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Modelling Time to Mortality with Congestive Heart Failure: A Case Study in Wollo General and Referral Government Hospitals

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Abstract: Congestive heart failure is a complex clinical syndrome of functional or structural impairment in the heart. Nowadays heart failure is common and increasing in the world and researches on this area is limited. Therefore the aim of the present study was to analyze and quantify the impact of modelling heart failure survival allowing for covariates with time varying effects known to be independent predictors of overall mortality in this clinical setting. A retrospective cohort study was conducted on CHF patients who were on treatment follow up at both WGH and DRH from January 1, 2010 to December 30, 2016. A total of 487 patients were selected by using simple random sampling from the patient's medical record. Semi parametric, parametric PH models and AFT models was employed to identify the best model which shown as the real causation of factors with the outcome of CHF which is death. The Weibull accelerated failure time model result showed that the risk factors related to accelerating or decelerating the lifespan were age (TR=0.962, p=0.000), Residence (rural) (TR=1.24, p=0.019), Nutritional (Poor) (TR=0.582, p=0.000), Smoking (TR=0.774, p=0.005), Alcoholism (TR=1.394, p=0.010), Diabetes mellitus (TR=0.49, p=0.000), Hypertension (TR=0.079, p=0.019), Stroke (TR=0.799, p=0.014), Coronary Artery disease (TR=0.276, p=0.012), Tuberculosis bacillus (TR=0.103, p=0.000) as a co morbidity and the interaction between age and Tuberculosis bacillus (p=0.000), age and Coronary artery disease (p=0.041), Diabetes mellitus with Hypertension (p=0.000), Hypertension with Nutritional status (p=0.000) and age with time (p=0.000) were found statistically significant. The Weibull accelerated failure time model performed better explain the effect of predictors than other Cox and parametric PH models. Thus, researchers should use parametric AFT models to see regression varying effect covariates. Frequent monitoring and follow up of Patients with heart failure should be adopted.

Keywords: CHF, Retrospective Cohort Study, Parametric AFT Model, Censoring, Mortality

1. Background

Heart failure is often used to mean chronic heart failure or congestive heart failure (CHF). Clinically it is impossible to define Heart Failure by a single term as a result it is defined as a complex clinical syndrome in which there is a functional or structural impairment in the heart. This can result from any functional or structural cardiac disorder and it impairs the ventricle's ability to fill with or eject blood and to deliver oxygenated blood corresponding to the requirements of the metabolizing tissues of the body and/or doing so at increased filling pressures [1]. Heart failure (HF) is progressive and irreversible which occurs more slowly because of damage to the heart muscle, building up through time due to disease of the heart or a blood vessel leading from the heart as a result of various diseases, accordingly it is a serious clinical condition which represents the end-stage of numerous other cardiac diseases [2].

Heart failure is a major clinical problem worldwide, reaching an epidemic level in the developed world with no known cure at this time. Approximately 26 million people worldwide are living with heart failure, and nearly 1 million

new cases are diagnosed annually worldwide, making it the most rapidly growing cardiovascular disorder. In economically developed countries, up to one person in five is expected to develop heart failure at some point in their life and it affects 1-3% of the general population [2]. It is predominantly seen in the geriatric population in these countries, with almost 80% of cases occurring in patients over the age of 65. Thus, prevalence of heart failure has been shown to follow an exponential pattern, which rises with age and affects 6-10% of people over age 65 [3].

Despite improvements in care over the past 20 years, the outlook for patients with heart failure remains poor, and it has a higher mortality than many of the common malignancies [1, 2]. One year mortality in developed countries is approximately 20% while the 5-year mortality is approximately 50-65% in population-based studies [1]. In a study conducted in Ghana the high prevalence of heart failure of 76% seen in the study supports the fact that HF is a major contributor to cardiovascular disease burden in sub-Saharan Africa [3]. Similar findings have been reported from Cameroon where heart failure is found to be the fifth to sixth cause of hospital admissions [4]. In other parts of sub-Saharan Africa, heart failure has been found to account to 5% to 10% of hospital admissions [3]. Compared to studies from other parts of the world, heart failure in Africa tends to occur at a much younger age with most cases recorded around the 5th and 6th decade and it is not a disease of the elderly in sub-Saharan Africa [2]. This young age reflect the major contribution of rheumatic valvular disease to heart failure, but could also be accounted for infections as it remain a common cause of heart failure in many parts of the world including Africa and can strike at any age. Hospital case fatality among those with heart failure in Africa ranges from 9% to 12.5%. This consistent death rate ranks heart failure among the major causes of death of cardiovascular origin in Africa [5].

In Ethiopia the prevalence and mortality associated with major non-communicable diseases in Ethiopia found cardiovascular disease accounted for 3%-12.6% hospital admission and found to have increased between 1970s and 2000s. And also they found congestive heart failure reported to have caused 2.5% of deaths among all age-groups in a sampled hospital-based mortality study [6]. Similarly a study conducted by analyzing surveillance data on causes of death in Addis Ababa found that, the leading cause of death was cardiovascular disease causing 24% of all death. Congestive heart failure is found to be the third cause of death following hypertension and stroke among the cardiovascular disease deaths [7]. Similar study conducted on Survival during Treatment Period of Patients with Severe Heart Failure Admitted to Intensive Care Unit (ICU) at Gondar University Hospital found that congestive heart failure reported to have caused 12.5% of deaths among all age groups [8]. Nowadays cardiovascular disease has become one of the major causes of premature death and disability in low and middle income countries. However, heart failure as cardiovascular complication remains unexplored largely in Africa [9]. The long-term prognosis associated with HF is also poor [10].

Thus, the limited work on the area and lack of appropriateness of the model applied for data have generated interest in assessing factors affecting timing of death by fitting a statistical model that can explain the data in most meaningful manner. However AFT models are relatively unfamiliar and seen rarely in medical research papers [11]. Primary Several models have been designed to predict survival of patients with heart failure. These, while available and widely used for both stratifying and deciding upon different treatment options on the individual level, have several limitations. Specifically, some clinical variables that may influence prognosis may have an influence that change over time. Statistical models that include such characteristic may help in evaluating prognosis. The aim of the present study is to analyze and quantify the impact of modelling heart failure survival allowing for covariates with time-varying effects known to be independent predictors of overall mortality in this clinical setting. Therefore, in this study the main objective was to compare cox proportional hazard and accelerated failure time models using heart failure dataset and explores the time-varying effect of the different covariates known to be predictive of mortality in such clinical scenario and highlight the importance of considering such details in the modelling of heart failure mortality.

2. Methods and Materials

2.1. Study Area and Settings

This study was conducted in both Woldia general and Dessie referral hospitals. Wollo found Northeast of Ethiopia, found in Amhara regional state of Ethiopia. Specifically, the data for this study was obtained from out ward patients in the internal medicine department in those hospitals.

2.2. Study Design and Period

Secondary data was taken from the patients follow up chart from January 1, 2010 to December 30, 2016. Retrospective cohort study was employed.

2.3. Source and Study Population

The source of population in this study was all CHF patients attend at Wollo general and referral hospitals during the study period January 1, 2010 to December 30, 2016. And the study population was All CHF patients were included as part of a secondary cohort of HF individuals who attend at a cardiology general and referral Wollo hospitals, Ethiopia. The ascertainment period was from January 1, 2010 to Dec. 30, 2016. The classification of the etiologies of heart failure was follow from the different literatures. As such, the diagnosis of chronic heart failure would make through both clinical and imaging procedures when necessary. Beginning of follow-up was defined as enrolment in the protocol. Last follow-up was evaluated in Dec. 30, 2016.

