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SURVIVAL ANALYSIS OF TIME TO BLINDNESS OF GLAUCOMA PATIENTS AT FELEGE HIWOT REFERRAL HOSPITAL, BAHIR DAR, ETHIOPIA

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between both authors. Author MWM designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author AST managed the analyses of the study. Author MWM managed the literature searches. Both authors read and approved the final manuscript.

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ABSTRACT

Purpose: The purpose of this study was to identify factors that affect the time to the blindness of glaucoma patients.
Design: This study was a retrospective, single-center cohort.
Participants: The medical charts of 328 randomly selected glaucoma patients under the follow-up from January 2014 to December 2018 were included.
Methods: A Cox proportional hazard model was employed to identify the risk factors of the blindness of glaucoma patients.
Main Outcome Measures: Coefficients of the Cox proportional hazard models.
Results: The Cox proportional hazard model showed that age (HR=1.018; P = 0.0344), had high blood pressure (HR=2.813; P < 0.0001), had diabetic disease (HR=1.595; P = 0.0442), the timolol with pilocarpine medication (HR=0.554; P = 0.0043), medium duration of treatment (HR = 0.0225; P < 0.0001), long duration of treatment (HR=0.0004; P < 0.0001), the cup- disk ratio greater than 0.7 (HR= 3.699; P < 0.0001) were a significant factor with glaucoma patients.
Conclusions: The age, blood pressure, diabetic disease, type of medication, duration of treatment, and cup-disk ratio were statistically significant factors on time to the blindness of glaucoma patients. Therefore, authorities and other concerned bodies give greater attention to reduce the chance of blindness of glaucoma patients by creating a focus for patients approximately irreversible blindness because of glaucoma disease.

Keywords: Glaucoma; time to blindness; cox proportional hazard model; survival analysis; ophthalmology.

ABBREVIATIONS

CI : *Confidence Interval;*
HR : *Hazard Ratio;*
SPSS : *Statistical Package for Social Science;*
POAG : *Primary Open-Angle Glaucoma*

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1. INTRODUCTION

Glaucoma is a leading cause of irreversible blindness worldwide and associated with characteristic damage to the optic nerve and patterns of visual field loss due to retinal ganglion cell degeneration [1]. Glaucoma encompasses a group of ophthalmic diseases that are believed to share the common pathophysiology of elevated intraocular pressure, or abnormal sensitivity to high normal IOP, resulting in damage to the nerve fiber layer of the retina and irreversible visual loss [2]. Primary open-angle glaucoma is a chronic, bilateral, and often asymmetrical disease in adults in whom acquired loss of optic nerve fibers and abnormality in the visual field occur with an open anterior chamber angle of normal appearance and IOP which is detrimental to the structural and functional integrity of the optic nerve head [3]. According to Faal's [4] study, POAG is sometimes known as the "thief of sight". Because blindness due to POAG is irreversible and there is no pain or discomfort. Vision loss is gradual that people often do not notice it. It cannot be cured as it is a chronic condition that requires ongoing treatment for the remainder of a patient's life.

The estimated prevalence of glaucoma is 60.5 million people with over 8.4 million people bilaterally blind due to glaucoma worldwide. Given the aging of the world's population, the prevalence of glaucoma is expected to rise to 80 million to 11.1 million people bilaterally blind due to glaucoma by 2020 [5]. Approximately, 15% of global blindness is due to glaucoma and around 600,000 people go blind annually [6].

In Africa, Glaucoma is the second leading cause of blindness, and approximately 15% of blindness in the Africa continent due to glaucoma. In many regions of Sub Saharan Africa, the ratio of an ophthalmologist to the patient is one for one million people. The shortage of trained eye care professionals is linked to a limited number of eye hospitals and the majority of eye hospitals are found in urban centers [7].

In Ethiopia, glaucoma is the fifth most common cause of blindness and the disease caused irreversible blindness in an estimated 62,000 people in 2006 [8]. Due to the nature of the disease, inadequate and inaccessible eye care service, and a very poor level of public awareness, glaucoma patients tend to come for help after they have become either unilaterally or bilaterally blind [9]. However, there was no study done in Ethiopia. Therefore, this study focused on identifying the risk factors of glaucoma patients attending an ophthalmology clinic at Felege Hiwot Referral Hospital, Bahir Dar, Ethiopia.

