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Research Article

Survival Pattern of Patients on Maintenance Haemodialysis for End Stage Renal Disease in a Nigerian Dialysis Centre

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Abstract

Background: The increasing incidence and prevalence of chronic kidney disease (CKD) is a serious health challenge globally. The need to examine the longevity of patients with CKD can never be over emphasized. We investigated the survival experience and factors that may contribute to the longevity of chronic kidney disease patient on haemodialysis.

Methods: Data for the study were extracted from the record of CKD patient on haemodialysis. Kaplan-Meier survival analysis was done to assess both short- and long-term survival. The impact of six covariates on survival chances were separately investigated using Log-rank test and collectively examined using both Cox and Weibull models. Akaike Information Criterion was then employed for determination of a better model between variables. P-value of <0.05 was considered as statistically significant.

Results: The overall median survival time was 182 days. Only 66.3% of all the patients survived their 90th days after starting dialysis and approximately 25% survived to 366 days. The hazard ratios for those patients with family history of chronic kidney disease was 0.45; 95% CI 0.23-0.90 and for those with urinary symptoms was 0.59; 95% CI 0.35-0.99. Model generated imply $\mathbf{h_i(t)= -5.1499\ exp\{-0.7850 Family\ His.\ Of\ CKD_i - 0.5353 Urinary\ symptom_i\}}$. The age of the patient was also found to be statistically significant when separately investigated.

Conclusion: Family history of chronic kidney disease and urinary symptoms were found to influence the survival of patients on haemodialysis. Early identification of at-risk family and prompt treatment of urinary symptoms is advocated.

Keywords: Chronic Kidney Diseases; Dialysis; Survival; Cox Proportional Hazard model; Weibull model

1. Introduction

The kidney is an important organ of the body which maintaining internal balance among other functions. When the kidney failed, the function is impaired with consequent retention of waste products of metabolism. Globally, the prevalence of renal disease is at a pandemic rate and has become a public concern. Report has shown that the prevalence of CKD is currently more than 10% in the general population and reaches 14% or more in high-risk subpopulations [1, 2]. There are currently over 1.4 million patients receiving renal replacement therapy (RRT) worldwide [3]. Haemodialysis, a form of RRT is beneficial to individuals with kidney failure. This treatment modality helps to remove waste and excess water from the blood. However, haemodialysis cannot completely reverse the function of the kidney. Mortality is substantially elevated in patients with chronic kidney disease (CKD) on dialysis [4, 5]. A Swedish population-based study compared the mortality in CKD stages 4 and 5 patients on renal replacement therapy. The authors found that during 6553 person-years, 766 patients with CKD stages 4 and 5 died (deaths/100 person-years 12, 95% CI 11 to 13) compared with 924 deaths during 3680 person-years in haemodialysis (25, 95% CI 23 to 27). In the same study, Neovius et al reported that against matched general population controls, the mortality HR was 3.6 (95% CI 3.2 to 4.0) for CKD and 12.6 (95% CI 10.8 to 14.6) for haemodialysis [6].

Survival of patient who cannot afford adequate treatment such as regular dialysis or renal transplant is unimaginable poor due to several complications that is associated with the disease [4, 5]. The financial burden of end stage renal disease (ESRD) is prohibitive. In our country, CKD patients are battling with poverty, inadequate health facilities, lack of subsidy for medical treatment among other challenges with a gloomy outlook. Survival analysis looks at how long it takes for an event to happen. The event outcome may either be positive or negative such as recovery or failure respectively. Analysis of survival data needs special consideration compared to other data because of the censored nature of the data as it does not follow a normal distribution. The survival analysis employed in this study is designed to handle time-to-event data, considering censored cases. These are cases where the event of interest has not occurred yet at the end of the study or before lost to follow-up or it has occurred due to some other causes. The degree of censoring can affect the reliability of the results. We investigated the survival experience and factors that may contribute to longevity of chronic kidney disease patient on haemodialysis in our dialysis centre. We determined the 4-week, 12-week, 26-week and 52-week survival probabilities and the best model while considering the effect of factors such as age, sex, blood pressure, family history of CKD, diabetes and urinary symptoms on the survival of the patient. Literature is scanty on the study of survival chance of dialysis patients in Nigeria. This study therefore, provided a scholarly impetus to improve the study of survival chance of dialysis patients in our practice.

