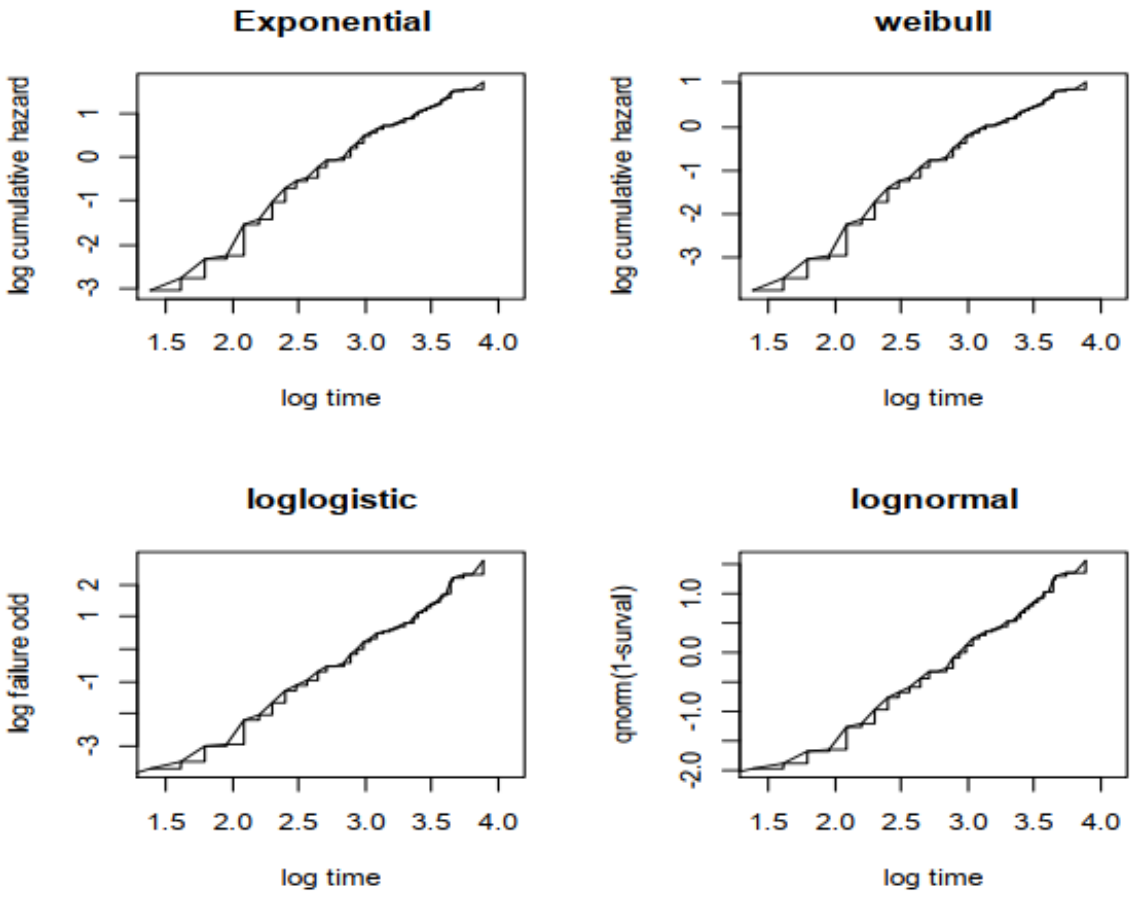

Figure 2: Diagnostic plot for hazard baselines

4.5.2 Cox Snell Residual plots

The cox-snell residual plot is one way of investigating which model is well fitted in the data. The Cox- Snell residuals plot of the cumulative hazard function with the fitting Weibull, log-logistic, exponential, and lognormal with maximum likelihood estimation and looking log-logistic residual plot is linear to the model in the covid-19 dataset that is shown in the figure below.

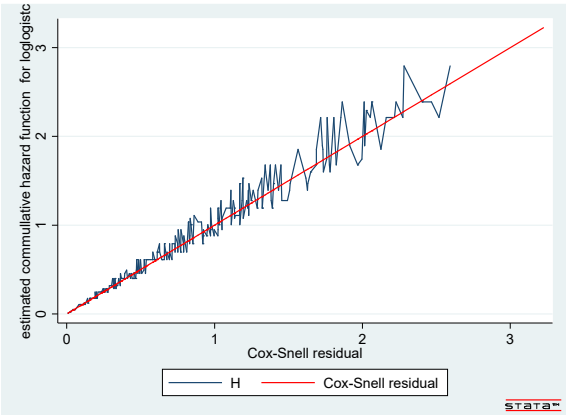

Figure 3: cox snail residual plot

4.5.3 Adequacy of Accelerated Failure Time

The Q-Q plot of the fitted model with adequacy fit for accelerated factor for the failure time has fitted linear or not. By plotting different prognostic covariates with q-q plots has checked the adequacy for fit failure-time of covid-19dataset. Graph of q-q plot of log-logistic with gamma frailty model. The adequacy of the failure time model is well-fitted within the significant prognostic covariate groups shown in the figure below