2.4. Inclusion and Exclusion Criteria

All CHF patients who follow up in hospital during the study period were included. All CHF patients who follow up in hospital during the study period and had other diseases as co morbidity was included. On the other hand all patients without CHF case are not included in the study. Also CHF patients died with other case were not considering as our failure event in the study. Finally, a patient's first seen department is not CHF case was not included in this study.

2.5. Sample Size and Sampling Procedures

Sample size is calculated based on the single population proportion formula to the size by considering the following points. Proportion of death in CHF is 12.5% [8]. (α=5%) level of significance and 3% margin of error (d).

$$n = \frac{z_{\frac{\alpha}{2}}^2 p\ (1-p)}{d^2}$$

where critical value at 95% CI of certainty 1.96

n= $(1.96)^2$ * 0.125 (1-0.125) =486.66 $(0.03)^2$

The total CHF patients attending at hospital between January 1, 2010 to Dec. 30, 2016 300 sample patients out of 6037 cases from DRH and 187 out of 3763 from WGH. The samples was allocated using probability proportion to size and a total of 487 CHF patients from the two sites was selected using simple random sampling method.

2.6. Variables in the Study

2.6.1. Dependent Variable

Survival analysis always measures the time from a defined starting point to the occurrence of a given event. In this study the response variable measures the length of treatment time from inward entry to event or censoring and the event of interest is death.

2.6.2. Independent Variables

The most important expected correlates of the survival experience of patients with CHF from literature reviews and their theoretical justification were included in this study. And they are grouped as clinical and demographic variables, and comorbidity conditions. Categorical predictors and Continuous predictors are systolic blood pressure, weight, heart rate, white blood cell count (WBCC) and duration of heart failure are included in this study.

2.7. Data Collection Tools and Techniques and Data Processing

The data was collected from heart failure patients follow up chart in Wollo general and referral hospitals by twelve trained nurses in profession as data collectors and with three supervisors. Three supervisor and six data collectors were selected from each hospital residing in Wollo zone and they were trained how they supervise and collect data accordingly for 3 days. Also they were practice how they review documents before the data collection. The supervisors and investigators were closely follow the data collection process and ensure completeness and consistency of the collected information daily until data collection ends. After the data collection, data editing, data entry and cleaning process of questionnaire was done and entered into SPSS version 20 and exported to STATA V. 12 for data analysis. Analysis of frequency of different variables was done using both STATA and SPSS.

2.8. Ethical Consideration

Prior to data collection ethical approval for the study was obtained from Institutionalized Review Board, Faculty of Natural and computational Science research and community service, Woldia University. And also the objectives of the study were explained to the medical directors to get permission. In addition, the participants identifier was not recorded anywhere for the sake of confidentiality.

2.9. Method of Data Analysis

2.9.1. Survival Analysis

The survival and hazard functions are key concepts in survival analysis for describing the distribution of survival times. The survivor function $s(t)$ is the probability that the survival time of a randomly selected subject is greater than some specified time, t or the probability of an individual being event-free beyond time, t [12]. In order to find the survival function, suppose T be random variable associated with the survival times,t be the observed value of the random variable T and $f(t)$ be the underlying probability density function of the survival time t. The cumulative distribution function, $F(t)$ represents the probability that an individual selected at random will have a survival time less than or equal to the specified value, t. Thus, the cumulative distribution function and the survivor function are given by:

$$F(t) = p(T \le t) = \int_0^t f(u)du, t \ge 0 \quad (1)$$

$$s(t) = p(T > t) = 1 - F(t), t \ge 0$$

The relationship between (t) and $f\ (t)$ is given as

$$\mathrm{f}(t) = \frac{d}{dt}F(t) = \frac{d}{dt}\big(1 - s(t)\big) = -\frac{d}{dt}s(t), t \ge 0 \quad (2)$$

Hazard function $h\ (t)$:

The hazard function is generally denoted by $h\ (t)$ and can be used to express the risk or hazard of death at time, t. It will be obtained from the probability that an individual dies in an infinite, simply small interval $(t, \Delta t)$ given that the individual has survived up to time, t. i.e.

$$\{t \le T < \frac{\nabla t}{T} \ge t\}$$

There is a clearly defined relationship between (t) and $h\ (t)$ which is given by the formula

$$h(t) = \frac{f\ (t)}{1 - F\ (t)} = \frac{f\ (t)}{s\ (t)} = \frac{-d}{dt} lnS\ (t)$$

$$S(t) = \exp[-\int_0^t \mathrm{h(u)du}] = \exp(-\mathrm{H(t)}, \mathrm{t} \geq 0 \quad (3)$$

Where $H(t) = \int_0^t h(u)du$ the cumulative hazard function, which can be obtained from

$$H(t) = -\log(S(t))$$

The probability density function of T can be written as $f(t) = h(t)S(t)$. The study was focus on time to event (time to death by CHF), so the appropriate method for this particular study is survival analysis. Kaplan-Meir estimator and Cox proportional hazard model and AFT model was used for summarizing and analysis and model building respectively. Also, we used log rank tests to study survival pattern and Wilcox on tests for comparison of survival functions.

2.9.2. Cox Proportional Hazards Model.

Cox proposed a semi parametric model for the hazard function that allows the addition of explanatory variables, but keeps the baseline hazard as an arbitrary, unspecified, nonnegative function of time. The Cox model specifies the hazard function as [13]

$$h(t;x) = ho(t)\exp(\beta' x) \quad (4)$$

Where x is a vector of covariates and β is the corresponding regression parameter and the baseline hazard $h_0(t)$ in (4) corresponding, t the hazard function when all covariates equal zero.

One of the restrictions underlying the Cox model with time-fixed covariates is its proportional hazards (PH) assumption. It follows from (3.4) that the hazard ratio between two sets of covariates is constant over time, because the common baseline hazard function cancels out in the ratio of the two hazards. For fixed-time covariates, the exponent of a coefficient describes the relative risk due to the covariate $h(t;x)$

$$\frac{h(t;x)}{ho(t)} = \exp(\beta' x)$$

2.9.3. Accelerated Failure Time Model

AFT models work to measure the effect of covariate to "accelerate" or to "decelerate" survival time meaning the effect of covariate is multiplicative on time scale (exp $(\beta' x)$). It is indicating how a change in covariate values changes the time scale from the baseline time scale. Under AFT models the survival function of the i^{th} individual with covariates $x_1, x_2, \ldots, x_p$ at time,t is the same as the survival function of an individual with a baseline survival function at a time, t. mathematically, it can be expressed with its corresponding hazard function as:

$$S_i(t;x) = S_0[\exp(\beta' x)t]$$

$$hi(t;x) = \exp(\beta' x)\, h_0\,(\exp(\beta' x)\, t)$$

Where $\hat{\beta}' = (\hat{\beta}_1, \hat{\beta}_{2,}, \widehat{\beta}_{3,,,} \widehat{\beta}_p)$ is a vector of regression coefficients $S_0\,(t)$ and $h_0\,(t)$ are the baseline survival and hazard functions respectively. The effect size for the AFT model is measured using the time ratio (TR) which is a ratio of the survival time of an individual with an exposure to the survival time of an individual without the exposure for a given survival probability.