2. MATERIALS AND METHODS

2.1 Study Area, Period, Design, and Population

A retrospective cohort study design was carried out from January 1, 2014, to December 30, 2018, in Felege Hiwot Referral Hospital, Bahir dar which is located 563 km far from Addis Ababa, Ethiopia. Currently, it delivers health care services with medical, surgical, gynecological, orthopedic, intensive care units, pediatrics, and ophthalmological wards with a total of 375 beds and 561 staff. The glaucoma patients were the source of the population for this study.

2.2 Inclusion and Exclusion Criteria

Glaucoma patients who have two and more than two visits in the study period were included in the study.

2.3 Sample Size and Sampling Procedure

The sample size was determined using the sample size determination formula [10] taking the prevalence of blindness 41% from previous studies in Ethiopia Menelik II hospital [11], by considering 5% margin of error, obtained 328 respondents. The respondents were selected using simple random sampling using their identification number.

2.3.1 Response variable

The response variable was time to the blindness of glaucoma patients.

2.3.2 Independent variables

The independent variables for this study were:
Gender (Female=0 and Male=1)
Place of residence (Rural=0 and Urban=1)
Age is a continuous variable measured in years.
Blood pressure (No=0 and Yes=1)
Diabetic disease (No=0 and Yes=1)
Type of medication (Timolol=0, Pilocarpine=1, Diamox=2, Timolol with Pilocarpine=3 Timolol with Diamox=4, and Timolol with Diamox with Pilocarpine=5)
Duration of treatment (Short=0, Medium=1 and long=2)
Stage of glaucoma (Early=0, Moderate=1 and Advanced=2)
Cup-disc ratio (less than or equal to 0.7=0 and greater than 0.7=1)

2.4 Data Collection Method and Quality Control

The data was collected from the medical chart of glaucoma patients in the ophthalmology clinic by optometry professionals.

2.5 Data Analysis

The data were entered in SPSS software Version 21 and then exported to R software version 3.5.3. We have used descriptive statistics to explore the entire variables of the study. Cox proportional hazard model was performed to see the relationship between the dependent and independent variables. A P-value of less than 0.05 was considered statistically significant.

3. RESULTS

3.1 Characteristics of the Study Participants

A total of 328 glaucoma patients were included and 106 (32.3%) were blind whereas 222 (67.7%) were censored. 28 (8.5%) female patients and 78 (23.8%) male patients were blind. Similarly, 74 (22.6%) and 33 (10.1%) blind patients had blood pressure and diabetic disease respectively. And also, 47 (14.3%), 45(13.7%), and 14 (4.3%) patients were blind from short treatment duration, medium treatment duration, and long treatment duration respectively (Table 1).

3.2 Cox Proportional Hazard Model Result

The result of the Cox proportional hazard model indicates that age, blood pressure, diabetic disease, and cup-disk ratio were positively associated with time to the blindness of glaucoma patients. But, pilocarpine medication and duration of treatment were negatively associated with time to the blindness of glaucoma patients at 5% of the level of significance.

The hazard ratio of blindness patients was increased by 1.018 (HR=1.018, P = 0.0344) for a unit increased in age. The risk of the blindness of the glaucoma patients who had blood pressure was 2.813 (HR=2.813, P < 0.0001) times the glaucoma patients who had no blood pressure. The risk of the blindness of the glaucoma patients who had the diabetic disease were 1.595 (HR=1.595, P = 0.0442) times the glaucoma patients who had no diabetic disease. The risk of the blindness of the glaucoma patients who take pilocarpine medication was 0.632 (HR=0.632, P = 0.0043) times the glaucoma patients who take timolol medication.

The risk of the blindness of the glaucoma patients who had a medium duration of treatment was 0.023

Table 1. Baseline characteristics of categorical variables of glaucoma patients

Variables	Categories	No. patient (%)	No. blind (%)
Gender	Female	108(32.9)	28(8.5)
	Male	220(67.1)	78(23.8)
Place of residence	Rural	146(44.5)	61(18.6)
	Urban	182(55.5)	45(13.7)
Blood pressure	No	230 (70.1)	32(9.8)
	Yes	98(29.9)	74(22.6)
Diabetic disease	No	280(85.4)	73(22.3)
	Yes	48(14.6)	33(10.1)
Type of medication	Timolol	65(19.8)	23(7.0)
	Timolol & Pilocarpine		
	Timolol & Diamox	82(25.0) 111(33.8)	22(6.7)
	Timolol, Pilocarpine & Diamox		35(10.7)
		70(21.3)	
Duration of treatment			26(7.9)
	Short	135(41.2)	47(14.3)
	Medium	106(32.3)	45(13.7)
Stage of glaucoma	Long	87(26.3)	14(4.3)
	Early	121(36.9)	13(4.0)
	Moderate	52(15.9)	11(3.4)
Cup-disk ratio	Advanced	155(47.3) 173(52.7)	82(25.0)
	≤ 0.7	153(47.3)	14(4.3)
	> 0.7		92(28.0)
	Minimum	Maximum	Mean
Age in years	6	89	55.86

