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Survival Analysis of Glaucoma Patients Until Blindness: The Case of University of Gondar Comprehensive Specialized Hospital, Gondar, Ethiopia

Körlüğe Kadar Glokom Hastalarının Sağkalım Analizi: Gondar Üniversitesi Kapsamlı Özel Hastane Vakası, Gondar, Etiyopya

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ABSTRACT Objective: The objective of the study was to identify the best-fitted survival regression model and to find factors that accelerate the time of blindness of glaucoma patients in University of Gondar Comprehensive Specialized Hospital. **Material and Methods:** Secondary data was taken from the patient's card, collected from January 2014-April 2018 in the hospital. In this study 401 glacoma patients' record was considered. Kaplan-Meier survival analysis, Semiparametric and Parametric AFT model were applied to identify factors that lead blindness of glaucoma patients. **Results:** From the total 401 glaucoma patients 23.69% was blind. From the total sample 38.41% and 61.59% were female and male glaucoma patients, respectively. The median time of blindness for the two eyes or one eye was 16 months after confirmation of glaucoma disease. In the multivariable Weibull accelerated failure-time model it has found that age group (18-43) (TR =1.29233, CI: 1.039576 to 1.606536), advanced stage of glaucoma (TR =1.281674, CI: 1.096103 to 1.498662), duration of diagnosis 1-5 years (TR = 1.944649, CI: 1.332738 to 2.83751) and duration of diagnosis >= 6 years (TR = 2.683586, CI: 1.367533 to 5.26615) were significantly associated with the time to blindness. **Conclusion:** The multivariable Weibull model revealed that age, duration of diagnosis and stage of glaucoma were major factors that affect the survival probability of glaucoma patients. Finally, based on the results of the study we can conclude that the Weibull regression model was the best fitted parametric accelerated failure-time model for identifying the major factors related to glaucoma patients.

Keywords: Glaucoma; risk factor; survival model; time of blindness

ÖZET Amaç: Çalışmanın amacı, en iyi sağkalım regresyon modelini belirlemek ve Gondar Üniversitesi Kapsamlı Özel Hastanesi'ndeki glokom hastalarının körlük süresini hızlandıran faktörleri bulmaktır. **Gereç ve Yöntemler:** İkinci veri Ocak 2014-Nisan 2018 arasında hastane tarafından toplanan hasta kartlarından alınmıştır. Bu çalışmada 401 glokom hastasının kayıtları dikkate alınmıştır. Glokom hastalarında körlüğe neden olan faktörleri belirlemek için Kaplan-Meier sağkalım analizi, Yarıparametrik ve Parametrik AFT model uygulanmıştır. **Bulgular:** 401 glokom hastasının %23.69'u kördü. Glokom hastalarının %38.41'i kadın, %61.59'u erkekti. Glokom hastalığı tanısı konduktan sonra bir ya da iki göz körlüğünün medyan süresi 16 aydır. Çok değişkenli Weibull hızlandırılmış başarısızlık-zaman modelinde yaş grubu (18-43) (TR =1.29233, CI: 1.039576;1.606536), ilerlemiş glokom evresi (TR =1.281674, CI: 1.096103;1.498662), tanı süresi 1-5 yıl (TR = 1.944649, CI: 1.332738;2.83751) körlük süresi ile anlamlı olarak ilişkili bulunmuştur. **Sonuç:** Çok değişkenli Weibull modeli yaş, hastalık süresi ve glokom evresinin glokom hastalarının sağkalım olasılığını etkileyen başlıca faktörler olduğunu ortaya çıkarmıştır. Sonuç olarak, çalışma sonuçlarına göre Weibull regresyon modeli; glokom hastaları ile ilişkili başlıca faktörleri belirlemede en iyi tahmini veren parametrik hızlandırılmış başarısızlık-zaman modelidir.