Suppose, T_i is a random variable representing the survival time for the , t_i individual. Then representation of the relationship between covariate values and survival time in the AFT model is the linear relationship between log time and the covariate values expressed as follows:

$$logTi = \mu + \beta' X_i + \delta\varepsilon_i$$

Where $\hat{\beta}' = (\hat{\beta}_1, \hat{\beta}_{2,}, \hat{\beta}_{3,,,}\hat{\beta}_p), \mu$ is intercept , δ is scale parameter and ε_i is a random variable used to model the deviation of values of $\log Ti$ from the linear part of the model. ε_i is random error distribution assumed to have a particular probability distribution supposed to be followed by the survival time under study.

Under the AFT formulation, the effect of treatments and covariates is assumed to act additively on the log time scale and therefore multiplicatively on the time scale itself. Three commonly adopted parametric AFT models are the Weibull, log-normal, and log-logistic in terms of the distribution of survival time. AFT models are fitted using the maximum likelihood estimation method. The likelihood function of n observed survival times, $(t_1, t_2, t_3, , , , , t_p)$ for the log-linear form of the AFT model is given by:

$$L(\beta, \mu, \sigma) = \prod_{i=1}^{n} [f_i\,(t_i)^{\delta i}\,[S_i\,(t_i)]^{(1-\delta i)}$$

Where $f_i\,(t_i)$ and $S_i\,(t_i)$ are the density and survival functions for the, i^{th} individual at time$t_i$and δ_i is the event indicator for the observation and has value zero for censored and one for uncensored individuals. If$f_{zi}\,(zi)$ and$f_{zi}\,(zi)$ are probability density function and survival function respectively of the random variable ε_i in such a way that

$$s_i(\mathrm{t}) = S_{zi}\,(zi).$$

$$f_i(t_i) = \frac{1}{\sigma t_i} f_{zi}\,(zi)$$

And, where

$$z_i = (logt_i - (\mu + \beta_1 x_{1i} + \beta_2 x_{2i} + \beta_3 x_{3i} + \cdots + \beta_p x_{pi}))$$

3. Result and Discussion

3.1. Descriptive Statistics

The medical cards of 487 patients have been reviewed of which 42.1% (total 205) are death cases. A death proportion seems lower for females (38.19%) than for males (47.74%). The Divorced group showed the highest percentage (62.86%) with respect to death proportions than the other three groups and HIV positive groups revealed the highest proportion of death (76.19%). A death proportion seems lower for rural residences (40.76%) than for Urban (43.19%) patients. While on the other hand the death proportion of patients who have had poor nutrition status (51.48%) seems higher than those of

who have good nutrition habit (26.37%). CHF patients with TB co infection have the highest death proportion (89.9%) than have no TB co infection. In the same fashion we describe the rest variables under table 1 below:

Table 1. *Demographic and Health factors by CHF death at medical wards of Woldia general and Dessie referral hospitals, Ethiopia, 2017/2018.*

Demographic and Health factors	Stratum	Value	Total	Median survival time (in months)	Status		
					Event/Death	Censored	Percent Death
Sex	1	(0) Male	199	15.19	95	104	47.74
	2	(1) Female	288	36.1	110	178	38.19
Residence	1	(0) Urban	276	35	119	157	43.11
	2	(1) Rural	211	16	86	125	40.76
Nutritional	1	(0) Poor	305	14.1	157	148	51.48
	2	(1) Good	182	42	48	134	26.37
Weight	1	(0) Under	202	26	97	105	48.02
	2	(1) Normal	231	36.2	72	159	31.17
	3	(2) Over	54	17.4	36	18	66.67
Marital Status	1	(0) Single	115	36.24	31	84	26.96
	2	(1) Married	294	26	128	166	43.54
	3	(2) Divorced	35	16	22	13	62.86
	4	(3) Widowed	43	37	24	19	55.81
Smoking Status	1	(0) No	430	29.95	153	277	35.58
	2	(1) Yes	57	23.93	52	5	91.23
Religion	1	(0) Orthodox	237	30.09	84	153	35.44
	2	(1) Muslim	250	25.23	121	129	48.4
Educational status	1	(0) Illiterate	168	31	70	98	41.67
	2	(1) Literate	139	25	135	184	97.12
Alcoholism	1	(0) No	444	35	177	267	39.86
	2	(1) Yes	43	14	28	15	65.12
Diabetes Miletus	1	(0) No	436	26	167	269	38.30
	2	(1) Yes	51	25	38	13	74.51
CKD	1	(0) No	439	35	168	271	38.27
	2	(1) Yes	48	17.4	37	11	77.08
Presence of pneumonia	1	(0) No	455	35	178	178	39.12
	2	(1) Yes	32	13	27	27	84.38
CAD	1	(0) No	467	35	188	279	40.26
	2	(1) Yes	20	13	17	3	85.0
HTN	1	(0) No	327	36.1	100	227	30.58
	2	(1) Yes	160	14	105	55	65.62
Stroke	1	(0) No	429	36.1	152	277	35.43
	2	(1) Yes	58	13	53	5	91.38
TB	1	(0) No	388	36.2	116	272	29.90
	2	(1) Yes	99	13	89	10	89.90
HIV	1	(0) No	403	35	147	262	36.48
	2	(1) Yes	84	17.4	64	20	76.19

The mean baseline age of the participants was 50 years. Ranging from 16 to 86 and standard deviation of 19 years. The mean systolic blood pressure of the participants was 116. Ranging from 80 and 180 and standard deviation of 20. Similarly for Heart rate of the patients in Table 2.

Table 2. *Continuous variable characteristics of the study participants.*

Variable	N	Minimum	Maximum	Mean	Std. Deviation
Baseline age of patients	487	16	86	49.81	18.984
Systolic blood pressure	487	80	180	116.12	19.490
Heart rate of the patients	487	23	120	82.57	13.957

3.2. Cox Proportional Hazards Model

The non parametric method does not control for covariates and it requires categorical predictors. Therefore here we used Cox PH for dealing the covariate effects along with the survival time. The Cox model identified significant predictors at 25% level. Consequently, the candidate variables for building a multivariable Cox model are place of residence, Sex, Age, Nutritional Status, Smoking Status, Religion, Alcoholism, Baseline Weight as (under, Normal & Over weight), Heart Rate, Systolic Blood Pressure, Presence of Diabetes Mellitus, Presence Of Hypertension, Presence of Coronary Kidney Disease, Presence of HIV, Presence of Pneumonia, Presence of Tuberculosis, Presence of Stroke And Presence of Coronary Artery Disease as co morbidity. Whereas Marital Status and Educational Status of the patients are not a candidate variable for main effect models at 25% level of significance. Hence the two covariates are not important for the building of the main effect only multivariable models. Univariable Cox proportional hazard

model STATA V. 12 summary results of the hazards ratio, 75% confidence intervals and standard errors for each covariate are presented in table 3.

