

Comparison of Cox Proportional Hazard Model and Accelerated Failure Time (Aft) Models: An Application to Neonatal Jaundice

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Abstract

A primary focus of Survival analysis in medicine is modelling time to surviving of a particular disease. In this paper, survival analysis was carried out on the neonatal jaundice data modeling time to surviving the disease. The data was gotten from collected from University College hospital (UCH), Ibadan, Nigeria. The Kaplan-Meier approach was used to describe the survival functions of the neonatal jaundice patients and Log-rank tests was used to compare the survival curves among groups. Different kinds of models such as Cox Proportional Hazard Model and Accelerated Failure Time (AFT) models like Weibull AFT model, Logistic AFT model, Log-normal AFT model, Log-logistic AFT model and Exponential AFT model are considered to be used for modelling the time to surviving neonatal jaundice. Models selection criteria were used as a guide to unravel the best model for modeling neonatal jaundice. The result revealed that the fitted cox proportional hazard model suggested that there were 0.2708 chances of male neonates having higher median time of surviving jaundice compared to female neonates. Based on the mother's health history, neonates whose mother had illness during pregnancy will have 0.5329 chance of having higher median time of surviving the Jaundice compared to neonates whose mother do not have any illness during pregnancy. The log-logistic AFT model out-performed the other models since it has the lowest AIC and the highest log-likelihood value with 1131.461 and -550.7305 respectively.

Keywords: Kaplan-Meier; Model selection criteria; Survival curves; Median time; Log-rank

Introduction

The use of statistics in medicine provides generalization from the public to better understand their risks for certain diseases, such as links between certain behaviors and heart disease or cancer [1]. Survival analysis is an application of statistics mostly used in medicine and has over the years become a discipline itself, enriching not only medicine but statistics in general [2]. Survival analysis is generally defined as a set of methods for analyzing data where the outcome variable is the time until the occurrence of an event of interest [3]. Survival analysis aims to estimate the three survival (survivorship, density, and hazard) functions, denoted by $S(t)$, $f(t)$ and $h(t)$, respectively [4]. There exist parametric as well as non-parametric methods for this purpose [5]. The survival function $S(t)$ gives the probability of surviving beyond time t , and is the complement of the cumulative distribution function, $F(t)$. The hazard function $h(t)$ gives the instantaneous potential per unit time for the event to occur, given that the individual has survived up to time t [5]. White et al. studied four survival analysis models to evaluate differences in length of stay based on Phototherapy treatment of neonatal jaundice and concluded that neonates who received Phototherapy had significantly longer length of Stay than untreated neonates [6]. Folorunso et al. concluded that Termed neonates are at lower risk than Preterm neonates and Rhesus compatibility are at lower risk than neonates with Rhesus incompatibility [7]. Onatunji and Folorunso studied the space-varying effects of jaundice and emphasize the importance of jaundice, which is widely the cause of neonatal mortality [8]. Their results shown a high risk of mortality associated with jaundice within the first 33 days. The estimated residual spatial effects for neonatal mortality shown clear differences between the significantly better survival chances of babies in the Northern state of Nigeria (FCT and some part of Kwara state). Modelling survival data plays an important role in the application of statistics in medicine and health science [9,10], therefore, in this study; survival analysis was carried out on the neonatal jaundice data modeling time to surviving the disease. The Kaplan-Meier approach was used to describe the survival functions of the neonatal jaundice patients and Log-rank tests was used

to compare the survival curves among groups. The time to surviving neonatal jaundice was modeled by using the following models viz: Cox Proportional Hazard Model and Accelerated Failure Time (AFT) models (Weibull AFT model, Logistic AFT model, Log-normal AFT model, Log-logistic AFT model and Exponential AFT model).