Anahtar Kelimeler: Glokom; risk faktörü; sağkalım modeli; körlük süresi

Glaucoma is one of the major eye diseases that cause visual impairment. It is most of the time related with elevated intraocular pressure (IOP) in which failure to the eye (optic) nerve can lead to loss of vision and even blindness.[1] According to Katz (2012) glaucoma is the leading cause of irreversible blindness in the world.[2] Glaucoma by its nature causes no symptoms early in its course when it can only be diagnosed by regular and frequent eye examinations based on age and the presence of other risk factors.[2]

The disease distribution was high (more than 66 million people worldwide) and is the second leading cause of irreversible blindness (more than 7 million people bilaterally blind worldwide).[3] Review of different studies revealed that glaucoma is responsible for 10-11% of eye failure in Western Europe and the U.S., and this percentage is increased in the last decade. The visual outcome is the main issue of glaucoma patients.[4] At medication, 34% are worried about blindness in the future; even if the percentage declines to 11% at follow-up, fear is still very high for patients with severe filed deterioration and progression.[5]

A study conducted in China on Angle-Closure Glaucoma (ACG) predicted blindness at presentation 6% and 30.1% based on visual acuity and visual field criteria with the progression to blindness in 7% over a 10-year follow-up.[6] Based on World Health Organization (WHO), glaucoma is the second main cause of avoidable blindness next to cataract,8% of total blindness worldwide.[7] This number could be as high as 15% in some Low and Middle- Income Countries (LMIC), specially in sub-Saharan-Africa. The Nigeria National Blindness and Visual Impairment Survey indicates that glaucoma related blindness was the most prevalent blinding condition after cataract.[8] In Ethiopia National Blindness and Low Vision Survey, which was studied in 2005, glaucoma was found to be the fifth major cause of blindness in Ethiopia (5.2% to the total blindness).[9]

Prevention of eye loss due to glaucoma is difficult in the Africa context. Patients frequently present late with advanced disease. Optometry services are not generally well established and only found in larger urban centers. Therefore, relatively little opportunistic detection of glaucoma and simple, cost-efficient systems are required to find persons with glaucoma before they exist substantial blindness. Generally, rural places of low income countries like Ethiopia have low access to eye care services.[10]

In medical research, most of the study was done by means of non-parametric [using Kaplan-Meier (KM) and cumulative hazard estimator] and semiparametric (Cox regression) methods and as well as performed by linear regression models.[11,12] Even if the semi-parametric and the non-parametric survival models have considerable success in analyzing time to event data, parametric survival models are usually advantageous for various reasons. Under the semi-parametric survival model the distribution of the baseline hazard model is not specified, but in the case of parametric model it assumes some well known distribution. If the assumption of the parametric model gets satisfied it will give a more reliable result with high precision. Uses of parametric model are as follows:distribution of survival time can be predicted, residual can show the difference between observed and predicted values of time, quantification, model building with time-dependent factors, complex models in large dataset and cause-specific or relative survival estimation is possible with parametric model..[12,13]

MATERIAL AND METHODS

This study was conducted in University of Gondar Comprehensive Specialized Hospital especially in the Ophthalmology Department. A retrospective study design was employed to retrieve relevant information from the medical records to address the objective of the study. The target population for the study was confirmed eye patients at Ophthalmology Department, University of Gondar Comprehensive Specialized Hospital.

Selected eye disease patients' medical records from January 2014 to April 2018 in Ophthalmology Department, University of Gondar Comprehensive Specialized Hospital were analysed.

For each patient, blindness from glaucoma of at least one eye occurring during the time of observation was considered as an event.

A simple random sampling method was employed for selecting a representative sample in which each of the patients had an equal chance of being selected to be part of the study. The total number of samples included in the study was 401 patients.

The response variable of this study was the survival time blindness of glaucoma patients. The survival time of glaucoma patients is the length of time from follow up start date until the date of blindness (or censor). Glaucoma patients, who stayed alive during study time, lost to follow up, or died by other causes were considered as censored. Independent variables that are assumed to influence the survival time glaucoma patients are: sex, place of residence, age, blood pressure, diabetic disease, duration of diagnosis, duration of treatment, stage of glaucoma, types of glaucoma, and family history of glaucoma.

