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Survival analysis of time to develop cardiovascular complications and its predictors among hypertensive patients treated in the Ayder Comprehensive Specialized Hospital, Ethiopia: a retrospective cohort study (RCD code: VIII)

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Abstract

Objective: Although hypertension is the leading cause of cardiovascular complications, time to develop cardiovascular complications among hypertensive patients has not been adequately investigated in Ethiopia. Therefore, the aim of this study was to assess time to develop cardiovascular complications and its predictors among adult hypertensive patients at the Ayder Comprehensive Specialized Hospital, Ethiopia. **Result:** A total of 578 hypertensive patients from the Cardiology Department were included in the study and followed for a total of 60 months (median 28 months). Half of the participants (290, 50.2%) were females. The median age of subjects was 54 years. Out of the 578 hypertensive patients who were analysed, 25.4% of them developed a cardiovascular complication. The incidence rate was 8.25 per 1000 persons per month. Significant predictors in the development of cardiovascular complications among hypertensive patients were age [AHR = 1.03 (95% CI=1.016, 1.046)], baseline cardiovascular complications [AHR=3.03 (95% CI=2.009, 4.870)], proteinuria [AHR=3.9 (95% CI=1.3, 11.68)], baseline systolic blood pressure [AHR =1.01 (95% CI=1.003, 2.012)], and baseline diastolic blood pressure [AHR = 1.013 (95% CI=1.005, 2.021)]. JRCD 2019; 4 (4): 96–100

Key words: rare disease, cardiovascular disease, Africa

Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide [1]. In 2017, the World Health Organization (WHO) reported that cardiovascular disease was responsible for 17.7 million deaths worldwide. Fourteen million of those deaths were in sub-Saharan Africa [1,2]. Currently, African populations are significantly affected by CVD [3].

Hypertension accounted for 45% of global cardiovascular morbidity and mortality [4]. Furthermore, ischaemic heart disease and stroke are among the top 10 causes of death in all low- and middle-income regions4,5,6). CVD risk is raised by a pathological increase in blood pressure, glucose, lipids, and body mass index [7]. Even in countries with a good health care system, the rate of death due to CVD is still high [8]. Ethiopian studies have indicated that the prevalence of uncontrolled hypertension among hypertensive patients varied from 52.7% in the Jimma University Special-

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ized Hospital, to 53.4% in the Gondar hospital, and up to 59.9% in the Tikur Anbessa Hospital [9–11]. Even with controlled hypertension, the magnitude of CVD among hypertensive patients ranges from 2.6% in Kenya to 17.8% in Namibia [16].

The WHO reported that more than one-third of annual deaths in Ethiopia were due to non-communicable diseases (NCDs). Of these, cardiovascular diseases were the most common, which accounted for 15% of cases [17]. The WHO estimated that worldwide, approximately 62% of CVD and 49% of ischaemic heart diseases are caused by hypertension [18]. In Ethiopia, hypertension contributed to 30.9% of cardiac deaths [19].

Results from Ethiopia's recent 10-year CVD study showed that prevalence increased by 50% since the previous study, which demonstrates the importance of CVD [17]. Another study performed in Addis Ababa showed that 51% of deaths were due to NCDs [20]. In the same study, among NCDs, cardiovascular disease was the leading cause of death (24%). A study carried out at the Ayder Comprehensive Specialized Hospital showed that patients with cardiovascular diseases were the leading cause of intensive care unit admissions (26%). The most common specific causes of admission were heart failure (16%) and stroke (15.2%), with the latter being the most frequent cause of death (17%)(21). Certain findings in the same region showed that the prevalence of stroke among hypertensive patients recieving anti-hypertensive treatment was nearly 38%. Approximately 66.2% of patients admitted to the hospital were hypertensive [22].

The World Economic Forum has stated that 5% of the global gross domestic product, or 47 trillion U.S. dollars, was spent on the treatment of NCDs [23]. Another study conducted in Ethiopia also showed that CVD expenses were approximately 67 U.S. dollars per disability-adjusted life year (DALY) and about 7 million U.S. dollars annually [24]

Because of this, investigating the time to develop cardiovascular complications among hypertensive patients is very important for prevention and control of CVD. However, there has been little research done in Ethiopia regarding time to develop cardiovascular complications, specifically in hypertensive patients. In addition, creation of awareness and understanding of CVD patterns, its factors, and time to develop CVD are crucial for guiding policy makers to focus on this emerging issue and to develop programs which play a key role in controlling CVD. This study can be also used as a baseline for future researchers and other concerned bodies.