Materials and Methods

Data source

Neonatal Jaundice data of 232 patients were used and the data were obtained from Children outpatients (CHOP) units, University College Hospital, Ibadan, Nigeria between 2005 and December 2010 with diagnoses time until death in days. Others variables that were considered are as follows age, sex, gestational age, mother illness, mother education, mode and place of delivery, parity, settlement, Rhesus factor, G6PD and jaundiced neonate which forms part of the predictor variables. Considering the data used, the survival of the jaundice neonates were used as the response variable that is when a jaundice neonate is alive or dead.

Ethical approval

This study will not be completed if the potential ethical problem that may arise in the study is not addressed. The following are some of

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the anticipated ethical problems that may arise:

- Confidentiality of data: The information extracted from the medical records department of University College Hospital are used specifically for this research work, therefore all information's was treated confidentially.
- Beneficence to participants: The information collected was used to evaluate the social and medical value of the study.

Data analysis

In this study, survival analysis was carried out on the data to model time to surviving neonatal jaundice. The Kaplan-Meier approach was used to describe the survival functions of the neonatal jaundice patients and the Log-rank tests was used to compare the survival curves among groups. The time to surviving neonatal jaundice was modelled by using the following models viz: Cox Proportional Hazard Model and Accelerated Failure Time (AFT) models (Weibull AFT model, Logistic AFT model, Log-normal AFT model, Log-logistic AFT model and Exponential AFT model).

The Kaplan Meier product limit method

In Kaplan Meier product limit method, survival probabilities can be obtained as:

$$S = \prod_{k=1}^{j-1} \left(\frac{n_j - d_j}{n_j} \right), k \leq n, t_j \leq t < t_{j+1}$$

Where; d_j = the number of failure in t_j , n_j is the number of incident cases at risk in t_j , k is the number of sequential observations, n is the total number of incident cases.

The log rank test

The log rank test is a hypothesis test to compare the survival distributions of two samples. It is appropriate to use when the data are right skewed and censored.

Hypothesis:

H_0 : No difference between survival curves

H_1 : There is difference between survival curves the log rank statistic for two groups is

$$\frac{(O_2 - E_2)^2}{var(O_2 - E_2)} \sim \chi_{G-1}^2$$

The expected frequency is calculated as

E_{ij} = proportion in risk set \times failures over both groups

$$E_{1j} = \left(\frac{n_{1j}}{n_{1j} + n_{2j}} \right) * (m_{1j} + m_{2j})$$

$$E_{2j} = \left(\frac{n_{2j}}{n_{1j} + n_{2j}} \right) * (m_{1j} + m_{2j})$$

Cox proportional hazard (ph) model

The Cox Proportional Hazards model is given as

$$h(t|x) = h_0(t) \exp(\beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p) = h_0(t) \exp(\beta'x)$$

where $h_0(t)$ is called the baseline hazard function which is the hazard function for an individual for whom all the variables included

in the model are zero., $x = (x_1, x_2, \dots, x_p)'$ is the value of the vector of explanatory variables for a particular individual, and $\beta = (\beta_1, \beta_2, \dots, \beta_p)$ vector of regression coefficients.

The corresponding survival functions are related as follows

$$S(t|x) = S_0(t) \exp\left(\sum_{i=1}^p \beta_i x_i\right)$$

This model, also known as the Cox regression model, makes no assumptions about the form of $h_0(t)$ (non-parametric part of model) but assumes parametric form for the effect of the predictors on the hazard (parametric part of model). The model is therefore referred to as a semi-parametric model.

The hazard ratio of two individuals with different covariates x and x^* is

$$HR = \frac{h(t) \exp(\beta'x)}{\beta'x^*} = \exp(\sum \beta' (x - x^*))$$

This hazard ratio is time-independent, which is why this is called the proportional hazards model.

Accelerated failure time (aft) model

The AFT model describes the relationship between survival probabilities and a set of covariates. For a group with covariates (X_1, X_2, \dots, X_p) , the AFT model is written mathematically as

$$S(t|x) = S_0(t | \eta(x))$$

Where $S_0(t)$ is the baseline survival function and h is an acceleration factor i.e. a ratio of survival times corresponding to any fixed value of $S(t)$.