Survival analysis is the phrase used to describe the analysis of data in the form of a well-defined time origin until the occurrence of some particular event or end point. Generally, survival analysis is a collection of statistical procedures for data analysis for which the outcome variable of interest is time until an event occurs. The term survival analysis suggests that the event is death, but that is not necessarily so. Events can also denote successful outcomes, such as recovery from therapy. Survival time then describes the time from a certain origin to the occurrence of an event. Let T be a random variable denoting a survival time, the distribution of survival time is characterized by any of three functions.[14,15,16]

The survival function: The survival function defined as the probability that the survival time is greater or equal to t. It gives the probability that a subject will survive past time t.

$$S(t) = P(T \geq t) = 1\text{-}F(t),\ t > 0$$

The probability density function: The probability density function is also very useful in describing the continuous probability distribution of random variable such as time, in survival analysis. Density functions for continuous random variable T is given by:

$$\begin{aligned} f(t) &= \frac{d}{dt} F(t) \\ &= \lim_{h\to 0} \frac{F(t+h)-F(t)}{h} \\ &= \lim_{h\to 0} \frac{f(t)h}{h} \\ &= f(t) \end{aligned}$$

The hazard function: The hazard function sometimes called instantaneous failure rate, incidence rate, the age-specific failure rate or conditional failure rate. The hazard function is the instantaneous probability of having an event at time t (per unit time) given that one has survived (i.e. not had an event) up to time t. For continuous random variables the hazard function is given by:

$$\begin{aligned} \lambda(t) &= \lim_{h\to 0} \frac{F(t+h)-F(t)}{h} \frac{1}{P(T>t)} \\ &= \lim_{h\to 0} \frac{F(t+h)-F(t)}{h} \frac{1}{1-F(t)} \\ &= \frac{f(t)}{1-F(t)} \\ &= \frac{f(t)}{S(t)} \end{aligned}$$

The KM estimator is a non-parametric estimator of the survivor function S (t).The KM estimator of the survivorship function (survival probability) *S(t) = P(T>t)*. S (t) is given by Smith.[17]

$$\tilde{S}(t)=\prod_{j:\tau<t}\{1-\frac{dj}{nj}\}^{\delta i}$$

Where d_j is the number of individuals who experience the event at timet_j,δ_i is tied indicator, and nj is the number of individuals who have not yet experienced the event at that time and are therefore still at risk for experiencing it.

The log-rank test, also referred to as the Mantel-Cox tests, is the most widely used method of comparing two survivals curves and can easily be extended to comparisons of three or more curves.[18]

Cox regression is considered as a semi-parametric procedure because the baseline hazard function,$ho(t)$ does not have to be specified, since the baseline hazard is not specified, a different parameter is used for each unique survival time. Because the hazard function is not restricted to a specific form, the semi-parametric model has considerable flexibility and is widely used. The hazard ratio (HR) of two individuals with different covariates x and x* is

$$HR=\frac{ho(t)\exp(\beta'X)}{ho(t)\exp(\beta'X*)}$$

This HR is time-independent, which is why this is called the proportional hazards (PH) model. The main assumption of the Cox PH model is PH. The PH model restricts the coefficients of the regressor's in the hazard function to be constant over time. These critical assumptions of PH model and must be checked for each covariate.

Parametric models are used only occasionally in analyzing clinical studies of survival despite offering some advantages over semi-parametric models. Parametric regression analysis is an attractive alternative to the widely used Cox model when hazard functions themselves are of primary interest, or when relative survival times are the primary measure of association. The key difference between the two kinds of models is that the baseline hazard function is assumed to follow a specific distribution when a fully parametric PH model is fitted to the data, whereas the Cox model has no such constraint.

In the parametric approach, a particular survival distribution is assumed to be exponential, Weibull, log-logistic and lognormal. In the statistical area of survival analysis, an accelerated failure time model (AFT model) is a parametric model that provides an alternative to the commonly used PH models. Whereas a PH model assumes that the effect of covariate is to multiply the hazard by some constant, an AFT model assumes that the effect of covariate is to accelerate or decelerate the life course of a disease by some constant. In full generality, the accelerated failure time model can be specified as:

$$\lambda(t/\theta)=\theta\lambda o(\theta t)$$

where θ denotes the joint effect of covariates, typically $\theta=\exp(-[\beta 1X1+\cdots+\beta pXp])$.[19]

Model comparison was performed using Likelihood ratio test, Maximum likelihood and information criteria.