Therefore, the primary purpose of this study was to assess time to develop cardiovascular complications and its predictors among adult hypertensive patients at the Ayder Comprehensive Specialized Hospital, Northern Ethiopia.

Methods

Study design and setting

A hospital-based retrospective cohort study was conducted in the Ayder Comprehensive Specialized Hospital. Data was collected between February and April 2018. The data pertained to patients who were hospitalised from January 2013 to January 2018. This hospital is the largest in the region and the second largest public referral centre and teaching hospital in Ethiopia which is affiliated with Mekelle University.

Study population

Hypertensive patients aged 18 years or greater who were followed-up for at least 3 months in the Ayder Comprehensive Specialized hospital from January 2013 to January 2018 were included in our study. Pregnant women and hypertensive patients who had developed CVD complications prior to commencement of the present study were excluded.

Sample size determination

All hypertensive patients during the follow-up time from January 2013 to January 2018, who met the inclusion criteria, were included in the study.

Data collection tools and procedures

A structured questionnaire in English and checklist were used. Four nurses served as data collectors while 1 nurse supervised. Secondary data were used to collect the required variables.

Study variables

In this study, the outcome variable was cardiovascular complication (time to event) among all adult hypertensive patients who received anti-hypertension treatment follow-up at the Ayder Comprehensive Specialized hospital from January 2013 to January 2018. The independent variables were socio-demographic characteristics (age, residence, sex, and educational status), hypertension status (baseline cardiovascular complications, baseline diastolic blood pressure, baseline systolic blood pressure, and pulse pressure), medical history (diabetes mellitus, chronic renal disease, dyslipidaemia, and obesity), and lifestyle (smoking, alcohol, and amount of salt in diet).

Data Quality Assurance

To ensure data quality, training by the primary investigator was provided to data collectors and the supervisor. The questionnaire was initially prepared in English, translated into Tigrigna, and then back to English to verify its consistency. The collected data was reviewed on-site for completeness and consistency by the supervisor and principal investigator on a daily basis during data collection.

Data processing and analysis

Data was coded, entered, edited, and organised by Epi-data manager version 4.2 and then exported into SPSS version 23 for analysis. The Kaplan-Meier (KM) survival function was applied to estimate the probability of patient survival after initiation of follow-up, while the log-rank test was used to compare the KM.

The Cox proportional-hazards model was used to determine the relationship between independent variables and the outcome variable. Every independent variable was tested via the log-rank test and bivariate Cox proportional-hazards against the depen-

Table 1. Kaplar Meier estimates of survival function for hypertensive among adult hypertensive patients attending at the Ayder comprehensive, specialized hospital, Tigray, Ethiopia, 2018 (n = 578)

Time in months	Beginning total	Event	S(t)	Std.err	(95% CI)
12	578	55	0.8958	0.0133	0.8665- 0.9190
24	423	53	0.7739	0.0193	0.7333 -0.8092
36	303	21	0.7147	0.0218	0.6696 -0.7549
48	225	18	0.6438	0.0252	0.5921- 0.6908
60	120	0	0.6438	0.0252	0.5921 -0.6908

dent variable and all variables with P-value <0.25 were included in the Cox-regression model. Cox-regression analysis was performed to estimate the hazard ratios. Finally, statistical significance was declared at P-values less than 0.05.

Operational definition

Censored

Individuals with unknown outcome, including a patient lost from follow-up who died but did not have any cardiovascular complications during the 5-year follow-up period.

Cardiovascular complications (event)

Cardiovascular complications were defined as the development of 1 or more of the following cardiovascular diseases in the study group: stroke, myocardial infarction, or heart failure in any time of the follow-up period diagnosed by physician. Cardiovascular complication was confirmed by reviewing the medical chart in the hospital and the appointment registration book. Survival time was calculated in months using the time interval between the date of anti-hypertensive therapy initiation or initiation of hypertension follow-up and the date of the event (cardiovascular complication) and date of censoring until the final date of the follow-up.

Baseline cardiovascular complication was defined as a complication which was present at the beginning of the follow-up period.

Results

Socio-demographic characteristics

A total of 578 hypertensive patients were included in the study group. The median age was 54 years. Half of the study cohort (290, 50.2%) was female. Analysis of the educational status of the participants showed that 242 (41.9%) were not formally educated and 146 (25.4%) achieved a primary level of education. Almost all (96.2%) of the participants were from Tigray. More than half lived in an urban area (323, 55.9%) and the rest in rural areas. Almost all were orthodox in religion (539, 93.3%).