Table 3. *Univariable analysis of Cox proportional hazard model result WGH&DRH, 2017.*

Factors	HR	S.E	P_value	75%CI	
				Lower	Upper
Sex (Ref.=Male)					
Female	0.62	0.09	0.001	0.53	0.73
Age	1.03	0.004	0.000	1.02	1.03
Residence (Ref.=Urban)					
Rural	1.44	0.21	0.011	1.22	1.70
Marital Status (Ref.=Windowed)*					
Single	0.75	0.21	0.309	0.55	1.04
Married	0.80	0.18	0.311	0.61	1.03
Divorced	0.93	0.28	0.813	0.66	1.32
Nutritional Status (Ref.=Poor)					
Good	0.36	0.06	0.000	0.30	0.44
Smoking (Ref.=No)					
Yes	1.59	0.26	0.005	1.31	1.92
Religion (Ref.=others)					
Orthodox	1.52	0.22	0.004	1.29	1.79
Muslim	Omitted				
Educational Status (Ref.=illiterate)*					
Literate	1.11	.16	0.465	0.94	1.32
Alcoholism (Ref.=No)					
Yes	1.38	0.29	0.119	1.09	1.76
Weight (Ref.=Normal)					
Under	1.65	0.26	0.001	1.37	1.97
Over	2.01	0.41	0.001	1.58	2.54
Heart rate	1.02	0.005	0.002	1.01	1.02
Systolic BP	1.01	0.003	0.002	1.006	1.01
Diabetes mellitus (Ref.=No)					
Yes	1.49	0.27	0.031	1.20	1.84
Hypertension (Ref.=No)					
Yes	2.78	0.40	0.000	2.352	3.28
Coronary Kidney Disease (Ref.=No)					
Yes	2.03	0.37	0.000	1.64	2.51
HIV (Ref.=No)					
Yes	1.95	0.30	0.000	1.63	2.33
Pneumonia (Ref.=No)					
Yes	3.33	0.70	0.000	2.62	4.25
Stroke (Ref.=No)					
Yes	1.94	0.312	0.000	1.61	2.33
Coronary Artery Disease (Ref.=No)					
Yes	3.10	0.80	0.000	2.31	4.18
Tuberculosis (Ref.=No)					
Yes	3.89	0.57	0.000	3.29	4.59

"*" represents insignificant variables at 25% level of significance

All the significant and clinical important variables at 25% level were included in the bivariable analysis with in a forward stepwise manner with an entry probability 0.05 and removal probability 0.25. Among the candidate variables considered for building multivariable Cox, stepwise procedure picked up eighteen variables. Finally, among the independent variables statistically significant and clinical important variables were selected for the multivariable analysis and the Cox proportional hazards model that were not statistically insignificant variables in the multivariable analysis were rejected and the analysis was run until the last best model was obtained with smaller -2 residual likelihood value or AIC&BIC minimum was better model fit. The final main effect only Multivariable Cox proportional hazard model STATA V. 12 summary results of Coefficients, Hazards ratio, 95% confidence intervals, standard errors for each variable with their AIC and BIC are presented in table 4.

Table 4. *Final Multivariable Cox regression model for CHF data, GH&DRH, 2017.*

Factors	Estimate	HR	S.E	P_value	95% CI for HR	
					Lower	Upper
Sex (Ref.=Male)						
Female	-0.56	0.57	0.12	0.007	0.38	0.86
Age	0.011	1.01	0.01	0.045	1.0002	1.02
Residence (Ref.=Urban)						
Rural	0.605	1.83	0.33	0.001	1.28	2.62
Nutritional Status (Ref.=Poor)						
Good	-0.78	0.46	0.10	0.000	0.30	0.70
Smoking (Ref.=No)						
Yes	0.15	1.16	0.25	0.494	0.76	1.77
Religion (Ref.=others)						
Orthodox	0.09	1.09	0.19	0.618	0.77	1.77
Muslim	Omitted					
Alcoholism (Ref.=No)						
Yes	0.041	1.04	0.33	0.898	0.56	1.96
Weight (Ref.=Normal)						
Under	-0.08	0.83	0.27	0.555	0.44	1.55
Over	0.11	0.90	0.26	0.708	0.50	1.60
Heart rate	0.005	1.005	0.01	0.463	0.99	1.02
Systolic BP	0.007	1.01	0.004	0.098	0.999	1.02
Diabetes mellitus (Ref.=No)						
Yes	-0.55	0.58	0.15	0.032	0.35	0.96
Hypertension (Ref.=No)						
Yes	0.74	2.10	0.37	0.000	1.48	2.97
Coronary Kidney Disease (Ref.=No)						
Yes	0.44	1.55	0.37	0.063	0.98	2.47
Stroke (Ref.=No)						
Yes	0.61	1.84	0.41	0.006	1.19	2.84
HIV (Ref.=No)						
Yes	0.28	1.33	0.30	0.214	0.85	2.07
Pneumonia (Ref.=No)						
Yes	0.52	1.68	0.44	0.045	1.01	2.79
Coronary Artery Disease (Ref.=No)						
Yes		3.10	0.80	0.000	2.31	4.18
Tuberculosis (Ref.=No)						
Yes		3.89	0.57	0.000	3.29	4.59
AIC						1968.87
BIC						2010.75

Log likelihood = -965.8977, prob. chi2=0.000, LR chi (19) = 221.62

3.3. Parametric Proportional Hazards Model

The parametric proportional hazards models are the parametric versions of the Cox proportional hazards model. It assumes the baseline hazard function follows a certain distribution and coefficients are estimated by maximum likelihood method, but not in Cox PH models. The results of Univariable parametric PH models are presented in table 5. In both models variables significant at 25% level in the Univariable analysis were taken as candidate variables for their multivariable analysis. Stepwise forward selection procedure was also implemented for these models as used in multivariable Cox model.

Table 5. *Results of Univariable Weibull, Exponential and, Log logistic PH model WGH&DRH, 2017.*

Factors	Weibull				Exponential			
	HR	75% CI	Pvalue	S.E	HR	75%CI	Pvalue	S.E
Sex (Ref.=No)								
Yes	0.62	(0.53,0.73)	0.001	0.87	0.63	0.54,0.74	0.001	0.09
Age	1.03	(1.023,1.032)	0.000	0.004	1.03	1.02,1.03	0.000	0.01
Residence (Ref.=Urban)								
Yes	1.51	1.28,1.78	0.004	0.215	1.48	1.26,1.74	0.005	0.21
Marital Status (Ref.=Divorced)								
Single	0.714	0.52,0.98	0.219	0.19	0.69	0.51,0.94	0.174	0.19
Married	0.73	0.56,0.94	0.151	0.16	0.72	0.56,0.93	0.140	0.16
Windowed	0.93	0.66,1.31	0.808	0.27	0.93	0.66,1.31	0.814	0.27
Educational status (Ref.=No)								
Literate	1.11	0.94,1.31	0.486	0.16	1.10	0.93,1.30	0.528	0.16
Alcoholism (Ref.=No)								
Yes	1.56	1.23,1.97	0.030	0.32	1.55	1.23,1.96	0.030	0.32

Factors	Weibull				Exponential			
	HR	75% CI	Pvalue	S.E	HR	75%CI	Pvalue	S.E
Weight (Ref.=Normal)								
Under	0.70	0.56,0.88	0.072	0.14	0.70	0.56,0.88	0.072	0.14
Over	0.44	0.35,0.56	0.000	0.09	0.44	0.35,0.56	0.000	0.09
Hrt	1.02	1.01,1.022	0.001	0.005	1.01	1.01,1.02	0.001	0.01
SBP	1.01	1.007,1.013	0.001	0.003	1.01	1.006,1.013	0.001	0.003
Dm (Ref.=No)								
Yes	1.60	1.30,1.97	0.009	0.30	1.63	1.33,2.01	0.007	0.29
HTN (Ref.=No)								
Yes	2.81	2.39,3.30	0.000	0.395	2.72	2.31,3.19	0.000	0.38
CKD (Ref.=No)								
Yes	2.13	1.73,2.62	0.000	0.39	2.13	1.73,2.63	0.000	0.39
HIV (Ref.=No)								
Yes	1.85	1.56,2.20	0.000	0.28	1.86	1.56,2.21	0.000	0.28
Pneumonia (Ref.=No)								
Yes	3.12	2.45,3.96	0.000	0.65	3.01	2.37,3.81	0.000	0.62
CAD (Ref.=No)								
Yes	3.34	2.49,4.49	0.000	0.85	3.17	2.37,4.24	0.000	0.80
Stroke (Ref.=No)								
Yes	0.54	0.45,0.64	0.000	0.09	1.89	1.57,2.27	0.000	0.30
Tuberculosis (Ref.=No)								
Yes	4.18	3.55,4.92	0.000	0.59	4.05	3.45,4.76	0.000	0.57

Results of multivariable Log logistic main effect model, WGH&DRH, 2017/2018.