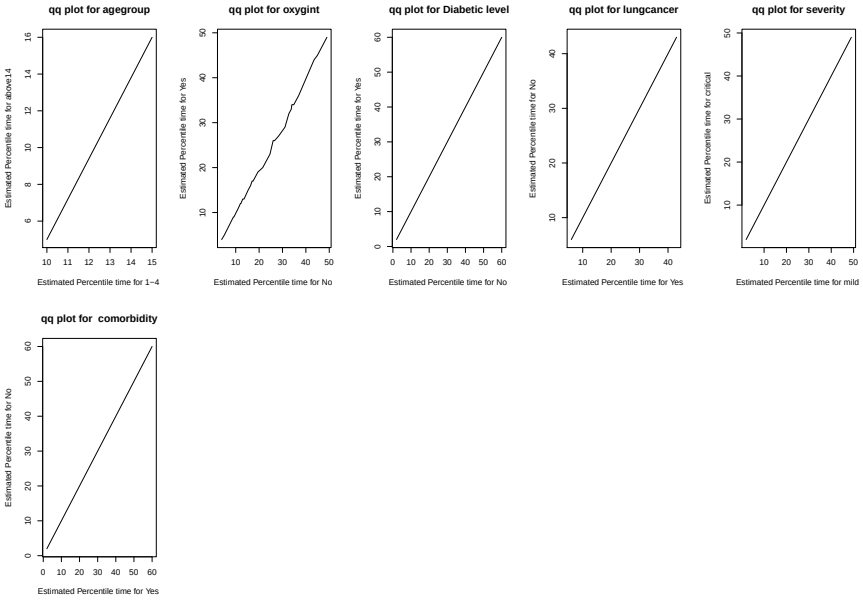

Figure 4: Q-Q plot

4.6 Discussion

Novel Corona viruses was the worst pandemic disease that causes Severe Acute Metabolic Syndrome (SAMS) [1].The distribution of Covid-19 was highly spread in the world and most of patients were cured [4].

The main objective of this finding was to spot the prognostic factors for covid-19 patients within the two treatments in the Jimma zone by using Gamma and Inverse-Gaussian frailty distribution among the various baseline hazard function. The population within the same treatment center relatively has same shared factors [68].

In this thesis (82.564) were cured in two treatment center in Jimma zone with median curing time of 19 days with maximum and minimum median curing time was 48 and 2 days respectively.In this result the same treatment care center shares skill of doctor, bedroom, environment, health facilities, covid-19 treatment, and other determinant factors for time-to-cure from covid-19 were considered. The result showed that there was frailty effect on the modeling time to cure of covid -19 due to heterogeneity in treatment centers.

Comparison of the various parametric frailty distribution with baseline of hazard function was done by smallest AIC value selected [85].From this thesis loglogstic-Gamma frailty distribution with smallest AIC(1609.625) was selected model to determine a clustering (frailty) effect on modeling time to Cure from covid-19 be due to the heterogeneity within two treatment care center (JUCC, SHGCC).

Clusters with smallest median Curing time have smaller frailties. So that these clusters are predicted to have a less hazard [53, 70].The random effect modify the hazard function, the hazard function should be evaluated conditionally on this effect. The treatment care centers which have more frail are les likely to cure than the less frail in the treatment care center.

This thesis showed that the median curing time of covid-19 was 19 days with 95% C.I [11, 23]. This study was agreed by study conducted in China which showed that the median curing time takes 4 to 53 days within China, and 4 to 21 days outside of China [38].

Depending on severity of covid 19 patients have different time lengths to cure of covid-19.The study conducted the median curing time of mild was 13 days with CI[10 ,20],moderate with median curing time 22 with CI[18, 32],sever was median curing time 24 days with C.I[21, 38] and critical was 48 days with C.I[31,56].How ever current study was in line with study was conducted in Singapore which reports severity of mild patent takes 7-21 days, moderate patients take 25-41 days and severe and critical takes 50-80 days [41, 42] .

In addition to this our current study was in line with the study conducted in the Indian which shown that time to cure was 25 days [35]. However current study was contradicted with the research conducted in New York which revealed that the median curing time of covid 19 patents were 3 days with in the 95%C.I [1 ,6] [37] and also research conducted on Italy were contradicted with this finding with median curing time of Covid-19 was 8 days with 95%C.I[5,11] [39].Also the study contradicted with study done in the Swiss medical hospital which revealed that the median curing time of 7 days with 95%C.I[4,10] [40].The causes of discrepancies may be due to severity of the disease, accesses given to covid-19 patents, sample of population ,co morbidity of the patients, skill of doctors , Living standard of patient, and as well as oxygen supply given to the patients makes the differences.

From this discovery the Severity was one prognostic factor that affect time to cure from covid-19. Our current study was supported by literature review in severity also affects the prolonging time to cure Covid-19 [35, 31, 36]. So the content of Severity of Covid-19 is curtail factor for time to cure from covid-19.Government give great attention to supply of oxygen for Sever (critical) patients especially. Attentively doctors treat are required for Sever (critical) patients that minimize content of Severity.