Ethical clearance was obtained from the ethical review committee of University of Gondar College of natural and computational sciences. The names of the subjects were not extracted to ensure privacy of patient information and confidentiality was maintained throughout the data collection process and analysis.

RESULTS

The study sample was obtained from a total population of 5980 glaucoma patients of which a random sample of 401 patients was taken, 23.69% of them were blind and 76.31% were censored. In this study, the minimum and maximum follow up time was 1 month and 55 months respectively. The total extent of follow-up time was 7,524 person-years with, an incidence rate of 0.04 blindness per100 person-years. The glaucoma patient's year range from 18 to 90 years with the survival median time of the glaucoma patients was 16 months. Out of the total patients 154(38.41%) were female and 247 (61.59%) were male. From the total patients 174 (43.39%) were from urban area while the remaining 227 (56.61%) were from rural area. The majority had been diagnosed between 1-5 years 229 (57.11%). From 401 glaucoma patients 30.67% had diabetic disease similarly 82 (20.45%) had blood pressure. Out of the study samples, 190(47.36%) had advanced glaucoma (determined by the extent of optic nerve damage). The most frequent types of glaucoma were primary open angle glaucoma (POAG) 195 (48.63%) and pseudoexfoliative glaucoma 151 (37.65%). During the follow up time period 95 (23.69%) of patients were blind and the remaining 306 (76.31%) glaucoma patients were censored at the end of the study and the majority of the patient were those age group between 44-69 (59.1%).

From the above Table 1 it is shown that there was a significant difference among the age groups regarding to the survival time of blindness.

TABLE 1: Comparison of Group difference of some socio demographic characteristics with survival pattern of glaucoma patients in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

Covariates	Category	No. of Censored	Percent of Censored	No. of Event	Percent of Event	Log-rank test Chi-square	p-value
Age	18-43	50	16.34%	8	8.42%	9.97	0.0068
	44-69	187	61.11%	50	52.63%		
	≥70	69	22.55	37	38.95%		
Sex	Female	118	38.56%	36	37.89%	0.45	0.5015
	Male	188	61.44%	59	62.11%		
Place of Residence	urban	136	44.44%	38	40.00%	1.27	0.2597
	rural	170	55.56%	57	60.00%		

TABLE 2: Comparison of various groups of clinical treatments of glaucoma patients in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

Covariates	Category	No. of Censored	Percent of Censored	No. of Event	Percent of Event	Log-rank test Chi-square	p-value
Age	Yes	100	32.68%	23	24.21%	1.77	0.1835
	No	206	67.32%	72	75.79%		
Blood pressure	Yes	59	19.28%	23	24.21%	0.13	0.7170
	No	247	80.72%	72	75.79%		
Duration of diagnosis	< 1 year	105	34.32%	47	49.47%	188.08	0.0000
	1-5 years	185	60.46%	44	46.32%		
	>= 6 years	16	5.22%	4	4.21%		
Duration of treatment	< 1 year	178	58.17%	42	3.16%	162.60	0.0000
	1-5 years	115	37.58%	50	52.63%		
	>= 6 years	13	4.25%	3	44.21%		
Stage of glaucoma	Early	119	38.89%	1	1.05%	31.76	0.0000
	Moderate	73	23.85%	18	18.95%		
	Advanced	114	37.26%	76	80.00%		
Type of glaucoma	ACG	37	12.09%	18	18.95%	1.22	0.5447
	XFG	111	36.27%	40	42.11%		
	POAG	158	51.64%	37	38.95%		
Family history of glaucoma	One or both parents in glaucoma	17	5.56%	4	4.21%	1.42	0.2326
	None	289	94.44%	91	95.79%		

ACG: Angle-Closure Glaucoma, POAG: Primary Open Angle Glaucoma, XFG: Pseudo-Exfoliation Glaucoma.

From the above Log-rank test it is shown that there was a significant difference occurred among the covariates of duration of diagnosis, duration of treatment and stage of glaucoma for the time of blindness (Table 2). The estimates of the overall KM survivor function presented below in Figure 1 showed thatblindness was higher in the beginning of the follow-up months and it strictly declined in the later months of follow-up.