The acceleration factor is given according to the formula

$$\eta(x) = \exp(\alpha_1 x_1 + \alpha_2 x_2 + \dots + \alpha_p x_p)$$

According to the relationship of survival function and hazard function, the hazard function for an individual with covariate X_1, X_2, \dots, X_p is given by

$$h(t|x) = \left[\frac{1}{\eta(x)} \right] h_0[t | \eta(x)]$$

Under an accelerated failure time model, the covariate effects are assumed to be constant and multiplicative on the time scale, that is, the covariate impacts on survival by a constant factor (acceleration factor). The corresponding log-linear form of the AFT model with respect to time is given by

$$\log T_i = \mu + \alpha_1 X_{1i} + \alpha_2 X_{2i} + \dots + \alpha_p X_{pi} + \sigma \varepsilon_i$$

Where μ is intercept, σ is scale parameter and is a random variable, ε_i assumed to have a particular distribution.

Weibull AFT Model

Suppose the survival time T has $W(\gamma; \lambda)$ distribution with scale parameter and shape parameter, under AFT model, the hazard function for the i th individual is

$$h_i(t) = \frac{1}{[\eta_i(x)]^\gamma} \lambda \gamma (t)^{\gamma-1}$$

Where $\eta_i = \exp(\alpha_1 x_{1i} + \alpha_2 x_{2i} + \dots + \alpha_p x_{pi})$ for individual i with p explanatory variables, so the survival time is given as The Weibull distribution has the AFT property.

If T_i has a Weibull distribution, then e_i has an extreme value distribution (Gumbel distribution). The survival function of Gumbel distribution is given as

$$S_{ei}(\varepsilon) = \exp(-\exp(\varepsilon))$$

The AFT representation of the survival function of the Weibull model is given by

$$S_i(t) = \exp\left[-\exp\left(\frac{-\mu - \alpha_1 X_{1i} - \dots - \alpha_p X_{pi}}{\sigma}\right) t^{\frac{1}{\sigma}}\right]$$

The AFT representation of hazard function of the Weibull model is given by

$$h_i(t) = \frac{1}{\sigma} t^{\frac{1}{\sigma}-1} \exp\left(\frac{-\mu - \alpha_1 X_{1i} - \dots - \alpha_p X_{pi}}{\sigma}\right)$$

The median survival time is

$$t(50) = \exp\left[\sigma \log(\log 2) + \mu + \alpha' x_i\right]$$

The log-logistic AFT model

The log-logistic survival and hazard function are given by

$$S(t) = \frac{1}{1 + e^{\theta} t^k}$$

$$h(t) = \frac{e^{\theta} k t^{k-1}}{1 + e^{\theta} t^k}$$

Where θ and k are unknown parameters and $k > 0$ suppose that the survival times have a log-logistic distribution with parameter k , under the AFT model, the hazard function for the i^{th} individual is

$$h(t) = \frac{e^{\theta - k \log \eta_i} k t^{k-1}}{1 + e^{\theta - k \log \eta_i} t^k}$$

Where $\eta_i = \exp(\alpha_1 x_{1i} + \alpha_2 x_{2i} + \dots + \alpha_p x_{pi})$ for individual i with p explanatory variables. Therefore, the survival time for the i^{th} individual has a log-logistic distribution with parameter $\theta - k \log \eta$ and k , log-logistic distribution has AFT property.

The AFT representation of survival function of the log-logistic model is given by

$$S_i(t) = \left[1 + t^{1/\sigma} \exp\left(\frac{-\mu - \alpha_1 X_{1i} - \dots - \alpha_p X_{pi}}{\sigma}\right)\right]^{-1}$$

The hazard function for the i^{th} individual is given by

$$h(t) = \frac{1}{\sigma t} \left[1 + t^{1/\sigma} \exp\left(\frac{-\mu - \alpha_1 X_{1i} - \dots - \alpha_p X_{pi}}{\sigma}\right)\right]^{-1}$$