Based on the socio-demographic characteristics, the findings showed that the distribution of cardiovascular complications was slightly higher among male participants (p=0.486; 53.1% vs. 46.9%) and significantly higher among participants living in urban areas (p=0.001; 77.6% vs 22.4%) and illiterate participants (p=0.035; 51.7% vs 23.8%) when compared with their counterparts.

Survival Analysis and Kaplan-Meier estimation of survival function

Out of 578 patients, 147 (25.4%) developed cardiovascular complications. The total person-month follow-up was 17 824 with an incidence rate of 8.25/1000 person-months.

The overall survival probability of hypertensive patients in the follow up at the end of 60 months was found to be 0.64 (95% CI=0.5921, 0.6908), while the survival probability of hypertensive patients at the end of 12 months and 24 months was 0.89 (95% CI=0.8665, 0.9190) and 0.77 (95% CI=0.7333, 0.8092) respectively (Table 1).

Discussion

One quarter (25.4%) of the study participants (95% CI= 21.97, 29.23) developed cardiovascular complications within the 5-year follow-up period. This result was in line with previous studies conducted in Bahir-dar (22%) [25] (25). A study conducted in Kenya showed that the prevalence of CVD complications was 33.4% [26], which is higher than in our study. This difference may be due to variations in study design, study population, and follow-up period. Our study also revealed a higher prevalence of CVD complications when compared with a study done in Spain (9%). This difference may be due to socio-demographic differences between the study populations.

The incidence rate was 8.6 per 1000 person-months (95% CI= 7.016, 9.694), which is lower than in the study conducted in Bahir-dar (12 per 1000 per person- month).

In the Cox-proportional hazards model analysis, age was a risk factor for cardiovascular disease complications with a hazard ratio AHR=1.03 (95% CI= 1.3, 11.68). This result is in accordance with studies conducted in Ethiopia, Spain, and Australia [25,28,29].

On the other hand, a systematic review conducted in Spain, based on the Cox proportional hazards model of age, revealed that the relative risk of cardiovascular events was 2 times higher in hypertension, which is higher than results from our study [28].

Table 2. Bivariate and multivariable Cox proportional regression analysis, among adult hypertensive patients attending at the Ayder comprehensive, specialized hospital, Tigray, Ethiopia, 2018 (n = 578)

Variables	Sub-category	Final outcome		Bivariate				Multivariable			
		Event (%)	Censored (%)	P-value	HR	95.0% CI		P-value	HR	95.0% CI	
						Lower	Upper			Lower	Upper
Blood Pressure	Controlled (Ref)	6(4.1)	322(74.7)								
	Uncontrolled	141(95.9)	109(25.3)	0.001*	40.89	18.05	92.64	0.130	2.330	0.780	6.960
Age	Mean ±SD(53.18±14.393)			0.001*	1.075	1.060	1.089	0.001**	1.030	1.016	1.046
Residence	Urban (Ref)	114(77.6)	209(48.5)	0.001*	0.370	0.251	0.546	0.170	0.720	0.868	2.25
	Rural	33(22.4)	222(51.5)								
Baseline cardiovascular complication	Yes	88(59.9)	68(15.8)	0.001*	5.889	4.223	8.212	0.001**	3.030	2.009	4.870
	No (Ref)	59(40.1)	363(84.2)								
Protein urea	Yes	137(93.2)	9(2.1)	0.001*	68.68	35.96	131.1	0.020**	3.900	1.300	11.68
	No (Ref)	10(6.8)	422(97.9)								
Chronic kidney disease	Yes	122(83.0)	6(1.4)	0.001*	29.34	18.91	45.50	0.570	1.190	0.647	2.197
	No (Ref)	25(17.0)	425(98.6)								
Baseline systolic BP	Mean ±SD(157.48±39.770)			0.001*	1.026	1.023	1.029	0.001**	1.007	1.003	2.012
Baseline diastolic BP	Mean ±SD(101.96±20.257)			0.001*	1.048	1.042	1.054	0.001**	1.013	1.005	2.021
Baseline pulse pressure	Mean ±SD(70.58±20.643)			0.001*	1.039	1.031	1.046	0.070	1.010	0.999	1.017
Baseline body mass index	Mean ±SD(24.09±3.076)			0.001*	1.396	1.331	1.464	0.910	0.995	0.920	1.078
Dyslipidemia	Yes	109(74.1)	49(11.4)	0.001*	10.60	7.329	15.45	0.460	1.180	0.759	1.833
	No (Ref)	38(25.9)	382(88.6)								
Diabetic mellitus	Yes	86(58.5)	77(17.9)	0.001*	4.079	2.936	5.666	0.130	0.752	0.518	1.091
	No (Ref)	61(41.5)	354(82.1)								
Cigarette smoking	Yes	84(57.1)	8(1.9)	0.001*	10.80	0.067	0.130	0.420	1.360	0.639	2.906
	No (Ref)	63(42.9)	423(98.1)								
Salt reduction	Yes	5(3.4)	171(39.7)	0.001*	0.061	0.025	0.150	0.100	0.452	0.175	1.171
	No (Ref)	142(96.6)	260(60.3)								