2. Methods and Materials

2.1 Study design

This study was a five-year (2010-2014) retrospective review of patients with CKD who received treatment at the haemodialysis unit of Ekiti State University Teaching hospital, Ado Ekiti (EKSUTH), Nigeria. The analyzed data were extracted from the patient's clinical and haemodialysis record. Patients with incomplete data were excluded from the study. The following information was extracted: date of first dialysis session, age of the patient, sex of the patient, blood pressure (BP) of the patient at commencement of dialysis, urinary symptoms, history of diabetes mellitus, family history of CKD, last date of dialysis session, status of patient after last dialysis and patient time. Ethical approval was obtained from the ethical committee of the institution.

2.2 Definition of terms

2.2.1 Date of first dialysis session: This is the date the patient commenced dialysis. This is the treatment starting point for the patient.

2.2.2 Age of the patient: This is the patient age at first dialysis. Age was categorized into two groups <60 and >/=60 using 60 years as cut off point. This was used in Cox proportional and Weibull analysis to determine whether age is a predictor of survival time.

2.2.3 Blood pressure (BP) of the patient at the commencement of dialysis: Blood pressure classification according to Eight Joint National Committee [7].

2.2.4 Last date of dialysis session: This is the date which the last dialysis was done for the patient. This is the treatment endpoint for the patient.

2.2.5 Status of the patient after last the dialysis: This is the treatment outcome of the patient after the last dialysis session. The status may be a failure (death) or censor.

2.2.6 Patient time: This is the time a patient spends in the study from the time of first to the last dialysis.

2.3 Data management and data analysis

Data analysis was performed with STATA version 12. Bivariate analysis was conducted using nonparametric technique; Kaplan-Meier Product Limit [8] Method was employed in estimation of the survival functions and hazard rates of the survival data. Also, both Log-Rank Test and Wilcoxon (Breslow) test was used for the comparison of survival functions. Cox's proportional hazard regression (Multivariate analysis) was initially used to model the relationship between the survival time and explanatory variables such as age, sex, hypertension, diabetes, family history and urinary symptoms. The data used in this study follows Weibull distribution which enabled the fitting of the probability distribution of real-life time data of dialysis patients. To be able to choose the better model between

Cox proportional and Weibull, Akaike Information Criterion (AIC) was employed. Model that has AIC estimate with the smallest value was considered to be more precise. Charts and tables were used to present the results.

3. Result

3.1 Sociodemographic distribution of the patients

One hundred and seven patients were the participants. Male constitute a higher proportion, 74 (69.2%). The mean age of the patients was 51 ± 15.4 years with a range of 21-89 years. The largest number of patients falls between age group 50-59 years (22.3%). Most of the patients (43.9%) were secondary school holders and petty trader (43.9%) constituted the highest proportion of their occupations (Table 1). The highest number of patient (46.7%) were treated in year 2013. Out of 107 patients, 40 (37.4%) were censored as alive up till or after the study time or were lost to follow up, 67 (62.6%) patients were reported to have died as a result of CKD.

Variables	Count	Percentage (%)
Age Group (Years)		
20-29	8	7.8
30-39	22	20.4
40-49	20	18.7
50-59	24	22.3
60-69	20	18.7
70 and above	13	12.1
All (21-89)	107	100.0
Sex		
Male	74	69.2
Female	33	30.8
Occupation		
Civil Servant	16	15.0
Petty Trader	47	43.9
Farmer	17	15.9
Artisan	9	8.4
Others	18	16.8
Education		
None	10	9.3
Primary	11	10.3
Secondary	47	43.9
Tertiary	39	36.4

Table 1: Social Demographic Characteristics of chronic kidney disease patients.