The median survival time is

$$t_i(50) = \exp(\mu + \alpha' x_i)$$

The Log-normal AFT model

If the survival times are assumed to have a log-normal distribution,

the baseline survival function and hazard function are given by

$$S_0(t) = 1 - \Phi\left(\frac{\log t - \mu}{\sigma}\right)$$

$$h_0(t) = \frac{\phi\left(\frac{\log t}{\sigma}\right)}{\left[1 - \Phi\left(\frac{\log t}{\sigma}\right)\right] \sigma t}$$

Where μ is intercept, σ is scale parameter and is a random variable; $\Phi(x)$ is the cumulative density function of the standard normal distribution. The survival function for the i^{th} individual is

$$S_i(t) = S_0(t|\eta_i) = 1 - \Phi\left(\frac{\log t - \alpha' x_i}{\sigma}\right)$$

Where $\eta_i = \exp(\alpha_1 x_{1i} + \alpha_2 x_{2i} + \dots + \alpha_p x_{pi})$. Therefore the log survival time for the i^{th} individual has normal $(\mu + \alpha' x_i, \sigma)$. The log-normal distribution has the AFT property.

The generalized gamma AFT model

The probability density function of the generalized gamma distribution with three parameters, λ , γ and α is defined by

$$f(t) = \frac{\alpha \lambda^{\alpha \gamma}}{\tilde{\Gamma}(\gamma)} t^{\alpha \gamma - 1} \exp\left[-(\lambda t)^{\alpha}\right], t > 0, \gamma > 0, \alpha > 0$$

Its survival function is given as

$$S(t) = 1 - \gamma \left\{ \frac{\alpha}{p}, (\lambda t)^p \right\} / \Gamma(\alpha / p)$$

Where $\gamma(s, t) = \int_x^t t^{s-1} e^{-t} dt$ is an incomplete gamma function, γ is the shape parameter of the distribution. The survival function and the hazard function do not have a closed form for the generalized gamma distribution. The exponential, Weibull and log-normal models are all special cases of the generalized gamma model. The generalized gamma distribution becomes the exponential distribution if $\alpha = \gamma = 1$; the Weibull distribution if $\gamma = 1$; and the log-normal distribution if γ tends to infinity.

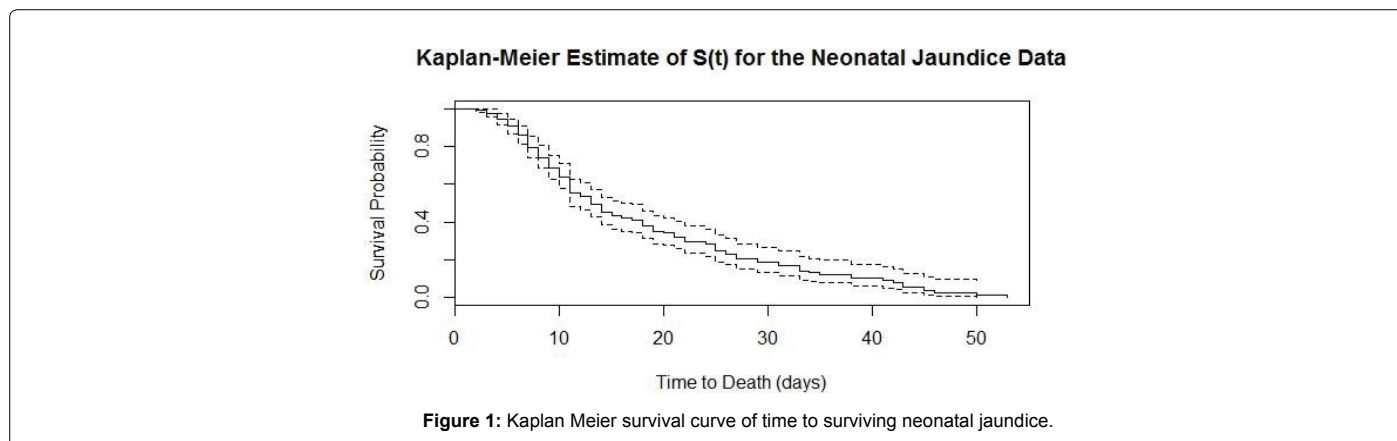
Results and Discussions

In Table 1, the overall median of time to surviving neonatal Jaundice is found to be 13 days, this indicates that 50% of the neonatal patients survive jaundice in less than or equal to 13 days and the other 50% survive jaundice longer than 13 days. This is the survival time at which the cumulative survival function is equal to 0.5. This is summarized in Figure 1.