Table 2. Result of the final Cox proportional hazards model for glaucoma patients

Covariates	Estimate	Std.error	HR (95% CI)	p-value
Age	0.0177	0.0084	1.0179(1.0013, 1.0347)	0.0344*
Blood pressure(ref=no)				
Yes	1.0341	0.2666	2.8127(1.6681, 4.7426)	<0.0001*
Diabetic disease(ref=no)				
Yes	0.4672	0.2322	1.5954(1.0121, 2.5149)	0.0442*
Type of medication (ref=timolol)				
Timolol & pilocarpine	-0.5902	0.2988	0.5542(0.3086, 0.9955)	0.0483 *
Timolol & Diamox	-0.3549	0.2698	0.7012(0.4133, 1.1898)	0.1883
Timolol, pilocarpine &Diamox	-0.0805	0.2865	0.9227(0.5262, 1.6179)	0.2241
Duration of treatment(ref=short)				
Medium	-3.7940	0.5370	0.0225(0.0079, 0.0645)	<0.0001*
Long	-7.7605	1.1528	0.0004(0.00004, 0.0041)	<0.0001*
Cup-disk ratio (ref ≤ 0.7)				
Greater than 0.7	1.3079	0.3208	3.6985(1.9724, 6.9354)	<0.0001*

** = Significance at 0.05 level of significance*

(HR=0.023, P < 0.0001) times the glaucoma patients who had a short duration of treatment. Similarly, the risk of the blindness of the glaucoma patients who had a long duration of treatment was 0.0004 (HR=0.0004, P < 0.0001) times the glaucoma patients who had a short duration of treatment. The risk of the blindness of the glaucoma patients who had greater than 0.7 cup-disk ratios were 3.699 (HR=3.699, P < 0.0001) times the glaucoma patients who had less than or equal to 0.7 cup-disk ratios (Table 2).

4. DISCUSSION

Age is an important socio-demographic predictor of time to blindness implies that the risk of blindness increases with an increase in age. This result consistent with another study [12], the result shows that higher age was a significant risk factor for the blindness of glaucoma patients [12]. The time to the blindness of glaucoma patients was significantly associated with the type of medication pilocarpine. Glaucoma patients who take pilocarpine medication reduce the risk of blindness. This finding was consistent with another study [13], the result showed that the use of any class of glaucoma medication was associated with a statistically significant reduced hazard of death or blindness. But, another type of medication in this study was statistically insignificant and contradict another study [13]. This is due to a lack of knowledge of glaucoma patients to take the medication and patients might be careless for medication due to the disease nature (the disease most of the time is painless). The risk of the blindness of patients who had a cup-disk ratio greater than 0.7 was higher compared to patients who had a cup-disk ratio less than or equal to 0.7. This finding was consistent with another study by Gardiner, Johnson [14], the result showed that increased the incidence of blindness in a larger cup–disc ratio > 0.7.

5. CONCLUSION

In conclusion, the analysis shows that the predictor age, blood pressure, diabetic disease, type of medication, duration of treatment, and cup-disk ratio were statistically significant factors on time to the blindness of glaucoma patients. The governments and concerned bodies give more attention to minimize the risk of the blindness of glaucoma patients by creating awareness for patients about irreversible blindness caused by glaucoma disease.

6. LIMITATION

Since this study was based on retrospective secondary data (record review), its quality (registering all required information) on entry and follow-up time, due to this some potentially important predictors were not available on patient's information charts, like patient's family history of glaucoma, types of glaucoma, and level of income.

ETHICS APPROVAL AND CONSENT

An ethical clearance certificate had been obtained from Bahir Dar University, Ethiopia. Hence all of the authors have the appropriate permission for the data we used. As per international standard or university

standard, patients' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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