From Figure 2 we can observe that patients who were diagnosed early (time of diagnosis >=6 years) lived longer or had a more favorable survival experience than those who diagnosed recently (time of diagnosis 1-5 years)) In addition those who were diagnosed before 1-5 years lived longer than those who were diagnosised less than one year (Table 2).

Figure 3 indicates that the glaucoma patients of age group 18-43 have higher survival curve as compare to other curve. This means the pattern of one survivorship function laying above had more favorable survival experience than that found below (Table 1).

Similarly, from Figure 4 we can conclude that the upper curve indicates that particular group experiences more survival time than the one below (i.e advanced, stage of glaucoma) (Table 2).

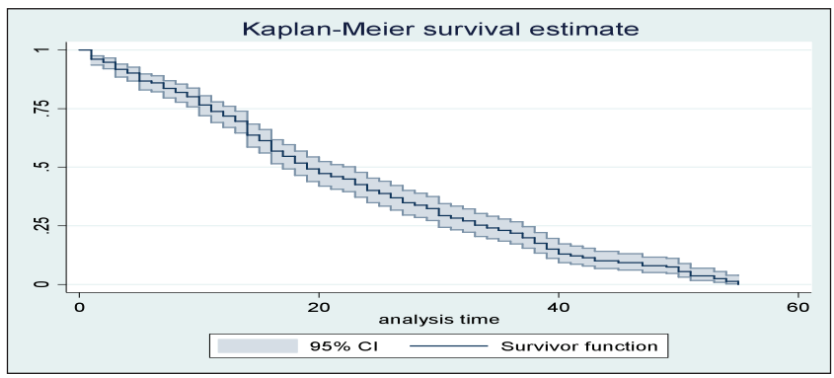

FIGURE 1: The plots of the overall estimate of Kaplan-Meier survivor function of glaucoma patients in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

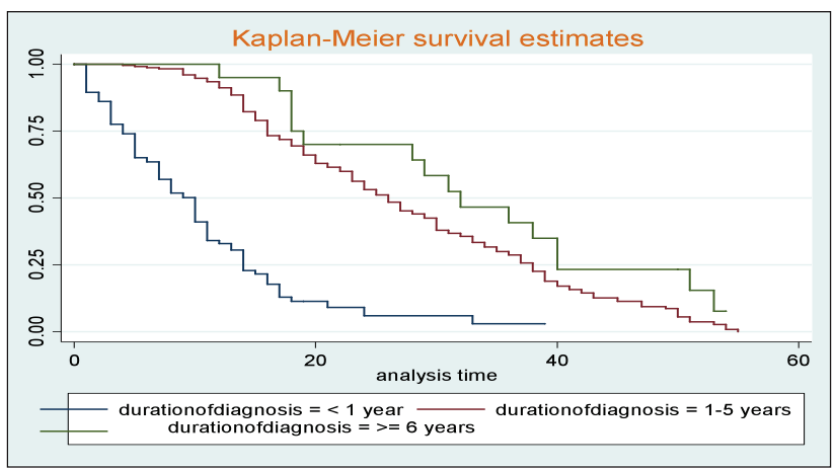

FIGURE 2: Estimated survivorship functions for duration of diagnosis for glaucoma patients in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

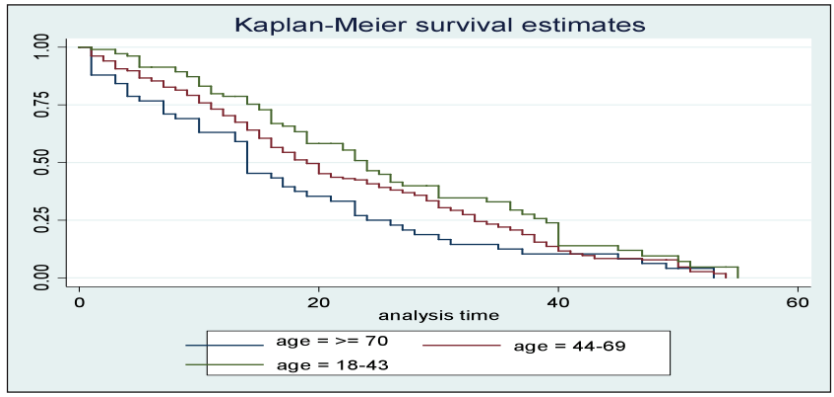

FIGURE 3: Estimated survivorship functions for the age group of glaucoma patients in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