3.2 Overall survivorship experience

In the overall cumulative survival, 66.3% of all the patients survived their 90th days after starting dialysis and approximately 25% survived to 366 days (Table 2. Figure 1). The median survival time was 182 days.

Time (days)	Start total	[S(t)]	SE[S(t)]	95% CI	
5	107	0.9907	0.0093	0.9355	0.9987
15	99	0.9438	0.0223	0.8792	0.9744
21	90	0.8663	0.0333	0.7845	0.9186
31	79	0.826	0.0374	0.7379	0.8867
60	71	0.7518	0.0433	0.6547	0.8252
90	56	0.6632	0.0482	0.5593	0.748
183	34	0.4824	0.0544	0.3727	0.5836
206	25	0.4239	0.0551	0.3152	0.5284
216	20	0.3524	0.0562	0.2447	0.4617
222	19	0.3338	0.0562	0.2271	0.444
275	15	0.2712	0.0561	0.1686	0.3844
360	12	0.2486	0.0558	0.1482	0.3626
366	11	0.2486	0.0558	0.1482	0.3626
367	10	0.2238	0.0555	0.126	0.3389
397	9	0.1741	0.0531	0.0853	0.2889
399	7	0.1492	0.051	0.0668	0.2625
428	6	0.1492	0.051	0.0668	0.2625
457	5	0.1193	0.0488	0.0451	0.2326
463	4	0.0895	0.0448	0.0267	0.2004
491	3	0.0597	0.0385	0.0121	0.1654
517	2	0.0597	0.0385	0.0121	0.1654
611	1	0.0597	0.0385	0.0121	0.1654

Table 2: Kaplan Meier Estimate of survivorship for all patients since first dialysis.

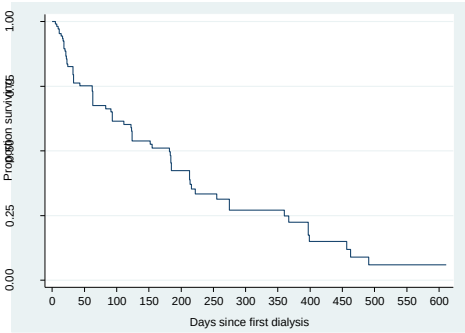

Figure 1: Survival curves of all patients since first dialysis.

3.3 Kaplan-Meier rate of survival according to selected characteristics and log rank or Wilcoxon test

3.3.1 Sex: There was no statistically significant association between sex and mortality. Log rank (Mantel-Cox): Chi-square=0.06; P-value=0.80. Median survival time was estimated for male and female to be 182 and 152 days respectively as shown in Figure 2.

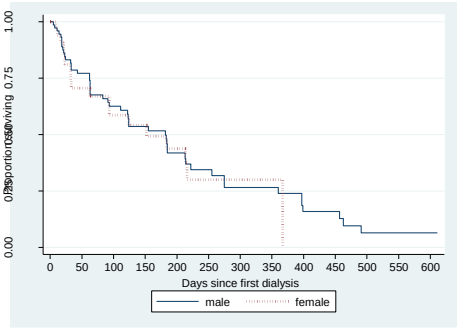

Figure 2: Survival Curves for male and female patients.

3.3.2 Age group: Figure 3 showed that survival (earlier survival difference) varies among the two age groups. Younger age group had a better survival experience. There was a statistically significant association between age group and mortality. Wilcoxon (Breslow): Chi-square=6.67; P-value=0.01.