Distribution=Log logistic						
Factors	Estimate	HR	S.E	P_value	95% CI for HR	
					Lower	Upper
Sex (Ref.=Male)						
Female	-0.73	0.48	0.10	0.001	0.31	0.73
Age	0.01	1.01	0.005	0.083	0.999	1.02
Residence (Ref.=Urban)						
Rural	0.72	2.06	0.38	0.000	1.43	2.96
Nutritional Status (Ref.=Poor)						
Good	-0.73	0.48	0.10	0.001	0.32	0.71
Religion (Ref.=Others)						
Orthodox	-0.18	0.84	0.15	0.334	0.59	1.20
Smoking (Ref.=No)						
Yes	0.17	1.18	0.26	0.444	0.77	1.81
Alcoholism (Ref.=No)						
Yes	-0.07	0.93	0.30	0.823	0.49	1.76
Weight (Ref.=Normal)						
Under	-0.07	0.93	0.19	0.742	0.63	1.39
Over	0.31	1.37	0.41	0.291	0.76	2.46
Hrt	0.004	1.004	0.006	0.501	0.992	1.02
SBP	0.007	1.007	0.004	0.113	0.998	1.015
Dm (Ref.=No)						
Yes	-0.45	0.64	0.16	0.068	0.39	1.03
CKD (Ref.=No)						
Yes	0.56	1.76	0.40	0.013	1.12	2.74
HTN (Ref.=No)						
Yes	0.92	2.52	0.45	0.000	1.77	3.58
Stoke (Ref.=No)						
Yes	0.50	1.64	0.34	0.018	1.10	2.48
HIV (Ref.=No)						
Yes	0.72	1.07	0.24	0.751	0.69	1.67
Pneumonia (Ref.=No)						
Yes	0.55	1.73	0.44	0.034	1.04	2.86
CAD (Ref.=No)						
Yes	1.11	3.05	0.94	0.000	1.67	5.57
Tuberculosis (Ref.=No)						
Yes	1.30	3.66	0.70	0.000	2.52	5.33
AIC						766.943
BIC						854.896

Log likelihood = -362.47, LR Chi2 (19)=239.62.16 & prob>chi2=0.0000

As we can seen above univariable analysis summary results table 5 indicates that in all distributions only Marital status and Educational status of a patients are not statistically significant at 25% level of significant, while all the remaining variables were considered as a candidate for the multivariable models. Therefore the next step is including all significant variables in a model simultaneously and the results of preliminarily final main effect only model are presented in these table.

Likewise from the preliminary main effect multivariate exponential, Log logistic and Weibull PH models, pick up all variables significance at 5% for the final model. Statistically significant predictors at 5% level of significance are sex, Nutritional Status, Presence of Hypertension, Presence of Tuberculosis, Presence of Stroke and Presence of Coronary Artery Disease as co morbidity are important variables for the decelerate or accelerate of the survival time of the CHF patient. While Age, Residence, Smoking, Alcoholism, Weight, Religion, Heart Rate, Systolic Blood Pressure, HIV, Presence of Diabetes mellitus and Pneumonia as a co morbidity are insignificant variables. Finally both clinically and statistically important variables with their interaction terms are analyzed together and it can be considered as a final model for each parametric PH models. Actually interaction add in the model by considering their effect have a significant effect even if there is no standards. However iteratively each interaction term importance was assessed at 5% level of significance. Therefore the final all significant interaction with main effect were modelled and the result was presented in (Tables 6-8).

Table 6. *Results of final weibull PH model WGH&DRH, 2017.*

Final Weibull PH model Summary results						
Factors	**HR**	**S.E**	**Z**	**P_value**	**95% CI**	
					Lower	**Upper**
Sex (Ref.=Male)						
Female	0.59	0.14	-2.23	0.026	0.371	0.940
Age	1.04	0.01	4.40	0.000	1.02	1.05
Residence (Ref.=Urban)						
Rural	1.74	0.33	2.94	0.003	1.20	2.53
Nutritional Status (Ref.=Poor)						
Good	3.12	0.88	4.04	0.000	1.80	5.42
Smoking status (Ref.=No)						
Yes	0.86	0.19	-0.71	0.479	0.560	1.31
Alcoholism (Ref.=No)						
Yes	1.24	0.38	0.70	0.482	0.68	2.27
Baseline Heart rate	1.005	0.006	0.79	0.431	0.993	1.02
Sbp	1.01	0.005	2.08	0.037	1.001	1.02
Dm (Ref.=No)						
Yes	0.39	0.12	-2.95	0.003	0.205	0.73
CAD (Ref.=No)						
Yes	33.7	43.18	2.75	0.006	2.73	425.28
Coronary kidney disease (Ref.=No)						
Yes	1.294	0.343	0.97	0.331	0.77	2.18
HIV (Ref.=No)						
Yes	1.23	0.30	1.13	0.257	0.83	2.04
HTN (Ref.=No)						
Yes	1.43	0.281	1.82	0.069	0.973	2.51
Stoke (Ref.=No)						
Yes	1.14	0.28	0.52	0.600	0.71	1.83
Pneumonia (Ref.=No)						
Yes	1.91	0.51	2.43	0.015	1.13	3.23
Tuberculosis (Ref.=No)						
Yes	101.31	76.89	6.11	0.000	23.06	447.8
Tb*Age (Ref.=No)						
Yes*Age	0.96	0.012	-3.69	0.000	0.934	0.980
CAD*Age (Ref.=No)						
Yes*Age	0.96	0.02	-2.04	0.041	0.92	0.998
Nut (Ref.=No)*Tb (Ref.=No)						
Yes	0.37	0.15	-2.5	0.012	0.17	0.81
Dm (Ref.=No)*HTN (Ref.=No)						
Yes	3.61	1.58	2.92	0.003	1.53	8.54
Constant	0.00007	0.0001	-11.79	0.000	0.000014	0.00033
/ln_p	0.31	0.06	5.32	0.000	0.19	0.42
P	1.36	0.08		1.21	1.52	
1/p	0.73	0.04		0.66	0.82	
AIC						735.4757
BIC						827.6175

Log likelihood =-345.7385 LR chi2 (21) =273.09 Prob >chi2 =0.0000

$$R^2 = 1 - \left\{exp\left[\frac{2}{486}(-482.2827 + 345.7379)\right]\right\} = 50.01\%$$