To describe how to evaluate whether or not K-M curves for two or more groups are statistically significant, a popular testing method called Log-rank test is used and the test used chi-square statistic. When two K-M curves are statistically the same or equivalent it means that based on testing procedure that compares the two curves in some overall sense, we do not have evidence to indicate that the true population survival curves (probabilities) are different. Table 2 suggest that there is a statistical difference between the survival probabilities of the levels of place of delivery, mother's education, jaundice level,

N	events	median	0.95LCL	0.95UCL
232	153	13	11	16

Table 1: Kaplan Meier estimate of time to surviving neonatal jaundice.



Variables	Levels	N	Observed	Expected	(O E)^2/E	Chi-square	P-value
Sex	Male	107	68	72.5	0.277	0.6	0.45
	Female	125	85	80.5	0.25		
Place of delivery	Not hospital	53	18	36	8.97	12.8	0.000353*
	Hospital	179	135	117	2.75		
Mother Education	Illiterate	83	50	64.8	3.39	6.5	0.0109*
	Literate	149	103	88.2	2.49		
Mode of Delivery	CS	85	61	56	0.449	0.8	0.379
	SVD	147	92	97	0.259		
Settlement	Rural	37	19	28	2.911	3.9	0.0494
	Urban	195	134	125	0.653		
Jaundice Level	Mild	112	105	86	4.2	10.6	0.00115*
	Severe	120	48	67	5.39		
GP6D	Normal	71	40	54.7	3.96	6.7	0.00945*
	Deficient	161	113	98.3	2.21		
Gestation Age	Not term/Preterm	110	71	81.8	1.42	3.3	0.0695
	Term	122	82	71.2	1.63		
Rhesus Factor	Incompatible	146	93	99.6	0.443	1.4	0.236
	Compatible	86	60	53.4	0.828		
Mother Illness	Present	43	14	24.5	4.524	5.8	0.0157*
	Absent	189	139	128.5	0.864		

Variables with * suggests that there is a significance difference between the survival probabilities of the groups.

Table 2: Log rank test showing the difference in survival function between the groups.

G6PD and mother illness since their SIG. values are less than 5% level of significance. This implies that the probability of surviving jaundice of infant born in the hospital is significantly different from the infant not born in the hospital. The infant whose mother has no form of education have a significantly different probability of survival jaundice compare to infant whose mother was literate. Infant whose jaundice level was mild has a significantly different probability of surviving jaundice compare to infant with severe jaundice level. There is a significance difference in the probability of surviving jaundice between the infant whose mother has the disease and who mother did not.

In Table 3, the fitted cox proportional hazard model suggested that there was 0.2708 chance of male infant having higher median time of

surviving jaundice compared to female infant. Based on the mother's health history, infant whose mother had jaundice will have 0.5329 chance of having higher median time of surviving the illness compared to infant whose mother do not have the illness. Based on the place of delivery, there was 1.0755 chance of infant born in the hospital having lower median time of surviving jaundice compared to infant not born in the hospital. Infant whose mode of delivery was CS and whose mother do not have any form of education would have 0.2024 and 0.3392 chance of having lower median time of surviving jaundice compared to infant who are born with SVD and whose mother are illiterate. There is 0.0860 chance of infant in urban settlement to have lower median time of surviving jaundice compared to infant in rural settlement. Infant whose gestation age was term and jaundice level was severe would have