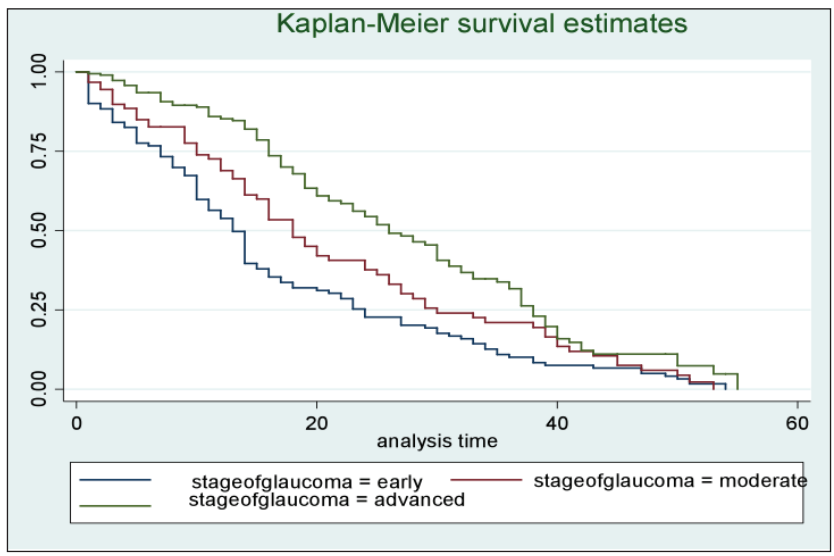

FIGURE 4: Estimated survivorship functions for the stage of glaucoma patients in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

TABLE 3: Multivariable Cox proportional hazard models of glaucoma patient's data in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

Covariates	Multivariable Cox proportional hazards model					
	Haz.Ratio	Std.Err	Z	P>|z|	[95% Conf.	Interval]
Age(>70Ref.)						
44-69	.8413266	.1404014	-1.04	0.301	606618	1.166847
18-43	.6316422	.1249502	-2.32	0.020	.4286356	.930795
Diabetic (yes Ref.)						
No	.8910983	.1118625	-0.92	0.358	.6967412	1.139672
Duration of diagnosis (< 1 year Ref.)						
1-5 years	.3262825	.1108364	-3.30	0.001	.1676661	.634954
>= 6 years	.165707	.1026497	-2.90	0.004	.0492098	.5579949
Duration of treatment (>=6 years Ref.)						
1-5 years	1.554868	1.04669	0.66	0.512	.4156144	5.816964
< 1 year	.8092724	.5400354	-0.32	0.751	.2188163	2.993021
Stage of glaucoma (early Ref.)						
Moderate	.9757026	.1515605	-0.16	0.874	.7196086	1.322935
Advanced	.6535582	.0913623	-3.04	0.002	.4969275	.8595587
Family history of glaucoma (one or both parents Ref.)						
None	1.017478	.2602214	0.07	0.946	.6163521	1.679658

Ref.: reference group.

Table 3 revealed that age, duration of diagnosis and stage of glaucoma have statistical relation with the time of blindness for glaucoma patient's (P-vlue<0.05). The PH assumption is not satisfied for the given data. The global test revealed the p-value that was less than 0.05 (P-value<0.05, Chi-square=21.45). Hence, the best one can hope for is to apply accelerated failure time model (AFT Model).

Table 4 shows that the result of time ratio and their corresponding p-value for different parametric survival models (Exponential, Weibull, Log-logistic and Log-normal). Next we select the best model using Log-likelihod, Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) model selection criteria.