Table 7. *Results of final Log logistic PH model WGH & DRH, 2017.*

Final Log logistic PH model Summary results						
Factors	**HR**	**S.E**	**Z**	**P_value**	**95% CI**	
					Lower	**Upper**
Sex (Ref.=Male)						
Female	0.46	0.18	2.55	0.011	0.105	0.81
Age	-0.025	0.01	-3.73	0.000	-0.04	-0.012
Residence (Ref.=Urban)						
Rural	-0.17	0.16	-1.11	0.267	-0.48	0.134
Nutritional Status (Ref.=Poor)						
Good	0.92	0.21	4.45	0.000	0.52	1.33
Smoking status (Ref.=No)						
Yes	0.29	0.19	1.51	0.13	-0.09	0.67
Alcoholism (Ref.=No)						
Yes	0.097	0.26	0.37	0.709	-0.414	0.61
Baseline Heart rate	-0.003	0.006	-0.49	0.627	-0.014	0.009
SBp	-0.006	0.004	-1.67	0.095	-0.013	0.001
Dm (Ref.=No)						
Yes	0.25	0.32	0.77	0.443	-0.39	0.88
CAD (Ref.=No)						
Yes	-3.78	0.886	-4.26	0.000	-5.52	-2.04
Coronary kidney disease (Ref.=No)						
Yes	-0.01	0.214	-0.04	0.971	-0.43	0.41
HIV (Ref.=No)						
Yes	-0.333	0.18	-1.86	0.063	-0.063	0.018
HTN (Ref.=No)						
Yes	-0.5	0.17	-2.90	0.004	-0.84	-0.16
Stoke (Ref.=No)						
Yes	-0.11	0.204	-0.53	0.599	-0.51	0.292
Pneumonia (Ref.=No)						
Yes	-0.335	0.235	-1.43	0.153	-0.795	0.125
Tuberculosis (Ref.=No)						
Yes	-4.054	0.629	-6.45	0.000	-5.29	-2.82
Tb*Age (Ref.=No)						
Yes*Age	0.06	0.01	5.4	0.000	0.036	0.077
CAD*Age (Ref.=No)						
Yes*Age	0.05	0.016	3.18	0.001	0.019	0.08
Nut (Ref.=No)*Tb (Ref.=No)						
Yes	-1.21	0.35	-3.47	0.001	-1.9	-0.53
Dm (Ref.=No)*HTN (Ref.=No)						
Yes	-0.55	0.417	-1.32	0.188	-1.37	0.27
Constant	5.58	0.62	-1.32	0.000	4.36	6.79
/ln_gamma	-0.55	0.59	9.01	0.000	-0.66	-0.434
Gamma	0.58	0.034			0.514	0.65
AIC						758.1743
BIC						850.3162

Log likelihood =-357.08717 LR chi2 (21) =269.25 Prob >chi2 =0.0000

$$R^2 = 1 - \left\{exp\left[\frac{2}{486}(-491.713 + 357.0872)\right]\right\} = 57.34\%$$

Table 8. *Results of final exponential PH model WGH & DRH, 2017.*

Final exponential PH model Summary results						
Factors	**HR**	**S.E**	**Z**	**P_value**	**95%CI**	
					Lower	**Upper**
Sex (Ref.=Male)						
Female	0.68	0.156	-1.68	0.093	0.436	1.027
Age	1.034	0.008	4.07	0.000	1.017	1.05
Residence (Ref.=Urban)						
Rural	1.478	0.27	2.11	0.035	1.03	2.13
Nutritional Status (Ref.=Poor)						
Good	3.09	0.865	4.03	0.000	1.786	5.349

Final exponential PH model Summary results						
Factors	**HR**	**S.E**	**Z**	**P_value**	**95%CI**	
					Lower	**Upper**
Smoking status (Ref.=No)						
Yes	0.956	0.202	-0.21	0.831	0.631	1.45
Alcoholism (Ref.=No)						
Yes	1.088	0.326	0.28	0.779	0.604	1.96
Baseline Hear trate	1.005	0.006	0.90	0.369	0.994	1.02
Sbp	1.008	0.0045	1.71	0.088	0.999	1.02
Dm (Ref.=No)						
Yes	0.534	0.168	-2.00	0.046	0.29	0.989
CAD (Ref.=No)						
Yes	19.99	23.29	2.57	0.010	2.04	196.08
Coronary kidney disease (Ref.=No)						
Yes	1.214	0.298	0.79	0.429	0.750	1.965
HIV (Ref.=No)						
Yes	1.35	0.30	1.37	0.17	0.878	2.09
HTN (Ref.=No)						
Yes	1.45	0.298	1.91	0.056	0.99	2.115
Stoke (Ref.=No)						
Yes	1.21	0.282	0.82	0.414	0.766	1.965
Pneumonia (Ref.=No)						
Yes	1.67	0.434	1.98	0.048	1.004	2.78
Tuberculosis (Ref.=No)						
Yes	75.03	55.28	5.86	0.000	17.7	317.98
Tb*Age (Ref.=No)						
Yes*Age	0.96	0.011	-3.41	0.001	0.94	0.983
CAD*Age (Ref.=No)						
Yes*Age	0.96	0.019	-1.87	0.062	0.926	1.002
Nut (Ref.=No)*Tb (Ref.=No)						
Yes	0.32	0.124	-2.94	0.003	0.149	0.683
Dm (Ref.=No)*HTN (Ref.=No)						
Yes	2.59	1.104	2.33	0.026	1.123	5.974
Constant	0.0003	0.0002	-11.10	0.000	0.0001	0.001
AIC						758.6276
BIC						846.5812

Log likelihood =-358.3138 LR chi2 (20) =249.59 Prob >chi2 =0.0000

$$R^2 = 1 - \left\{exp\left[\frac{2}{486}(-483.1094 + 358.3138)\right]\right\} = 87.37\%$$

From the above final three parametric PH model exponential have better performance to explain the effect of covariates on the survival time of patient with CHF since it have high R^2 type statistic which is it accounts around 87.37%. We can take is as thee alternative model for Cox model even if the assumption is violated.

3.4. AFT Model Results

The AFT model which is another alternative of the Cox PH model when the PH assumption is violate. It can be used to express the magnitude of effect in a more accessible way in terms of difference between covariates in survival time. We fitted the dataset using exponential, Weibull and log-logistic AFT model. Similarly we done the same procedure for AFT models like so far in parametric Cox proportional models. In all models variables significant at 25% level in the Univariable analysis were taken as candidate variables for their multivariable analysis. Finally all variables in a main effect model and it's interaction term significant at 5% with a stepwise forward selection procedure was also implemented and reported in (Tables 9-11).

Table 9. *Results of final Log logistic AFT model WGH & DRH, 2017.*

Final Log logistic AFT model Summary results						
Factors	**TR**	**S.E**	**Z**	**P_value**	**95% CI**	
					Lower	**Upper**
Sex (Ref.=Male)						
Female	1.285	0.137	2.35	0.019	1.043	1.583
Age	0.965	0.004	-8.61	0.000	0.957	0.973

Final Log logistic AFT model Summary results						
Factors	**TR**	**S.E**	**Z**	**P_value**	**95% CI**	
					Lower	**Upper**
Residence (Ref.=Urban)						
Rural	1.167	0.117	1.54	0.124*	0.958	1.421
Nutritional Status (Ref.=Good)						
Poor	0.64	0.784	-3.64	0.000	0.504	0.835
Smoking status (Ref.=No)						
Yes	0.669	0.090	-2.97	0.003	0.513	0.872
Alcoholism (Ref.=No)						
Yes	1.677	0.268	3.23	0.001	1.226	2.295
Dm (Ref.=No)						
Yes	0.363	0.063	-5.79	0.000	0.268	0.512
Baseline Heart rate	0.999	0.003	-0.33	0.745*	0.992	1.006
SBP	0.999	0.002	-0.37	0.709*	0.995	1.003
CAD (Ref.=No)						
Yes	0.201	0.110	-2.94	0.003	0.069	0.587
Coronary kidney disease (Ref.=No)						
Yes	0.714	0.099	-2.42	0.016	0.543	0.938
HIV (Ref.=No)						
Yes	0.841	0.102	-1.44	0.151*	0.663	1.065
HTN (Ref.=No)						
Yes	0.789	0.079	-2.35	0.019	0.648	0.962
Stoke (Ref.=No)						
Yes	0.805	0.098	-1.77	0.076*	0.634	1.023
Pneumonia (Ref.=No)						
Yes	1.064	0.161	0.41	0.682*	0.791	1.431
Tuberculosis (Ref.=No)						
Yes	0.029	0.012	-8.23	0.000	0.012	0.067
Tb*Age (Ref.=No)						
Yes*Age	1.041	0.007	5.90	0.000	1.027	1.054
CAD*Age (Ref.=No)						
Yes*Age	1.021	0.009	2.23	0.026	1.002	1.040
Nut (Ref.=No)*Tb (Ref.=No)						
Yes	2.227	0.447	4.03	0.000	1.508	3.287
Dm (Ref.=No)*HTN (Ref.=No)						
Yes	2.79	0.703	4.07	0.000	1.703	4.573
Time*Age	1.001	.00007	18.53	0.000	1.0011	1.0014
Constant term	78.396	30.473	11.22	0.000	36.596	167.941
/ln_gamma	-1.067	0.058	-18.40	0.000	-1.180	-0.953
Gamma	0.344	0.020			0.307	0.385
AIC						542.722
BIC						639.0521