From this result age group was significant prognostic factor of time to cure of covid-19.In addition to this our current study supported with study was conducted in India, Italy, Japan, Singapore, Canada, and the Republic of Korea [49]. Because the similarity due to age increases the metabolic activity also decreased and various amounts of co morbidity increase, for such cases the variation of patients' quality is additionally decreasing. So elder person consumes more prolonged time to cure from Covid-19 compared with counterparts.

From the result of these diabetics was the prognostic factor for time to cure of Covid-19 with accelerated factor 2.262 with C.I [1.011, 3.313]. So current Study was argued by study was conducted in China, by using Coxph model which shown that diabetics was prognostic factor for time to cure with 95 %C.I [23, 91]. Diabetics are one prognostic factor to increase severity of Covid 19 and have longer prolonged time to cure from covid-19. The median curing time of covid-19 was 12 days with in 95% C.I (7–15) with P value 0.022 in China [44, 45]. From this thesis the diabetic patients consumes prolonged time to cure from Covid-19 and most of the diabetic patients are not cured.

This thesis was report based on patient's intake of oxygen was leading prognostic factor for time to cure from covid-19.In addition to current study was supported by The scholars conducted on the prevalence of oxygen with covid-19.By using multiple logistic regration models to analysis

prevalence of oxygen with Covid-19 and conclude that Oxygen treatment was highly required in COVID-19 patients. A scholar conducted on the prevalence of Oxygen therapy was required for patients. The oxygen supply of patients (odds ratio [OR] 2.072, 95% confidence interval CI[1.312-3.27] [50].

Lung cancer was prognostic factor for time to cure of covid-19 and the patient having lung cancer has low chance to cure from this result. Current study was agreed with the study conducted on literature review [42, 6, 46].

The most appropriate model was checked by Cox snail. Log-logistic-Gamma frailty model was best fitted model for Covid-19 dataset. Adequacy of model can be checked by using graphs under Q-Q plot used to check accelerated failure time.Adequacy fit For different group of population compared with reference group with graph showed that linear comparative group of covariates.

5 CONCLUSION AND RECOMENDATION

5.1 Conclusion

Various parametric frailty models were used for this thesis to find time to cure of covid-19.From that frailty model log-logistic-gamma frailty model was best fitted model for covid 19 dataset. There was a frailty (clustering) effect on the time to cure from covid-19 due to heterogeneity between the treatment care center (JUCC, SHGCC). Based on this result patient was cured with average median curing time of 19 days in two treatment care center. From these finding elders, co morbid, severe, critical, lung cancer, diabetics, and oxygen intake have had more prolonged time to cure from Covid-19 than the counterparts. In generally the median curing time of covid-19 in Jimma zone is 19 days was more prolonged time compare to developed countries.

5.2 Recommendations

The study has a small print of implications in general. Hence, supported the results of this study we must attentively make the subsequent recommendations:

⋆ every person should manage themselves from the attack of covid 19 by keep the principle of WHO especially the co morbid person and Aged person has managed to realize themselves from Covid-19.

⋆ this study finds that some unobserved characteristics were not assumed. The study recommends further Study must be carried out to explore those unobserved impact on covid-19

⋆ Additional treatment and attention will give the diabetic,, co morbid ,elders, severity of disease ,lung cancer patients to control covid-19 to adapted severity of the disease.

⋆ From this result there was scarcity of oxygen supply in both treatment care center.Especially Government should fulfill oxygen supply in every treatment center

⋆ Jimma University and , Shenen Gibe covid care center must recorded BMI,height,weight, blood type for the further study.

⋆ Federal ministry of health must keep variation of treatment care center by fulfilling equal access.

⋆ WHO must give special treatment for elders, co morbid, diabetics, hypertensive, critical (sever) patients.

⋆ For further study interested to comparing parametric frailty models, researcher Recommend that simulation studies to get more appropriate results.

5.3 Limitations of the study

There are some limitations on this finding. The main challenge was lack of literature review. In addition to the required variables such as BMI, Height, Weight and Blood type have not recorded.

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6 ANNEX

6.1 Annex1:Univariable Analysis for Frailty Models

Table 6.1: Weibull- Gamma Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Sex	Coef	3.1865	24.20	0.0903	0.0023	[24.02,24.37]*
	female(rf)					
	Male	0.0774	1.08	0.0696	0.487	[0.94 , 1.214]
AGe group	Coef	1.08	2.9586847	0.244	0.018	[1.835, 4.769]*
	1-4(rf)					
	5-14	1.20	3.3320097	0.0047	0.0089	[2.059 , 5.39]*
	$>= 15$	2.22	9.1958910	0.229	0.0056	[5.86, 14.41]*
Co-morbidity	Coef	2.917	18.48	0.0903	0.0637	[18.30,18.66]*
	No(rf)					
	Yes	0.728	2.070	0.0658	0.0498	[1.94 2.19]*
Lung cancer	Coef	3.16	23.57	0.351	0.0001	[22.88,24.25]*
	No(rf)					
	Yes	1.18	3.25	0.235	0.009	[2.79 3.71]*
Hypertension	Coef	3.138	23.05	3.138	0.0019	[16.907,29.20]*
	No(rf)					
	Yes	0.519	1.68	0.0993	0.008	[1.48 , 1.87]*
Severity	Coef	2.791	16.29	0.5920	0.078	[15.13,17.45]*
	mild(rf)					
	moderet	0.528	1.69	0.0669	0.045	[1.56 , 1.82]*
	Sever	0.721	2.05	0.0689	0.028	[1.92 , 2.19]*
	critical	0.825	2.28	0.089	0.005	[2.107, 2.45]*
Oxygen	Coef	3.125	22.75	0.0811	0.002	[22.60,22.91]*
	No(rf)					
	Yes	0.211	1.23	0.0663	0.007	[1.36 1.10]*
Diabetics	Coef	3.022	20.53	0.4380	0.024	[19.67,21.39]*
	No(rf)					
	Yes	0.699	1.99	0.0818	0.012	[1.83 2.15]*

