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Determinants of hypertensive heart disease among adult hypertensive patients in the University of Gondar Referral Hospital, Gondar, Ethiopia: A case-control study

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ABSTRACT

Introduction: Hypertensive heart disease (HHD) is the constellation of abnormalities characterized by cardiac complications. Despite advancements in the management of hypertension and access to medical care, the incidence of HHD is an alarmingly increasing through time. However, there is a dearth of information on the determinants of HHD in Ethiopia. Therefore, this study aimed to assess the determinants of HHD among adult hypertensive patients at Gondar University Referral Hospital, Gondar, Ethiopia.

Materials and Methods: This case-control study was conducted from April 1st to 26th in 2018. The cases were adult hypertensive outpatients with cardiac complications who were diagnosed within the last two years and were on follow-up and care in Gondar University Referral Hospital Gondar, Ethiopia, during the study period. On the other hand, the controls were adult hypertensive outpatients without a history of any of the cardiac complications who were diagnosed within the last two years and were on follow-up and care in Gondar University Referral Hospital, Gondar, Ethiopia, during the study period. A total of 159 participants included 53 cases and 106 controls were selected using a simple random sampling method. Data were collected using a checklist, and an interviewer administered a structured questionnaire. Moreover, multivariate logistic regression analysis was used to identify the predictors of hypertensive heart disease. In addition, a p-value of less than 0.05 was considered statistically significant.

Results: According to the results of this study, the majority of the cases (70.9%) and controls (54.5%) were in the age group of ≥60 years. Furthermore, hypertensive patients who had a family history of cardiovascular disease (Adjusted odds ratio (AOR)=4.7, 95% CI: 1.8-11.9**)**, sedentary lifestyle (AOR=3.2, 95% CI: 1.3-7.8), uncontrolled blood pressure (AOR=4, 95% CI: 1.8-9.0), and hypertension duration ≥10 years (AOR=3, 95% CI: 1.1-8.7**)** were more likely to develop hypertensive heart disease than their counterparts.

Conclusion: Multiple factors predicted HHD; accordingly, it is highly recommended to consider the early management guidelines and provide professional advice regarding physical exercise, especially for older individuals.

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Introduction

Globally, cardiovascular diseases (CVDs) are the leading cause of deaths, of which more than a quarter occurs in Sub Saharan Africa (SSA) (1, 2). High blood pressure is the leading risk factor for CVDs (3). The increasing burdens of CVDs in SSA are due to the increasing prevalence of hypertension,

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and (4, 5) hypertensive heart diseases (HHDS) are becoming the growing public health concern (6, 7). Hypertension causing left ventricular hypertrophy (LVH) leads to the development of heart failure (8). The LVH, which is the commonest complication of hypertension, is a complex cardiac pathology (9-11). Moreover, the HHD is an increasingly costly (9, 11, 12) and the resulted burden calls for an urgent public awareness and provision of access to care (13) since it causes frequent hospital admission and prolonged hospital stays (14). The LVH has been detected among 46.6% and 80.9% of hypertensive patients in Ghana and Nigeria, respectively (15). On the other hand, the prevalence of hypertension in Ethiopia ranges from 13.2% in southwest Ethiopia to 31% in Addis Ababa (16, 17) among which about 13.5% were HHD patients (18). During 2015, 23% of hypertensive patients have developed cardiac complications (19). Despite the advances in medical options, the incidence of HHD is dramatically increasing in Ethiopia (20, 21) and its predictors are not being well recognized in this region. Therefore, this study aimed to assess the determinants of HHD among hypertensive patients.

Methods

Study setting, population, and design

A hospital-based case-control study was conducted among adult hypertensive patients who were on follow-up from 2016 to 2017 in Gondar University Referral Hospital, Gondar, Ethiopia, located about 750 km far from the national capital city, Addis Ababa. Chronic disease follow-up is given at this hospital to patients with hypertension, diabetes, asthma, and heart failure.

The HHD patients are appointed for care and follow-up every month except for those with clinical urgency and chronic management. During the study, there were 511 hypertensive outpatients who were on follow-up. The inclusion criteria of the cases were: 1) adult primary hypertensive outpatients, 2) a history of either one or a combination of the common cardiac complications, such as LVH, myocardial ischemia, and heart failure diagnosed by a physician, 3) ≥ 18 years of age, 4) being diagnosed within the last two years, and 5) being on follow-up and care in Gondar University Referral Hospital during the study period.

On the other hand, the inclusion criteria for the controls were: 1) adult primary hypertensive outpatients, 2) no history of any of the cardiac complications, such as LVH, myocardial ischemia, and heart failure confirmed by a physician, 3) ≥ 18 years of age, 4) being diagnosed within the last two years, and 5) being on follow-up and care in Gondar University Referral Hospital during the study period. The data were collected from April 1st to 26th in 2018.

Sample size determination and sampling technique

The required sample size was determined using EpiInfo software with a 95% confidence level and 80% power and 1 to 2 case to control ratio. The duration of hypertension above 10 years, uncontrolled blood pressure, and the age above 50 years were considered to calculate the required sample size by reviewing different pieces of literature (20, 21). Among these factors, uncontrolled hypertension was chosen as an exposure variable because it gave the maximum sample size, compared to other variables. Since the proportion of exposure was a common one among controls (36.3) in the previous pieces of literature, it was possible to get a generalizable sample size (22). After adding 10% non-response rate, the final sample size was obtained at 165 participants including 55 and 110 cases and controls, respectively.