Log likelihood =-248.361 LR chi2 (21) =486.70 Prob >chi2 =0.0000

$$R^2 = 1 - \left\{exp\left[\frac{2}{486}(-491.713 - (-248.361))\right]\right\} = 63.27\%$$

Table 10. *Results of final Weibull AFT model WGH & DRH, 2017.*

Final Weibull AFT model Summary results						
Factors	**TR**	**S.E**	**Z**	**P_value**	**95%CI**	
					Lower	**Upper**
Sex (Ref.=Male)						
Female	1.137	0.111	1.31	0.190*	0.938	1.377
Age	0.962	0.004	-9.71	0.000	0.954	0.969
Residence (Ref.=Urban)						
Rural	1.237	0.112	2.34	0.019	1.035	1.478
Nutritional Status (Ref.=Good)						
Poor	0.582	0.073	-4.33	0.000	0.456	0.744
Smoking status (Ref.=No)						
Yes	0.774	0.071	-2.78	0.005	0.646	0.927
Alcoholism (Ref.=No)						
Yes	1.394	0.179	2.59	0.010	1.084	1.793
Dm (Ref.=No)						
Yes	0.490	0.072	-4.85	0.000	0.367	0.653
Baseline Heart rate	0.999	0.003	-0.33	0.745*	0.992	1.006

Final Weibull AFT model Summary results						
Factors	**TR**	**S.E**	**Z**	**P_value**	**95%CI**	
					Lower	**Upper**
SBP	0.999	0.002	-0.37	0.709*	0.995	1.003
CAD (Ref.=No)						
Yes	0.276	0.141	-2.52	0.012	0.101	0.752
Coronary kidney disease (Ref.=No)						
Yes	0.81	0.095	-1.79	0.074*	0.64	1.02
HIV (Ref.=No)						
Yes	1.014	0.101	0.14	0.891*	0.834	1.233
HTN (Ref.=No)						
Yes	0.789	0.079	-2.35	0.019	0.648	0.962
Stoke (Ref.=No)						
Yes	0.799	0.073	-2.45	0.014	0.668	0.956
Pneumonia (Ref.=No)						
Yes	1.250	0.144	1.95	0.052*	0.98	1.566
Tuberculosis (Ref.=No)						
Yes	0.103	0.036	-6.52	0.000	0.052	0.204
Tb*Age (Ref.=No)						
Yes*Age	1.021	0.0055	3.83	0.000	1.010	1.032
CAD*Age (Ref.=No)						
Yes*Age	1.018	0.009	2.05	0.041	1.001	1.036
Nut (Ref.=No)*Tb (Ref.=No)						
Yes	2.05	0.365	4.04	0.000	1.448	2.908
Dm (Ref.=No)*HTN (Ref.=No)						
Yes	2.18	0.45	3.78	0.000	1.455	3.268
Time*Age	1.001	.00007	16.49	0.000	1.001	1.002
Constant term	125.078	43.931	13.75	0.000	62.836	248.97
/ln_p	0.824	0.06	13.8	0.000	0.707	0.941
P	2.279	0.136			2.028	2.562
1/p	0.439	0.026			0.390	0.493
AIC						532.1867
BIC						628.5167

Log likelihood =-243.09333 LR chi2 (21) =478.38 Prob >chi2 =0.0000

$$R^2 = 1 - \left\{exp\left[\frac{2}{486}(-(-243.09333) - (-(-532.1867)))\right]\right\} = 69.58\%$$

Table 11. *Results of final exponential AFT model WGH & DRH, 2017.*

Final exponential AFT model Summary results						
Factors	**TR**	**S.E**	**Z**	**P_value**	**95% CI**	
					Lower	**Upper**
Sex (Ref.=Male)						
Female	1.081	0.228	0.37	0.712	0.715	1.635
Age	0.948	0.008	-6.49	0.000	0.932	0.963
Residence (Ref.=Urban)						
Rural	1.269	0.249	1.22	0.224*	0.864	1.865
Nutritional Status (Ref.=Good)						
Poor	0.357	0.099	-3.72	0.000	0.208	0.614
Smoking status (Ref.=No)						
Yes	0.583	0.124	-2.55	0.011	0.384	0.883
Alcoholism (Ref.=No)						
Yes	1.493	0.425	1.41	0.159*	0.855	2.610
Baseline Heart rate	0.993	0.0061	-1.16	0.244*	0.981	1.005
SBp	0.999	0.0043	-0.12	0.905*	0.991	1.008
Dm (Ref.=No)						
Yes	0.428	0.137	-2.65	0.008	0.228	0.802
CAD (Ref.=No)						
Yes	0.165	0.179	-1.66	0.097*	0.020	1.385
Coronary kidney disease (Ref.=No)						
Yes	0.683	0.164	-1.59	0.113*	0.427	1.094
HIV (Ref.=No)						
Yes	0.81	0.169	-1.01	0.311*	0.536	1.219
HTN (Ref.=No)						
Yes	0.661	0.126	-2.16	0.031	0.455	0.962
Stoke (Ref.=No)						

Final exponential AFT model Summary results						
Factors	**TR**	**S.E**	**Z**	**P_value**	**95% CI**	
					Lower	**Upper**
Yes	0.615	0.128	-2.33	0.020	0.409	0.926
Pneumonia (Ref.=No)						
Yes	1.01	0.260	0.05	0.956*	0.613	1.678
Tuberculosis (Ref.=No)						
Yes	0.014	0.010	-5.81	0.000	0.003	0.059
Tb*Age (Ref.=No)						
Yes*Age	1.039	0.012	3.33	0.001	1.016	1.059
CAD*Age (Ref.=No)						
Yes*Age	1.022	0.019	1.19	0.236*	0.986	1.060
Nut (Ref.=No)*Tb (Ref.=No)						
Yes	4.097	1.585	3.64	0.000	1.919	8.746
Dm (Ref.=No)*HTN (Ref.=No)						
Yes	2.335	1.02	1.93	0.054	0.987	5.526
Time*Age	1.001	.0001	9.42	0.000	1.001	1.002
Constant term	1338.39	996.71	9.62	0.000	310.95	5760.724
AIC						673.8928
BIC						666.0346

Log likelihood =-314.9464 LR chi2 (21) =336.33 Prob >chi2 =0.0000

$$R^2 = 1 - \left\{exp\left[\frac{2}{486}(-(-483.1094) - (-(-314.9464)))\right]\right\} = 49.94\%$$

3.5. Discussion

For this study, based on AIC, weibull AFT model were found to be the better among all semi and parametric models. In our case the weibull AFT model produced a consistence a far from zero parameter as compared to the other parametric model as well as Cox PH suggesting that the exponential PH model was better than the rest parametric as well as semi parametric model.