Table 6.2: Lognormal-Gamma Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Sex	Coef	2.9313	18.7	0.1389	0.042	[18.47,19.02]*
	female(rf)					
	Male	0.0754	1.07	0.0797	0.89	[0.92 1.23]
AGe group	Coef	0.922		0.275	0.0001	[6.67,7.96]*
	1-4(rf)					
	5-14	1.263	2.5148	0.298	0.0189	[1.46, 4.31]*
	$>= 15$	2.124	8.36838	0.277	0.006	[4.86, 14.403]*
Co-morbidity	Coef	2.657	14.25	0.6752	0.0023	[12.93,15.57]*
	No(rf)					
	Yes	0.839	2.31	0.0639	0.0012	[2.18 2.43]*
Lung cancer	Coef	2.90	18.17	0.440	0.0045	[19.03,17.31]*
	No(rf)					
	Yes	1.21	3.35	0.175	0.0012	[3.694 3.01]*
Hypertension	Coef	2.867	17.58	0.2741	0.012	[17.04,18.12]*
	No(rf)					
	Yes	0.656	1.92	0.0983	0.002	[1.73 2.11]*
Severity	Coef	2.544	12.73	0.6346	0.001	[11.48,13.97]*
	Mild(rf)					
	moderate	0.598	1.81	0.0732	0.021	[1.67 , 1.96]*
	Sever	0.699	2.01	0.0699	0.0006	[1.87 , 2.14]*
	Critical	1.475	4.37	0.1367	0.0045	[4.10 , 4.63]*
Oxygen	Coef	2.815	16.69	0.4518	0.021	[15.80,17.57]*
	No(rf)					
	Yes	0.664		0.0814	0.018	[0.94 1.214]*
Diabetics	Coef	2.750	15.64	0.6027	0.0001	[14.46,16.82]*
	No(rf)					
	Yes	0.821	2.27	0.0756	0.0012	[2.12 , 2.42]*

Table 6.3: Exponential -Gamma Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI (ϕ)
Sex	Coef female(rf)	3.148	0.1	23.28	0,0001	[23.08,23.287]*
	Male	0.0898	1.09	0.132	0.23	[0.88 , 1.34]
AGe group	Coef 1-4(rf)	1.00	2.7307	0.502	0.009	[1.021, 7.29]*
	5-4	1.24	1.86	3.4536	0.00006	[1.19, 9.98]*
	$>= 15$	2.30	9.979	0.505	0.0089	[3.71, 26.83]*
Co-morbidity	Coef No(rf)	2.78	16.11	0.0846	0.001	[15.95,16.28]*
	Yes	1.11	3.03	0.1419	0.0056	[2.75 3.31] *
Lung cancer	Coef No(rf)	3.09	21.97	0.0645	0.0089	[21.85,22.10]*
	Yes	2.08	8.00	0.4518	0.050	[7.12 8.88]*
Hypertension	Coef No (rf)	3.080	21.75	0.034	0.0682	[20.87,22.64]*
	Yes	0.807	2.24	0.1921	0.0089	[1.86 , 2.61]*
Severity	Coef mild(rf)	2.64	14.01	0.103	0.00091	[13.81,14.21]*
	moderate	0.62	1.85	0.163	0.0067	[1.65 , 2.06]*
	Sever	1.01	2.74	0.165	0,025	[2.42 , 3.06]*
	Critical	2.61	13.59	0.455	0.014	[12.70 , 14.49]*
Oxygen	Coef No(rf)	3.09	21.97	0.0887	0.045	[21.80,22.15]*
	Yes	0.27	1.309	0.1276	0.008	[1.05 , 1.56]*
Smoking	Coef No(rf)	3.008	20.24	3.23	0.034	[13.91,26.57]*
	Yes	0.811	2.25	0.1609	0.009	[1.93 , 2.56]*
Diabetics	Coef No(rf)	2.90	18.17	0.083	0.011	[18.01,18.33]*
	Yes	1.11	3.034	0.164	0.012	[2.712 , 3.35]*