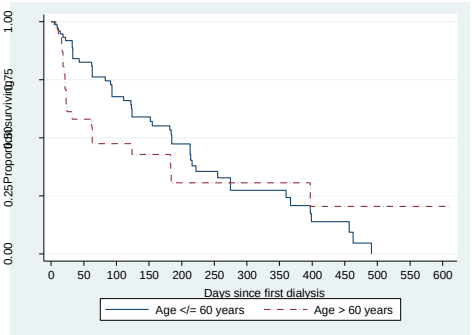

Figure 3: Survival curves for age group ≤ 60 years versus age group >60 years.

3.3.3 Diabetes status: Median survival time for CKD patients with no diabetes is 183 days while patients with diabetes is 93 days (Table 4 and Figure 4). The relationship between the two diabetes status group was not statistically significant (Long-rank: Chi-square is 0.06, P-value=0.80) as shown in Table 4.

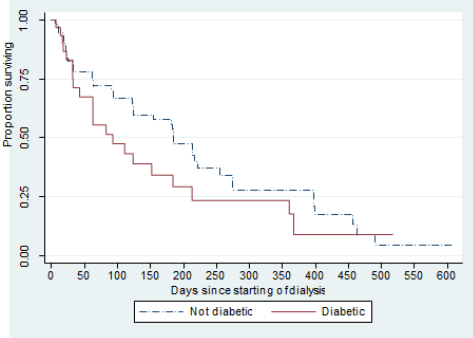

Figure 4: Survival curves by diabetes status.

3.3.4 Family history of chronic kidney diseases (CKD): The median survival time for patient with or without family history of CKD was 124 and 367 days respectively (Log rank statistic 6.78, p-value=0.009). Survival is better if there is no family history of CKD Figure 5.

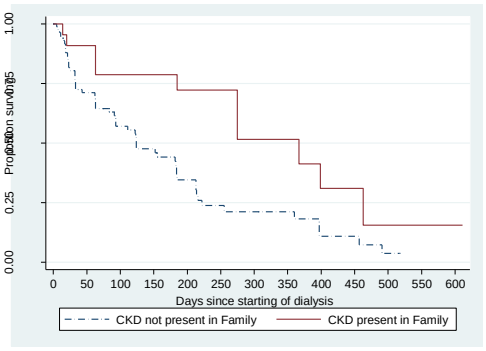

Figure 5: Survival curves by family history of chronic kidney disease patients.

3.3.5 Urinary symptoms: We found a statistically significant relationship among patient with and without urinary symptoms a median survival time of 83 and 213 days. (Long-rank: Chi-square is 5.79, P-value=0. 016) Figure 6.

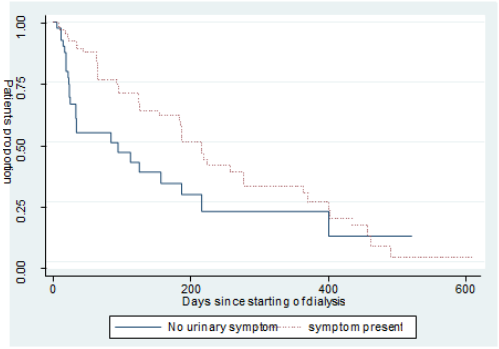

Figure 6: Survival curves for patient with or without urinary symptoms.

3.3.6 Blood pressure at commencement of dialysis: There was no statistically significant relationship in the median survival time among patient with normal BP, 1st stage hypertension and 2nd stage hypertension, Log rank (Mantel-Cox): Chi-square=0.836; P-value=0.80 Figure 7.

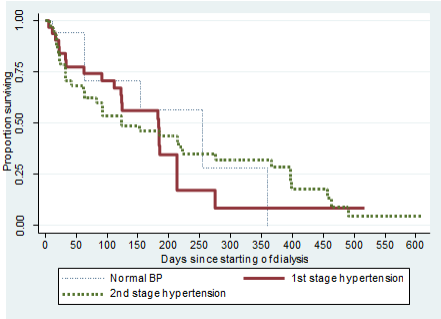

Figure 7: Survival curves of patients in different stages of blood pressure.