Variables	Levels	Value (B)	exp(B)	Std. Error	z	P
Sex	Male (RC)					
	Female	0.270758	1.310957	0.206015	1.314	0.188758
Mother Illness	Present (RC)					
	Absent	0.532936	1.703928	0.306157	1.741	0.081731
Place of Delivery	Not hospital (RC)					
	Hospital	1.075458	2.931335	0.312804	3.438	0.000586*
Mother Education	Illiterate (RC)					
	Literate	0.33918	1.403797	0.198802	1.706	0.087985
Mode of Delivery	CS (RC)					
	SVD	0.202361	1.22429	0.181097	1.117	0.263815
GP6D	Normal (RC)					
	Deficient	0.29507	1.343221	0.229669	1.285	0.198874
Settlement	Rural (RC)					
	Urban	-0.08601	0.917584	0.301631	-0.285	0.775528
Gestation Age	Not term/Preterm (RC)					
	Term	-0.20864	0.811685	0.227235	-0.918	0.358524
Jaundice Level	Mild (RC)					
	Severe	-0.15477	0.856617	0.195494	-0.792	0.428559
Rhesus Factor	Incompatible (RC)					
	Compatible	-0.19332	0.824219	0.189992	-1.018	0.30891
Age		0.000577	1.000577	0.015513	0.037	0.970342
Parity		-0.0358	0.964832	0.057892	-0.618	0.536297
Weight		0.522485	1.686213	0.128933	4.052	5.07E-05*

Table 3: Parameter estimate of cox proportional hazard model of time to surviving neonatal jaundice.

Variables	Levels	Value (B)	exp(B)	Std. Error	z	p
Intercept		4.0454	57.13404	0.2958	13.6749	1.43E-42
Sex	Male (RC)					
	Female	-0.17125	0.843455	0.1159	-1.4684	1.42E-1
Mother Illness	Present (RC)					
	Absent	-0.30251	0.738963	0.1585	-1.9082	5.64E-2
Place of Delivery	Not hospital (RC)					
	Hospital	-0.68343	0.504882	0.177	-3.8605	1.13E-4
Mother Education	Illiterate (RC)					
	Literate	-0.10524	0.900108	0.1187	-0.8868	3.75E-1
Mode of Delivery	CS (RC)					
	SVD	-0.05342	0.947986	0.1089	-0.4906	6.24E-1
GP6D	Normal (RC)					
	Deficient	-0.10036	0.904515	0.1372	-0.7317	4.64E-1
Settlement	Rural (RC)					
	Urban	0.069102	1.071546	0.1734	0.3985	6.90E-1
Gestation Age	Not term/Preterm (RC)					
	Term	0.186279	1.204758	0.1473	1.2642	2.06E-1
Jaundice Level	Mild (RC)					
	Severe	0.130109	1.138953	0.1131	1.1501	2.50E-1
Rhesus Factor	Incompatible (RC)					
	Compatible	0.028747	1.029164	0.1119	0.257	7.97E-1
Age		-0.00082	0.999177	0.0106	-0.0778	9.38E-1
Parity		0.05417	1.055664	0.0371	1.4616	1.44E-1
Weight		-0.31353	0.73086	0.0749	-4.1864	2.83E-5
Log (Scale)		-0.99032	0.371459	0.0657	-15.0631	2.83E-51

Table 4: Parameter estimate of log-logistic accelerated failure time model of time to surviving neonatal jaundice.

0.2086 and 0.1548 chance of having lower median time of surviving jaundice respectively compared to infant whose gestation age was not term and jaundice level was mild. Also, there is 0.0928 chance of infant whose rhesus factor was compatible was expected to have lower median time of surviving jaundice compared to infant whose rhesus factor was incompatible. A unit increase in the age and weight of the infant will

cause 0.00058 and 0.5225 increase in the median time of surviving Jaundice. Also, a unit increase in the parity of infant will cause 0.0358 decreases in the median time of surviving jaundice.

Also, place of delivery and weight have significant effect on the median time to surviving neonatal jaundice.