Table 6.4: Weibbull - Inverse-Gaussian Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Sex	Coef	3.1844	24.15	0.0967	0.0125	[23.96,24.34]*
	female(rf)					
	Male	2.193		0.1548	0.077	[0.94 1.214]
AGe group	Coef	1.08	2.94200	0.249	0.021	[1.81, 4.79]*
	Age1-4(rf)					
	Age5-14	1.20	3.3335683	0.246	0.005	[2.06, 5.39]*
	Age>=15	2.22	9.2088599	0.229	0.002	[5.87,14.43]*
Co-morbidity	Coef	2.911	18.37	0.1057	0.031	[18.16,18.58]*
	No(rf)					
	Yes	0.727	2.06	0.0658	0.009	[1.93 , 2.19]
Lung cancer	Coef	3.15	23.33	0.006	0.0884	[23.16,23.50]*
	No(rf)					
	Yes	1.18	3.25	0.23548	0.044	[2.79 , 3.71]*
Hypertension	Coef	3.134	22.96	0.0828	0.007	[22.80,23.127]*
	No(rf)					
	Yes	0.519	1.68	0.0994	0.0012	[1.48 1.87]*
Severity	Coef	2.786	16.21	0.10343	0.0056	[16.01,16.41]*
	Mild(rf)					
	Moderate	0.527	1.69	0.0669	0.0044	[1.56 , 1.82]*
	sever	0.720	2.05	0.0688	0.0089	[1.91 2.18]*
	Critical	1.447	4.25	0.1914	0.0071	[4.11 , 4.38]
Oxygen	Coef	3.123	22.71	0.0878	0.0031	[22.54,22.88]*
	No(rf)					
	Yes	0.211	1.23	0.0663	0.0043	[0.94 , 1.36]*
Diabetics	Coef	3.016	20.40	0.0141	0.1071	[20.19,20.6]*
	No(rf)					
	Yes	0.698	2.00	0.0818	0.0022	[1.84 2.17*

Table 6.5: Loglogstic - Inverse-Gaussian Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value 95% CI (ϕ)	
Sex	Coef	2.9493	19.09	0.1278	0.0025	[18.84,19.34]*
	female(rf)					
	Male	0.0441	1.08	0.18	0.0801	[0.72 1.43]
AGe group	Coef	0.872	7.86	0.257	0.012	[1.44,3.95]*
	1-4(rf)					
	5-14	1.320	1.71	0.278	0.0126	[2.17, 6.45]*
	>=15	2.176	2.63	0.259	0.0078	[5.305, 14.636]*
Co-morbidity	Coef	2.664	14.35	0.1308	0.000	[14.09,14.60]*
	No(rf)					
	Yes	0.799	2.22	0.0595	0.0012	[2.10 , 2.33]*
Lung cancer	Coef	2.90	18.17	0.174	0.0012	[17.83,18.51]*
	No(rf)					
	Yes	2.864	17.53	0.11388	0.05	[17.30 ,17.75]*
Hypertension	Coef	0.615	1.84	0.0911	0.045	[1.67,2.02]*
	No(rf)					
	Ys	2.553	12.84	0.1525	0.001	[12.54 , 13.14]*
Severity	Coef	2.553	12.84	0.1525	0.002	[12.54,13.14]*
	Mild(rf)					
	moderate	0.578	1.78	0.0699	0.0034	[1.64 , 1.91]*
	Sever	0.788	2.19	0.0636	0.00031	[2.07 , 2.32]*
	critical	1.413	4.10	0.1334	0.0016	[3.84 , 4.36]*
Oxygen	Coef	2.868	17.60	0.1260	0.0039	[17.35,17.84]*
	No(rf)					
	Yes	0.223	1.24	0.0727	0.0068	[1.107 , 1.39]*
Diabetics	Coef	2.75	15.64	0.1295	0.0015	[15.38,15.89]*
	No(rf)					
	Yes	0.77	2.15	0.0704	0.009	[2.021 , 2.29]*

Table 6.6: Lognormal- Inverse-Gaussian Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI (ϕ)
Sex	Coef	2.9247	18.62	0.1355	0.001	[18.36,18.89]*
	female(rf)					
	Male	1.978	7.22	0.179	0.87	[6.87 , 7.57]*
AGe group	Coef	0.922	1.1813	0.296	0.019	[-0.52,2.88]
	1-4(rf)					
	5-14	1.269	2.619	0.286	0.0023	[1.42 , 3.82]*
	>=15	2.138	1.6135	0.266	0.009	[1.48 2.75]*
Co-morbidity	Coef	2.648	14.12	0.1330	0.0017	[13.86,14.38]*
	No(rf)					
	Yes	0.83	2.29	0.0639	0.021	[2.16 2.41]*
Lung cancer	Coef	2.89	17.99	2.125	0.0001	[13.82,22.15]*
	No(rf)					
	Yes	1.21	3.35	0.175	0.0014	[3.01 3.69]*
Hypertension	Coef	2.859	17.44	0.1204	0.005	[17.20,17.68]*
	No(rf)					
	Yes	0.657	1.92	0.0984	0.0007	[1.73,2.12]*
Severity	Coef	2.532	12.57	0.1531	0.001	[12.27,12.87]*
	mild(rf)					
	moderate	0.598	1.81	0.0732	0.00189	[1.67 , 1.96]*
	Sever	0.848	2.33	0.0700	0.006	[2.19 , 2.47]*
	critical	1.474	4.36	0.1366	0.0068	[4.09 , 4.63]*
Oxygen	Coef	2.874	17.70	0.1321	0.0031	[17.44,17.96]*
	No(rf)					
	Yes	0.196	1.21	0.0753	0.001	[1.36 , 1.06]*
Diabetics	Coef	2.74	15.48	0.13445	0.0011	[15.22,15.75]*
	No (rf)					
	Yes	1.82	6.17	0.578	0.004	[5.90 , 6.43]