Note * Variables with significant association at bivariate analysis. ** Variables with significant association at multivariable analysis. Ref: Reference category. HR: Hazard ratio. BP: Blood pressure.

A study conducted in Japan demonstrated that level of proteinuria was a risk factor for cardiovascular disease, which is in line with our study. This could be due to the nature of the study design. Similarly, a systematic review and meta-analysis conducted in Australia indicated that the presence of proteinuria was associated with an approximate 50% increase in coronary heart disease risk (HR 1.47, 95% CI= 1.23, 1.74) after adjustment for known risk factors, which is lower than our study (HR 3.9, 95% CI= 1.3, 11.68) [29]. Baseline cardiovascular complications were another risk factor for cardiovascular complications with a hazard ratio HR =3.03 (95% CI= 2.009, 4.870), which is compatible with a study conducted in America and Ethiopia [25,31,32].

In our study, diastolic blood pressure and systolic blood pressure were significant predictors of cardiovascular disease complications with hazard ratios of 1.13 and 1.07 respectively. This result is in line with other studies conducted in the US, UK, and South Africa [25,33–35]. Review articles in the US National Library of Medicine show that systolic blood pressure was a powerful predictor for cardiovascular disease at every age [36].

Conclusion

Cardiovascular complications among hypertensive patients were frequent in the study region. Age, baseline systolic blood pressure, baseline diastolic blood pressure, proteinuria, and baseline complications were major predictors for the development of cardiovascular complications.

Limitations

The inherent retrospective nature of the study design leads to the exclusion of patients with incomplete medical records.