As we could observe from the Table 5 both AIC and BIC criteria the Weibull distribution had minimum AIC and BIC value therefore, it is considered as the best fitted model for predicting survival time of blindness of glaucoma patients data in University of Gondar Comprehensive Specialized Hospital. The Accelerated Failure- Time Weibull regression model in the multivariable analysis belongs to the socio demographic covariates age group [18-43: TR= 1.29233, Confidence Interval (CI)=1.039576-1.606536] was found to be statistically significantly associated with the time to blindness. On the other hand duration of diagnosis 1-5 years (TR= 1.944649, CI=1.332738-2.83751) and >= 6 years (TR=2.683586, CI= 1.367533-5.26615), stage of glaucoma advanced (TR=1.281674, CI=1.096103 1.498662) were statistically significant associated with time to blindness from clinical covariates.

TABLE 4: Parametric regression models fitted to glaucoma patient's data in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

Predictor variables	Model							
	Exponential		Weibull		Log-Logistic		Log-Normal	
	Time ratio	p-value	Time ratio	p-value	Time ratio	p-value	Time ratio	p-value
Age(> 70) (Ref.)								
44-69	1.116849	0.505	1.103273	0.293	1.118798	0.321	1.147588	0.233
18-43	1.429423	0.070	1.29233	0.021	1.439147	0.005	1.475194	0.004
Diabetic (yes) (Ref.)								
No	1.217843	0.114	1.081756	0.267	1.233793	0.011	1.1957	0.037
Duration of diagnosis (<1 year)	2.24125	0.014	1.944649	0.001	2.796469	0.000	3.130824	0.000
1-5 years	3.1498	0.060	2.683586	0.004	3.353322	0.003	3.751908	0.001
>= 6 years (Ref.)								
Duration of treatment								
>=6year	.9073249	0.884	.7997247	0.551	.7862717	0.586	.7981392	0.618
1-5 years	1.074915	0.913	1.090244	0.819	.8934778	0.7900	.8808944	0.768
< 1 year (Ref.)								
Stage of glaucoma(early)	1.135823	0.408	1.013209	0.880	1.086093	0.432	1.110353	0.338
Moderate	1.693168	0.000	1.281674	0.002	1.420683	0.000	1.507246	0.000
Advanced (Ref.)								
Family history of glaucoma (one or both parents in glaucoma)	.9259554	0.763	.9717681	0.842	.8343628	0.267	.814129	0.246
None (Ref.)								

Ref.=Reference Category.

TABLE 5: Selection of the best fitted models for glaucoma patient data in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

No.	Model	Log –likelihood	AIC	BIC
1	Exponential	-436.7389	895.4778	939.4114
2	Weibull	-373.2652	770.5305	818.458
3	Log-logistic	-380.4753	784.9506	832.8782
4	Log-normal	-384.2576	792.5153	840.4428

AIC: Akaike Information Criteria, BIC: Bayesian Information Criteria.

TABLE 6: The Accelerated Failure Time Weibull model for glaucoma patients in University of Gondar Comprehensive Specialized Hospital, 2014-2018.

Covariates	Time Ratio	Std. Err	Z	P>|z|	[95% Conf. Interval]
Age (> 70)					
44-69	1.103273	.1030924	1.05	0.293	.9186391 1.325017
18-43	1.29233	.1435	2.31	0.021	1.039576 1.606536
Diabetic (yes)					
No	1.081756	.0765497	1.11	0.267	.9416609 1.242693
Duration of diagnosis (< 1 year)					
1-5 years	1.944649	.3748932	3.45	0.001	1.332738 2.83751
>= 6 years	2.683586	.9230411	2.87	0.004	1.367533 5.26615
Duration of treatment (>=6 years)					
1-5 years	.7997247	.2999897	-0.60	0.551	.3833902 1.668169
< 1 year	1.090244	.4124071	0.23	0.819	.5194445 2.288274
Stage of glaucoma (early)					
Moderate	1.013209	.0881588	0.15	0.880	.8543514 1.201605
Advanced	1.281674	.1022779	3.11	0.002	1.096103 1.498662
Family history of glaucoma(one or both parents in glaucoma)					
None	.9717681	.1396238	-0.20	0.842	.7332666 1.287844

Among the glaucoma patients who aged between 18-43years had 29.23% increase in survival time than those aged greater than 70 years. We could observe that among the glaucoma patients, who were diagnosed before >= 6 years had 2.68 times increase in the survival time than those who were diagnosised < 1 year. Similarly, in the glaucoma patients who were diagnosed between 1-5 yearshad 94.5% increase in the survival experience than who were diagnosised < 1 year,keeping all other covariates at some constant level. Glaucoma patients, with advanced stage of glaucoma had 28.16% increase survival experience than those with early stage of glaucoma, keeping all other covariates at some constant level (Table 6).