Table 6.7: Exponential vs Inverse-Gaussian Univariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Sex	Coef	3.151	23.35	0.121	0.000	[23.12,23.59]*
	female(rf)					
	Male	0.116	1.12	0.132	0.91	[0.86 1.38]
AGe group	Coef	.0127272	2.514	0 .498	0.00001	[-1.64,3.67]
	1-4(rf)					
	5-14	1.097829	3.55592	0.171	0.0015	[1.597 4.39]*
	>=15	1.72914	8.4818	0.1810	0.00065	[4.23, 7.04]*
Co-morbidity	Coef	2.78	16.11	0.113	0.009	[15.89,16.34*
	No(rf)					
	Yes	0.839	2.31	0.0639	0.0038	[2.18 2.43]*
Lung cancer	Coef	2.0915	8.09	0.0915	0.0006	[7.91,8.27]*
	No(rf)					
	Yes	2.09	8.08	0.4518	0.00036	[7.19 8.97]*
Hypertension	Coef	2.78	16.11	0.113	0.001	[15.89,16.34]*
	No (rf)					
	Yes	0.839	2.31	0.0639	0.008	[2.18 2.43]*
Severity	Coef	2.643	14.05	0.133	0.0012	[13.79,14.31]*
	Mild (rf)					
	moderate	0.624	14.05	0.163	0.018	[13.79 14.31]*
	Sever	1.013	2.75	0.165	0.0017	[2.43 3.07]
	critical	2.618	13.70	0.455	0.00089	[12.81 14.60]
Oxygen	Coef	3.088	21.93	0.104	0.00015	[21.72,22.13]*
	No(rf)					
	Yes	0.268	1.307	0.128	0.0066	[1.05 1.55]*
Diabetics	Coef	2.90	18.17	0.114	0.0082	[17.95,18.39]*
	No(rf)					
	Yes	1.12	3.06	0.164	0.00014	[2.74 3.38]*

6.2 Annex2:Multivariable Analysis for Frailty Models

Table 6.8: Weibull-gamma Multivariable Analysis for Frailty Models

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Intercept	Coeff	1.0622	2.879	0.89	0.6661	[0.783 ,10.673]
Sex	female(rf)					
	Male	0.0148	1.0149	0.0491	0.45	[0.921 .1.117]
Agegroup	1-4(rf)					
	5-14	1.2185	3.382	0.1915	0.019	[1.70 ,2.25]*
	>15	1.7574	5.797	1.7574	0.03	[1.17 , 2.09]*
Comorbidity	No(rf)					
	Yes	0.2850	1.3297	0.0711	0.023	[1.06 , 1.36]*
Lungcancer	No(rf)					
	Yes	1.233484	3.433	0.1376	0.0091	[8.80 , 9.10]*
hyphertension	No(rf)					
	Yes	0.989	2.688	0.0766	0.014	[2.53 , 2.83]*
Severity	mild rf)					
	moderate	0.2984	1.3477	0.0666	0.034	[1.08 ,1.31]*
	Sever	0.4693	1.5988	0.0646	0.031	[1.35 1.59]*
	critical	0.9102	2.4848	0.1701	0.0018	[1.85 , 2.41]*
Oxygin	No(rf)					
	Yes	2.8802	17.81	0.0423	0.0061	[17.73 , 17.9]*
Diabtics	No(rf)					
	Yes 1	0.6993	2.01234	0.0747	0.0019	[1.86 , 2.15]*
	$\tau = 0.05$	θ= 0.942 λ=0.003	ρ= 2.883		AIC=1622.098	

Data, Jimma university and shenen gibe covid center 2021

$\hat{\beta}$= coefficient, St. err= standard error, ϕ = acceleration factor, τ=Kendaell's tau, θ=variance of random effect, λ scale, ρ =shape

Table 6.9: Result of lognormal-gamma multivariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Intercept	Coeff	0.88422	2.421095	0.7202	0.89	[0.59, 9.93]
Sex	female(rf)					
	Male	-0.02522	0.9750	0.0465	0.90	[0.89, 1.07]
Agegroup	1-4(rf)					
	5-14	1.27199	2.15	0.0728	0.0067	[2.44, 5.21]*
	>15	1.72914	3.58	0.1024	0.0001	[3.95 ,8.03]*
Comorbidity	No					
	Yes	0.32125	1.42	0.0685	0.0017	[1.21 ,1.58]*
Lungcancer	No(rf)					
	Yes	0.27832	1.230	0.1218	0.0019	[1.04, 1.67]*
Hyphertension	No (rf)					
	Yes	-0.01165	1.70	0.0773	0.0034	[1.55 , 1.85]*
Severity	Mild(rf)					
	Moderat	0.24500	1.27	0.0615	0.0056	[1.15, 1.39]*
	Sever	0.43864	1.55	0.0660	0.0026	[1.42 1.67]*
	critical	0.75867	2.13	0.1187	0020	[1.90 2.36]*
Oxygin	No (rf)					
	Yes	.1940511	1.214	.1940511	0.0039	[1.05 2.38]*
Diabetics	No(rf)					
	Yes	.8276743	2.28799	.0773089	0.0082	[1.12, 3.45]*
AIC=1625.238	$\tau = 0.005$	θ= 0.954λ=3.774	ρ= 1.209		AIC=116.2073	