Age is an important demographic variable that affects the Lifespan of patients with CHF. As the age of the patient increases in years (TR=0.962) the lifespan of CHF patients were found to be prolonged. Our finding was similar with the previous study [14]. On the other hand study suggest that age were not significantly associated with CHF complications [11, 15]. In this study, the weibull AFT model as compared to the above studies might have contributed for the statistically significant association between the age and time to event. One of the other predictor variable was the presence of coronary kidney disease as a co morbidity which is not statistically significant. This study is not consistent with other studies suggests that more than 40% of HF patients have CKD and worsens their survival time [16].

A meta-analysis of 8 studies conducted in patients with CKD (stages 3–5) and CHF showed that beta blocker therapy lowered all-cause and cardiovascular mortality with an increased risk of bradycardia and hypotension [17]. They also suggests that older patients having CKD as a co morbidity accelerating the mortality of patients with CHF. In this study, the weibull AFT model and the study design as well as the number of subjects as compared to the above studies might be the statistically insignificant association between the presence of coronary kidney disease and time to event. Additionally May be physicians were not evaluated well even if it needs further study. Place of residence of the patients with CHF were found statistically significant with a probability value of (p=0.019). Based on the multivariate Weibull AFT model result patients with CHF who lived rural area were 1.24 times longer live than urban patients. This might be due to the different poisoning chemicals from the vehicles, industries, and suffocations. Actually there is no enough research which is conducted on the relationship between place of residences and CHF. Malnutrition were found statistically significant (p=0.000). CHF patients who do not intake good nutrition can decelerate their life by 0.582 than patients who intake of nutrationous food. Therefore intake of good food prolong the life of CHF patients. This study is confirmed with a study on nutrition using Cox PH model suggests that patients had CHF had intake of poor diet was fastening mortality patients (p<0.001). In other words patients with heart failure being malunutrishes had higher mortality [1, 18].

Similarly smoking were found statistically significant at a probability value of (p=0.005). Hence, smoker had shorter life span than non smokers (time ratio=0.7724). In other words smoking were accelerating the hazard of death of the patient with CHF. This study is confirmed with the previous report [19]. It suggests that smoking status at baseline for a one year survival study did not show any significant effect on the outcomes of patients with CHF. However, the study also suggests that smoking status was significantly associated with HF patients' for 1-year health status. Meaning smoking long time accelerate the mortality.

The other predictor variable under this study were alcoholism which is an important variable for the accelerate or decelerate of the survival time of patients with CHF. However this study indicates that drunkenness made prolong the life of patients with CHF at a time ratio of (TR=1.394). Therefore patients with CHF drinking little to moderate alcohol were improve the function of heart and the patients can live longer than non drunker with a probability value of

(p=0.010). Our study also comparable with other studies [19, 20]. It was shown that that a 59% lower risk of HF among men who consumed 8 to 14 drinks per week compared with abstainers and only a modest and non-statistically significant association in women. Altogether, there appears to be substantial evidence supporting possible benefits of light-to moderate alcohol consumption on the risk of HF from these observational data. Thus, for patients who do not consume any alcohol, it would be premature to recommend light-to-moderate drinking as a means to lower the risk of HF, given the possible risk of abuse and resulting consequences.

Diabetes Mellitus as a co morbidity were found statistical significant (p=0.000). Diabetes and congestive heart failure (HF) commonly coexist in the same patient, and the presence of diabetes in HF patients is associated with increased adverse events compared to patients without diabetes. Meaning the presence of Diabetes Mellitus as a co morbidity will accelerate the mortality of patients with CHF (TR=0.49). This study also confirmed with [8, 21]. Stroke as a co morbidity were found statistical significant (p=0.014). The presence of stroke in HF patients is associated with increased adverse events compared to patients without stroke. Meaning the presence of stroke as a co morbidity will accelerate the mortality of patients with CHF (TR=0.799). The complication of CHF were increase as the co morbidity increases. This study is confirmed by the previous study [19].

Coronary artery disease as a co morbidity were found statistical significant (p=0.012). The presence of Coronary artery disease in HF patients is associated with increased adverse events compared to patients without Coronary artery disease. Meaning the presence of Coronary artery disease as a co morbidity will accelerate the mortality of patients with CHF (TR=0.276). The complication of CHF were increase as the comorbidity increases. This study also confirmed within a study carried out previously [20, 21]. Therefore physicians should give due attention especially for minimizing the burden of complication of CHF had disease as a co morbidity. TB is an important clinical variable that affects the lifespan of patients with CHF. Patients with CHF had TB as a co morbidity had a worse survival rate. In other words Patients with CHF had TB as a co morbidity had accelerate the mortality by (TR=0.103) and it is statistically significant at a p-value of (p-0.000). Our study is also confirmed with the study [20].

4. Conclusion and Recommendation

This study is based on a CHF data set derived from a five-year retrospective cohort study of patients CHF follow up in the Woldia general and Dessie referral hospital, Northen Ethiopia with an aim of investigating the comparative performance of Cox and parametric models in a survival analysis of time-to death with CHF data. We used AIC and standardized variability of the coefficients for covariates in the models to evaluate the performance among models. In our dataset the proportional hazard assumptions were violated. However, based on AIC the Weibull AFT model indicated an improved fit as compared to the rest parametric counter parts for any combination of variables in the data set. We also found that from different combinations of covariates in the dataset Age, Residence, Nutritional statues, Smoking, Alcoholism, Diabetes mellitus, hypertension, Stroke, Coronary artery disease, Tuberculosis bacillus as a co morbidity and the interaction between age and Tuberculosis bacillus, age and Coronary artery disease, Diabetes mellitus with Hypertension, Hypertension with Nutritional status and age with time yield the smallest possible AIC value for Weibull AFT model suggesting that Weibull model with these predictors is the best to explain the given time to death with CHF in this dataset compared to the rest parametric models.

Based on the result of the study different factors and parsimonious model are identified for time to mortality data. Researchers in the field of medical sciences are often interested in Cox proportional hazard model more than parametric models. However, it does have the requirement of proportional hazards, which is not always satisfied by the data. If this assumption does not hold, the Cox model can lead to the unreliable conclusions. In these situations, parametric models (such as log logistic, Weibull and Exponential) provide an alternative method to fit survival data even when hazards are not proportional Moreover, under these models we measured the direct effect of the explanatory variables on the survival time and not on a conditional probability, as we do in the Cox regression model. This characteristic allows for an easier interpretation of the results because the parameters measure the effect of the correspondent covariate on the mean lifetime. Parametric models are, therefore, based on a specific distribution for duration times without need to proportional hazard assumptions.

Abbreviations

AFT: Accelerated Failure Time, CHF: Congestive Heart Failure, DRH: Dessie Referral Hospital, WGH: Woldia General Hospital, HF: Heart Failure, SPSS: Statistical Package for Social Science, STATA: South Texas Art Therapy Association

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

Habtamu D. conceived the study, participated in data

collection, performed analysis and interpretation of the data and drafted the paper and prepared all versions of the manuscript. Yenefenta W., Belete A. and Eskeziaw A. assisted in the design, participated in data collection, analysis and revised subsequent drafts of the paper. All authors read and approved the final manuscript.

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