DISCUSSION

From Table 5 in the listed parametric survival models, the Weibull regression model had the lowest value in terms of AIC and BIC. Therefore, the Weibull survival regression model was performed for a more accurate identification of the major risk factors for glaucoma patients. Among different socio-demographic characteristics age is one of the factors in determining the survival of glaucoma patients. This result is consistent with the finding of Steven and Austim (2013).[20] In the published document different socio demographic factors such as age, sex and level of residence are the important factors for glaucoma patients.[21] But the finding of this study showed that age was the major factor for blindness in glaucoma patients on the other hand sex and place of residence were not statistically associated with an increased risk of blindness. This study showed that duration of diagnosis is another predictor of blindness for glaucoma patients.

The estimated plot of survivorship function showed that patients who were diagnosed (1-5 years and >= 6 years) had longer survival time before the occurrence of blindness. This can be explained as follows. Those diagnosed early would start proper treatment early and the disease can be controlled well. As explained by George and Louis (2013), glaucoma patients who receive diagnosis may have become more anxious or depressed because they perceived that laser trabeculoplasty was being used because medications had failed, that their disease may be more severe or difficult to control and that there will be a greater risk of disability, loss of independency or blindness.[22] Similarly, in the plot of survivor function in advanced stage of the disease showed more survival time than the early stage. This is because patients with glaucoma in

general has no symptoms early in the course of the disease, and by the time a patient is aware of vision loss, the disease is usually quite advanced and they will begin treatment at that stage. Hence, stage of glaucoma was found to be statistically significant factors for the survival of glaucoma patients, this result also similar with the earlier study.[23]

CONCLUSION

This study was a five year (January, 2014 to April, 2018) retrospective study based on 401 glaucoma patients who were attending their follow-up in University of Gondar Comprehensive Specialized Hospital, out of which it has been found that 23.69% of patients were blind and the remaining 76.31% glaucoma patients were censored at the end of the study. Based on the minimum Akaike Information criteria (AIC), it has been found that the Weibull regression model was the best fitted model for predicting survival time of glaucoma patients regarding to blindness in University of Gondar Comprehensive Specialized Hospital. The multivariable Weibull model revealed that age, duration of diagnosis and stage of glaucoma were major factors that affect the survival probability of glaucoma patients until blindness. Finally, according to the result of the study parametric accelerated failure-time model has advantageous over non parametric and semi-parametric survival models for identifying the major factors. Because of the parametric model the result revealed a more accurate result with a complete specification of the base line hazard model.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Mulu Tiruneh Asemu;* ***Design:*** *Kasim Mohammed Yesuf;* ***Control/Supervision:*** *Kasim Mohammed Yesuf, Yohannes Tadesse Asnaqew;* ***Data Collection and/or Processing:*** *Mulu Tiruneh Asemu;* ***Analysis and/or Interpretation:*** *Mulu Tiruneh Asemu, Kasim Mohammed Yesuf;* ***Literature Review:*** *Mulu Tiruneh Asemu;* ***Writing The Article:*** *Mulu Tiruneh Asemu;* ***Critical Review:*** *Yohannes Tadesse Asnaqew;* ***References and Fundings:*** *Yohannes Tadesse Asnaqew;* ***Materials:*** *Mulu Tiruneh Asemu, Kasim Mohammed Yesuf.*

Limitation

Due to our data limitation, this study missed few important variables such as household income, marital status, educational level of patients, etc. Future studies, where possible should include all important risk factors for blindness.

Availability of data and materials

Data can be found from the corresponding author based on request.

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