Data, Jimma university and shenen gibe covid center 2021

$\hat{\beta}$= coefficient, St. err= standard error, ϕ = acceleration factor, τ=Kendaell's tau, θ=variance of random effect, λ scale, ρ =shape

Table 6.10: Result of exponential -gamma multivariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Intercept	Coef	0.95081	2.5878	0.527	0.65	[0.92,7.27]
Sex	female(rf)					
	Male	0.00547 0	1.005	0.137	0.88	[0.76, 1.31]
Agegroup	1-4(rf)					
	5-14	1.23852	3.450	0.546	0.0016	[1.18, 10.06]*
	>15	0.76982	2.159	0.0728	0.009	[2.01, 14.98]*
Comorbidity	No(rf)					
	Yes	0.41502	1.42	0.205	0.0034	[1.012, 2.26]*
Lungcancer	No(rf)					
	Yes	1.06180	2.891	0.478	0.0026	[1.13, 7.37]*
Hyphertension	No(rf)					
	Yes	0.07233	1.0750	0.247	0.73	[0.66, 1.74]
Severity	mild(rf)					
	moderate	0.24500	1.27	0.0615	0.0045	[1.15, 1.39]*
	sever	1.4086814	4.090	0.0660	0.00023	[1.22, 2.60]*
	critical	1.7805054	5.932	0.1187	0.0018	[2.3,15.6]*
oxygin	No					
	Yes	3.215	24.90	0.0423	0.0001	[24.81 24.99]*
Diabetics	No(rf)					
	Yes	0.24289	1.27	0.0747	0.0078	[1.11 1.43]*
	$\tau = 0.003$	θ= 0.00615 λ= 0.022			AIC=2030.071	

Data, Jimma university and shenen gibe covid center 2021

$\hat{\beta}$= coefficient, St. err= standard error, ϕ = acceleration factor, τ=Kendaell's tau, θ=variance of random effect, λ scale, ρ =shape

Table 6.11: Results of Weibull-InversGaussian multivariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Intercept	Coef	1.0574	2.8788	0.2221	0.089	[1.86, 4.44]
Sex	female(rf)					
	Male	0.0155	1.01562	0.0491	0.71	[0.92, 1.11]
AgeGroup	1-4(rf)					
	5-14	1.2172	3.3777	0.1915	0.0016	[2.32, 4.91]
	>=15	1.7545	5.780	0.1798	0.002	[4.06, 8.22]
Co-morbidity	No(rf)					
	Yes	0.2845	1.3290	0.0711	0.008	[1.15, 1.52]
Lung cancer	No(rf)					
	Yes	0.3610	1.434763	0.1676	0.0075	[1.03, 1.99]
Hypertension	No(rf)					
	Yes	0.0268	1.0271	0.0872	0.284	[0.86, 1.21]
Severity	mild(rf)					
	moderate	0.2981	1.3472	0.0666	0.0043	[1.18 ,1.53]
	Sever	0.4693	1.5988	0.0646	0.0036	[1.40, 1.81]
	critical	0.9094	2.4828	0.1700	0.0021	[1.77, 3.46]
Oxygen	No(rf)					
	Yes	0.0571	1.0587	0.0478	0.0071	[24.81 24.99]
Diabetics	No(rf)					
	Yes	.6990915	2.011924	.0791182	0.0041	[0.84 3.17]
	$\tau = 0.078$	θ= 0.199 λ=0.002	ρ= 2.929		AIC=1622.609	

Data, Jimma university and shenen gibe covid center 2021

$\hat{\beta}$= coefficient, St. err= standard error, ϕ = acceleration factor, τ=Kendaell's tau, θ=variance of random effect, λ scale, ρ =shape

Table 6.12: Results of Loglogstic-InversGaussian multivariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI (
Intercept	Coef	0.83133	2.29637	0.2321	0.268	[1.45, 3.6
Sex	female(rf)					
	Male	-0.03411	0.9664	0.0454	0.058	[0.88,1.0
AgeGroup	1-4(rf)					
	5-14	1.30585	3.6908	0.1855	0.0081	[2.56,5.3
	>=15	1.76622	5.8487	0.1743	0.0092	[4.15, 8.2
Co-morbidity	No(rf)					
	Yes	0.31920	1.3760	0.0695	0.00389	[1.20,1.5
Lung cancer	No(rf)					
	Yes	0.28729	1.3328	0.1244	0.0001	[1.00 , 1.4
Hypertension	No(rf)					
	Yes	-0.01449	0.9856	0.0773	0.93	[0.84 ,1.1
Severity	mild(rf)					
	moderate	0.33576	1.3990	0.0622	0.0056	[1.23, 1.5
	Sever	0.46326	1.589	0.0646	0.0048	[1.40 ,1.8
	critical	0.92820	2.5299	0.1216	0.001	[1.99,3.2
Oxygen	No(rf)					
	Yes	0.08906	1.093	0.0440	0.034	[1.00, 1.1
Diabetics	No(rf)					
	Yes	0.7712102	2.162382	.0718838	0.0081	[1.01 3.3
	$\tau = 0.388$	θ= 0.0506 λ=3.159	ρ= -11.492		AIC=1610.186	