3.4 Justification that collected CKD data follows Weibull distribution

A straight (approximately) line in the plot of Log {-log S(t)} versus Log (t) indicates a Weibull models. In Figure 8 Gender and Age covariates showed linearity hence, Weibull model was considered appropriate for the data used for the study.

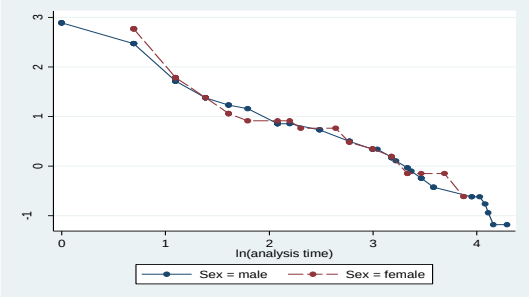

Figure 8: Justification that collected CKD data follows Weibull model.

3.5 Cox proportional hazard and weibull models

The consideration of only three variables here was as a result of their statistical significances among the initial six covariates. Under the Cox Proportional Hazard model (Table 3) therefore, only Family history of CKD is statistically significant among others (Age group and urinary symptoms). Computation from Weibull model (Table 4) on the other hands, confirmed family history of CKD and urinary symptom to be statistically significant.

Explanatory Variables	Hazard Ratio	S.E.	Z	P-values	95% CI	
Age group	1.146831	0.328604	0.48	0.633	0.654038	2.010926
F.history of CKD	0.450776	0.157754	–2.28	0.023	0.227025	0.895051
Urinary symptoms	0.62633	0.169884	–1.72	0.085	0.368066	1.065814
_cons	-	-	-	-	-	-

Log likelihood= –246.18

Table 3: Cox proportional Hazard model.

Explanatory Variables	Hazard Ratio	S.E.	Z	P-values	95% CI	
Age group	1.181071	0.331647	0.59	0.553	0.681172	2.047836
Family history of CKD	0.456093	0.158785	–2.25	0.024	0.230523	0.902385
Urinary symptoms	0.585528	0.157515	–1.99	0.047	0.345592	0.992046
_cons	0.005763	0.003747	–7.93	0	0.001612	0.02061

Log likelihood= –133.811

Table 4: Weibull model.

3.6 Comparison of the result form the Cox and the Weibull model

The comparison of both the Cox proportional hazard and the Weibull model as shown in table 5. gives different results. However, the Weibull model is supported by Akaike Information Criterion. Hence, computation of hazard ratio from Weibull model implies 0.45; 95% CI 0.23-0.90 for family history of CKD history, taking the patient with no family history of CKD as the reference category. Also, for urinary symptom, hazard ratio from Weibull model imply 0.59; 95% CI 0.35-0.99 for patients with urinary symptoms, taking patients with no urinary symptoms as the reference category.

Covariate		Cox Model	Weibull Model
		HR (95% Conf. Interval)	HR (95% Conf. Interval)
Age Class	≤ 60 years (ref.)	1.15 [0.65-2.01]	1.18 [0.68-2.05]
	>60 years		
Family history of CKD	Not present (ref.)	0.45 [0.23-0.90]	0.46 [0.23-0.90]
	Present		
Urinary symptoms	No urinary symptoms (ref.)	0.63 [0.37-1.07]	0.59 [0.35-0.99]
Akaike Information Criterion		496.36	267.62

Table 5: Comparison of the result form the Cox and the Weibull model.

3.7 Model fitting

Family history of CKD and urinary symptoms are the only covariates compared to others that influence survival chance in this study. The hazard ratios of the two covariates are supportive. Therefore, better model using computations in table 6 imply; $\mathbf{h_i(t) = –5.1499 \exp \{– 0.7850 Family\ His.\ Of\ CKD_i – 0.5353 Urinary\ symptoms_i\}}$

Covariate	HR	β
Urinary status	0.5855	–0.5352891
Family his. Of CKD	0.4561	–0.7850432
Constant	0.0058	–5.14989736

Table 6: Model fitting.