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References

1. Kotwani P, Kwarisiima D, Clark TD, et al. Epidemiology and awareness of hypertension in a rural Ugandan community: a cross-sectional study. BMC Public Health 2013;13:1151.
2. Ekanem US, Opara DC, Akwaowo CD. High blood pressure in a semiurban community in south-south Nigeria: a community-based study. Afr Health Sci 2013; 13(1): 56–61.
3. Keates AK, Mocumbi AO, Ntsekhe M, et al. Cardiovascular disease in Africa: epidemiological profile and challenges. Nature Reviews Cardiology 2017;14:273.
4. Klabunde R. Cardiovascular physiology concepts. Lippincott Williams & Wilkins. 2011.
5. World Health Organization. Global Burden of Deaths and DALYs. http://www.who.int/healthinfo/statistics/ bodgbddeathdalyestimates.xls. 2010.
6. Hajar R. ramingham Contribution to Cardiovascular Disease. Heart Views 2016; 7 (2): 78–81
7. World Health Organization. Cardiovascular disease On World Heart Day WHO calls for accelerated action to prevent the world's leading global killer. 2017.
8. Lopez AD. Global Burden of Disease and Risk Factors. Washington, DC Oxford University Press. 2006.
9. Tesfaye B, Haile D, Lake B, et al. Uncontrolled hypertension and associated factors among adult hypertensive patients on follow-up at Jimma University Teaching and Specialized Hospital: cross-sectional study. Research Reports in Clinical Cardiology 30 March 2017; 8: 21–29.
10. Yohannes SM, Mengesha ZB. Adherence to antihypertensive treatment and associated factors among patients for follow up at the University of Gondar Hospital, Northwest Ethiopia. BMC Public Health 2012;12(1):282.
11. Tesfaye A. Blood pressure control associates and antihypertensive pharmacotherapy patterns in Tikur Anbessa General Specialized Hospital Chronic Care Department, Addis Ababa, Ethiopia. Am J Biomed Life Sci 2015;3(3):41–48.
12. World Health Organization. Causes of Death [online database]. Geneva. 2008.
13. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990- 2010: a systematic analysis of the Global Burden of Disease Study 2010. Lancet 2012:2224–2260.
14. Mendis S, Pekka P, Norrving B. Global Atlas on cardiovascular disease prevention and control. 2011: 155.
15. McGill HC, McMahan CA, Gidding SS. Preventing heart disease in the 21st century: implications of the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study. Circulation 2008;117 (9): 1216–1227.
16. Hendriks ME, Wit FW, Roos MT, et al. Hypertension in sub-Saharan Africa: cross-sectional surveys in four rural and urban communities. PLoS One 2012;7(3):1–10.
17. Ethiopia Ministry Of Health. Health Sector Transformation Plan 2015/16 – 2019/20. 2015.
18. World Health Organization Report. Reducing Risks, Promoting Healthy Life. http://wwwwhoint/wh. 2013.
19. Belete H, Fessahaye A. The pattern of cardiac diseases at the cardiac clinic of Jimma University Specialized Hospital, South West EthiopiaEthiop J Health Sci 2010;20(2): 99-105.
20. Gidey K, Hailu A, Bayray A. Pattern and outcome of medical intensive care unit admissions to ayder comprehensive specialized hospital in tigray, ethiopia. Ethiopia Med J 2018;56(1).
21. Sennay A, Gebremariam A, Hannah S. Types, risk profiles, and outcomes of stroke patients in a tertiary teaching hospital in northern Ethiopia. NeurologicalSci 2016;3:41–47.
22. Bloom DE, Cafiero E, Jané-Llopis E, et al.The global economic burden of noncommunicable diseases. PGDA working paper No. 87. Boston, MA: Harvard Institute for Global Health, Program on the Global Demography of Aging. Available at http://wwwhsphharvardedu/program-on-the-global-demography-of aging/WorkingPapers/2012/PGDA_WP_87pdf. 2012.
23. Tolla G. Prevention and treatment of cardiovascular disease in Ethiopia: a cost-effectiveness analysis. Cost Effectiveness and Resource Allocation. 2016.
24. Unated Nations General Assembly Resolution. Resolution 70/1. t. A/Res/70/1. Transforming our world: the 2030 Agenda for Sustainable Development. United Nations General Assembly. New York 2015.
25. Tadege GM. Survival Analysis of Time to Cardiovascular Disease Complication of Hypertensive Patients at Felege Hiwot Referral Hospital in Bahir-Dar, Ethiopia: A Retrospective Cohort Study. J Biom Biostat 2017;8(5).
26. Mugure G, Karama M, Kyobutungi C, et al. Correlates for cardiovascular diseases among diabetic hypertensive patients attending outreach clinics in two Nairobi slums Kenya Gladys. Pan Afr Med J 2014;19:1–11.
27. Weycker D, Nichols GA, Keeffe-Rosetti MO, et al. Risk-Factor Clustering and Cardiovascular Disease Risk in Hypertensive Patients. American Journal of Hypertension. 2007;20 (6).
28. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. The Lancet 2014;383(9932):1899–1911.
29. Tefera T. The changing trend of cardiovascular disease and its clinical characteristics in Ethiopia: hospital-based observational study. 2017.
30. Trijp MJ, Grobbee DE, Hoes AW, et al. Prediction of cardiovascular disease on the basis of blood pressure measurements more reliable with systolic than with diastolic measurement. 2003;147 (30): 1456–1459.
31. Haines A, Patterson D, Rayner M, et al. Prevention of cardiovascular disease. Occas Pap R Coll Gen Pract 1992: 67–78.
32. Thom T. Heart Disease and Stroke Statistics 2006 Update A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee 113: 2006:85-151.
33. AMKDG. Explaining the sex difference in coronary heart disease mortality among patients with type 2 diabetes mellitus a meta-analysis. Arch Intern MED 162: 2002:1737–1745.
34. Prescott E, Hippe M, Schnohr P, et al. Smoking and risk of myocardial infarction in women and men longitudinal population study. BMJ 316. 1998:1043–1047.
35. Van den Hoogen P, Feskens E, Nagelkerke N, et al. The Relation between Blood Pressure and Mortality Due to Coronary Heart Disease among Men in Different Parts of the World. N Engl J Med 2000; 2:1–8.
36. Verdecchia P. Systolic, diastolic and pulse pressure: prognostic implications. 2001; 2 (4): 369–374.