Data, Jimma university and shenen gibe covid center 2021

$\hat{\beta}$= coefficient, St. err= standard error, ϕ = acceleration factor, τ=Kendaell's tau, θ=variance of random effect, λ scale, ρ =shape

Table 6.13: table Results of lognormal-InversGaussian multivariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Intercept	Coeff	0.87223	2.3922	0.2388	0.289	[1.49, 3.81]*
Sex	female(rf)					
	Male	-0.02505	0.9752	0.4585	0.816	[0.89, 1.06]
Agegroup	1-4(rf)					
	5-14	1.27190	3.567	0.1930	0.0018	[2.44,5.20]*
	$>= 15$	1.72887	5.6342	0.0811	0.0029	[3.95, 8.03]*
Co-morbidity	No(rf)					
	Yes	0.32126	1.378	0.0685	0.0018	[1.21, 1.57]*
Lung cancer	No(rf)					
	Yes	0.27859	1.3212	0.1219	0.0014	[1.1,1.67]*
Hypertension	No(rf)					
	Yes	-0.01133	0.9887	0.0783	0.156	[0.84, 1.15]
Severity	mild(rf)					
	moderate	0.33865	1.4030	0.0630	0.0019	[1.24, 1.58]*
	sever	0.47815	1.613	0.0663	0.001	[1.41, 1.83]*
	critical	0.94491	2.5725	0.1244	0.0034	[2.01, 3.28]*
Oxygen	No (rf)					
	Yes	0.08684	1.090	0.034	0.0011	[1.1,1.19]*
Diabetics	No(rf)					
	Yes	0.8277297	2.2881	0.0772966	0.00145	[1.12 , 3.45]
	$\tau = 0.195$	θ= 0.0563 λ= 4.179	ρ= 3.774		AIC=1625.720	

Data, Jimma university and shenen gibe covid center 2021

$\hat{\beta}$= coefficient, St. err= standard error, ϕ = acceleration factor, τ=Kendaell's tau, θ=variance of random effect, λ scale, ρ =shape

Table 6.14: table Results of exponential-InversGaussian multivariable frailty model

Covariate Variable	category	$\hat{\beta}$	ϕ	St. err	p-value	95% CI(ϕ)
Intercept	Coeff	0.94274	2.567	0.535	0.080	[0.89, 7.32]
Sex	female(rf)					
	Male	0.00325	1.0032	0.137	0.44	[0.76, 1.31]
AgeGroup	1-4(rf)					
	5-14	0.30348	1.51	0.0830	0.001	[1.18, 10.08*
	$>= 15$	0.67027	1.95	0.0811	0.0010	[2.02, 15.07]*
Co-morbidity	No(rf)					
	Yes	0.41606	1.5159	0.205	0.0006	[1.01, 2.26]*
Lung cancer	No(rf)					
	Yes	1.06068	2.8883	0.478	0.0017	[1.13, 7.36]*
Hypertension	No(rf)					
	Yes	0.07005	1.0725	0.247	0.27	[0.66, 1.73]
Severity	mild(rf)					
	moderate	0.30404	1.355	0.183	0.0016	[1.156, 1.39]
	Sever	0.58276	1.7909	0.0660	0.004	[1.22, 2.61]
	critical	1.80334	6.069	0.485	0.0017	[2.3, 15.70]
Oxygen	No(rf)					
	Yes	0.07017	1.0726	0.0423	0.0005	[24.81 24.99]*
Diabetics	No(rf)					
	Yes	1.111	3.0373	0.0747	0.00116	[1.65 4.41]*
	$\tau = 0.001$	θ= 0.006 λ=0.022	ρ= 1.67		AIC=2029.364	

Data, Jimma university and shenen gibe covid center 2021

$\hat{\beta}$= coefficient, St. err= standard error, ϕ = acceleration factor, τ=Kendaell's tau, θ=variance of random effect, λ scale, ρ =shape

6.3 coxsnail for non selected model

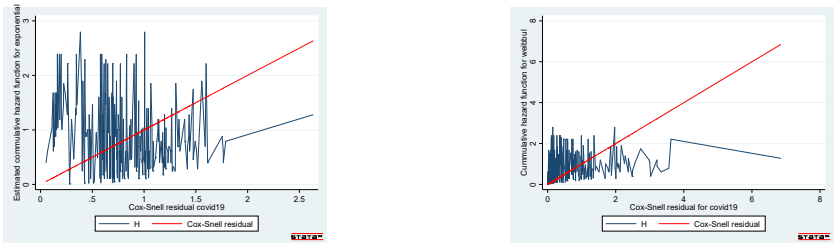

Figure 5: cox snail for non selected model