4. Discussion

Chronic kidney disease is common among young adults between 20 to 50 years in sub-Saharan Africa [9]. In this study, we found that the overall median survival time was 182 days. However, the overall cumulative survival was 66.3% for all the patients that survived their 90th days from starting of dialysis and approximately 25% survived to 366 days. This is higher than the 90th days reported in an Ethiopia study (61.5%) [10] and Ghana (45%) [11]. Van-Djik et al. in their analysis of renal data collected from the national renal registries of six European countries found that the 2-, 5- and 10-year patient survival was 67, 35 and 11% respectively among their dialysis patients. This figure is much higher than what we obtained in this study probably because Europe is a developed country with better healthcare system compared to Nigeria [12]. Individuals with a family history of kidney disease appear to be at higher risk of developing kidney disease. The presence of genes coding for susceptibility factors for the development or progression of kidney disease in general, as well as genes coding for specific kidney diseases such as nephropathic cystinosis, autosomal dominant polycystic kidney disease [2]. A family history of kidney disease is a risk factor for CKD. A high number of ESRD patients have an affected first-degree relative. This association has been found to be much stronger in African Americans than whites [13, 14]. Song et al. screened incident dialysis patients over 8 years period in the United States, nearly 23% of incident dialysis patients had close relatives with ESRD [15]. McClellan et al. [16] reported a significantly increased risk for ESRD associated with a positive family history of chronic kidney disease even after adjusting for confounders such as age, sex, race, diabetes, hypertension, and socio-economic status (adjusted hazard ratio of 1.93; 95% confidence interval, 1.22-3.07). In this study, patients with family history of CKD are 0.46 times as likely to be at the risk of death compared to those without family history. Similarly, Patients with urinary symptoms at starting dialysis are 0.59 times as likely to be at the risk of death compared to those without urinary symptoms similar to other reports [17, 18].

The presence of co-morbidity such as diabetes mellitus, high blood pressure and other covariates such as sex and age group which did not reach statistically significant were presumed not to have any influence on the survival chances of CKD patients on dialysis except age group when separately investigated. Reindl-Schwaighofer et al. [19] retrospectively analyzed the Austrian Dialysis and Transplant Registry and identified 8,622 patients who started maintenance hemodialysis after the age of 65 years between 2002 and 2009. The data set was compared with a cohort of 174 patients aged over 65 Years with CKD Stage 5 who progressed to an ESRD and were managed conservatively. Their result suggested that the benefit of dialysis treatment decreases with age when the data was further subjected to time to event analysis. The influences of family history of CKD and urinary symptoms in the patient may be supportive. Awareness of chronic kidney disease among members of family will enable other members to practice preventive measures as they are now better informed. Such an individual is expected to present early and comply with medical treatment. It is also likely that patient with urinary symptoms is likely to present or referred to the nephrologist early. The data used for this study followed Weibull regression model, being the one with the least AIC value when compared with the Cox model which indicates the best model for registered chronic disease patients in our institution. Cox regression model with highest AIC was considered to be comparatively less

efficient. This result agreed with the results obtained by Hui et al. [20] where comparison of Cox and Weibull model was done using gastric cancer data.

5. Conclusion

This study provided information on the survival experience among a fairly large population of patients treated with dialysis at haemodialysis centre of Ekiti State University Teaching Hospital patient. Out of the entire explanatory variables investigated for their influence on survival chances during dialysis, only family history of chronic kidney disease and urinary symptoms were statistically significant among variables considered. Though the age-group of patients at the start of dialysis was also statistically significant when separately investigated. This study hence recommends appropriate attention to be paid to those with family history of CKD and urinary symptoms at the start of dialysis in addition to other treatment strategies.

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