Model	AIC Value	Log-Likelihood
Weibull AFT	1142.529	-556.264
Exponential AFT	1207.064	-589.532
Logistic AFT	1213.737	-591.869
Log-Logistic AFT	1131.461	-550.731
Cox PHM	1292.453	-633.227

Table 5: Performance comparison of the models.

In Table 4, the fitted log-logistic AFT model suggested that there was 0.17125 chance of male infant having higher median time of surviving jaundice compared to female infant. Based on the mother's health history, infant whose mother had jaundice will have 3.0251 chance of having higher median time of surviving the illness compared to infant whose mother do not have the illness. Based on the place of delivery, there was 0.6834 chance of infant born in the hospital having lower median time of surviving jaundice compared to infant not born in the hospital. Infant whose mode of delivery was CS and whose mother do not have any form of education would have 0.0534 and 0.1052 chance of having higher median time of surviving jaundice compared to infant whose mother was literate and born with SVD. There was 0.0239 chance of infant in urban settlement to have higher median time of surviving jaundice compared to infant in rural settlement. Neonates whose gestation age was term and jaundice level was severe would have 0.1863 and 0.1301 chance of having higher median time of surviving jaundice respectively compared to infant whose gestation age was not term and jaundice level was mild. Also, there was 0.0287 chance of infant whose rhesus factor was compatible to have higher median time of surviving jaundice compared to infant whose rhesus factor was incompatible. A unit increase in the age and weight of the infant will cause 0.00082 and 0.3135 decrease in the median time of surviving Jaundice. Also, a unit increase in the parity of infant will cause 0.05417 increases in the median time of surviving jaundice (Supplementary Tables 1-4).

Table 5 showed the performance comparison of the models. The model with the lowest AIC and highest log-likelihood is chosen as the best model. The log-logistic AFT model outperformed the other models since it has the lowest AIC and the highest log-likelihood value

with 1131.461 and -550.7305 respectively.

Conclusions

From our findings, we are able to determine that the log-logistic AFT model outperformed the other models. Also, the fitted log-logistic AFT model suggested that there was chance of male neonates having higher median time of surviving jaundice compared to female neonates. There was chance of neonates in urban settlement to have higher median time of surviving jaundice compared to neonates in rural settlement. Also, there was chance of neonates whose rhesus factor was compatible to have higher median time of surviving jaundice compared to neonates whose rhesus factor was incompatible.

References

- Andersen PK (1991) Survival analysis 1982-1991: The second decade of the proportional hazards regression model. *Statistics in Medicine* 10: 1931-1941.
- Angelis RD, Cappocaccia R, Hakulinen T, Soderman B, Verdecchia A (1999) Mixture models for cancer survival analysis: Application to population based data with covariates. *Statistics in Medicine* 18: 441-454.
- Farewell VT (1986) Mixtures models in survival analysis: Are they worth the risk? *Canadian J Stat* 14: 257-262.
- Collet D (1994) Modelling survival data in medical research. Chapman and Hall, 1st edtn, New York, USA.
- Kleinbaum DG, Klein M (2010) Survival analysis: A self-learning text. Springer, USA.
- Lauren A (2013) Effect of phototherapy on neonatal hospital stay, Emory University, Georgia.
- Folorunso SA, Chukwu AU, Tongo O (2015) Prevalence and factors associated with neonatal Jaundice: A case study of university college hospital, Ibadan. *IOSR-JDMS* 14: 17-23.
- Onatunji AP, Folorunso SA (2017) Semi parametric analysis of neonatal mortality caused by jaundice. *Int J Sci Eng Res* 8: 1371-1376.
- Joseph GC (2010) Survival analysis: Overview of parametric, nonparametric and semi-parametric approaches and new developments. SAS Global Forum, Michigan State University, USA.
- Hosmer DW, Lemeshow S (1999) Applied survival analysis: Regression modelling of time to event data. John Wiley and Sons, Inc. New York, USA.