A simple random sampling technique was used to select the cases and controls. Out of 511 hypertensive outpatients who were on follow-up and care, 155 hypertensive outpatients were identified as patients with HHDs, out whom 90 cases were diagnosed within the last two years. A total of 65 patients from cases and 146 patients from controls were excluded from the study due to being below 18 years of age, diagnosed more than the last two years ago, missing outcome variables under study, transferred to other facilities, incomplete patient cards, had a diagnosis of stroke or renal disease and undocumented patient status. The cases and controls were coded by numbers for identification. After the coding process, the information of 90 cases and 210 controls

were imported into the EpiData software separately, and eventually, 55 cases and 110 controls were selected randomly. Moreover, the cards were reviewed and checked for the completeness of the necessary information.

Variables and measurement

The major outcome variable was HHD (i.e., LVH, myocardial ischemia, and heart failure), and the predictor recorded variables included socio-demographic variables as well as medical and behavioral risk factors.(Figure 1)

Operational definition

The HHD was defined as a history of hypertension with the presence of at least one of the cardiac complications, such as hypertension and myocardial ischemia obtained from electrocardiography results according to Minnesota Code criteria, the diagnosis of heart failure according to Framingham's criteria, and LVH obtained from echocardiographic results using a two-dimensional echocardiography.

Likewise, hypertensive heart failure was defined as a history of hypertension and heart failure diagnosis according to Framingham's criteria that are the presence of either two major criteria or one major and two minor criteria. The major criteria include cardiomegaly, hepatojugular reflex, neck vein distension, pulmonary edema, pulmonary rales, paroxysmal nocturnal dyspnea or orthopnea, S3 gallop rhythm. On the other hand, the minor criteria include hepatomegaly, ankle edema, dyspnea, nocturnal cough, pleural effusion, and tachycardia. Hypertensive LVH was considered when a history of hypertension exists with echocardiographic documentation of LVH (Left ventricular mass index [LVM] >95g/m2 for female and LVM > 115g/m2 for male).

Furthermore, the hypertensive myocardial ischemia was defined when a history of hypertension exists with a history of angina and documented ischemic electrocardiographic abnormalities.

The hypertension is defined in this study as a previous diagnosis of and ongoing treatment for hypertension or record of sustained blood pressure ≥140/90 mm Hg on two or more occasions. Similarly, the duration of the hypertension was started from the time of the first diagnosis and lasted to the end of the study period. If it lasted for 10 years or longer, it was considered a long term duration. A family history of CVD was obtained from a self-report history of CVD in the parents or siblings that occurred at 60 years of age or younger.

Regarding the baseline blood pressure, the values of blood pressure at the first diagnosis of hypertension were categorized as high blood pressure stage 1 and 2 if they were lower than 140/90 and higher than 140/90 mmHg systolic and diastolic blood pressure, respectively. Diabetes mellitus was defined as fasting blood glucose levels >126 mg/dl, random blood sugar level >200 mg/dl) with typical clinical manifestation, the use of insulin, and/or oral hyperglycemic medications.

With regard to cholesterol level, if at least one of the components has an abnormal value, it was considered as dyslipidemia or abnormal lipid profile (elevated total cholesterol if >200mg/dl, low HDL cholesterol if <40 mg/dl, high LDL cholesterol if >160 mg/dl).

The patients were considered physically active if they involved in vigorous-intensity exercise for at least 20 min or moderate-intensity exercise for 30 min at least 3 days per week in either at work, leisure time, or commuting from place to place. Otherwise, they were regarded as sedentary.

Data collection technique and procedures

The review of patient medical records was conducted by two physicians to identify cases and controls using data extraction checklist.

The data collectors completed the checklists using the relevant information available on the patient's medical records. Echocardiography, electrocardiography, and biochemical test results were among the variables reviewed during the data collection. Moreover, the patients were interviewed by one physician and two nurses with bachelor degrees using an interviewer-administered questionnaire and data extraction format adapted from a standard source and similar other studies (23).

The validity of the interview questionnaire was determined using the content validity.

The reliability of the interview questionnaire in assessing the determinants of HHD among hypertensive patients was estimated to be the Cornbrash's alpha coefficient of 0.76.

The questionnaire sought information regarding socio-demographic characteristics, medical history, and behavioral factors. Physical activity was measured using 14 items according to World Health Organization wise approach and grouped into three categories, namely physical exercise at the workplace, at leisure time, and at the time of commuting from place to place (24). Stress was measured through a 10-item questionnaire consisting of psychosocial factors.

Data processing and data analysis

Data coding, entry, and cleaning were performed using EpiData software (version 3.1) and analyzed in SPSS software (version 21.0).

Variables with p-values of <0.25 in bivariate analysis were imported into multivariable logistic regression analysis using backward LR (left right) method. Moreover, the Hosmer-Lemeshow test was performed for goodness of model fitness, and it was significant at p-value=0.92. The effect modifier was checked using an interaction term in binary logistic regression model and Breslow day test. Finally, AOR with a 95% confidence intervals and 5% p-value was considered to predict the determinant factors.

Data quality control and management

The data collection process was supervised by two trained medical doctors, and an appropriate data collection tool was designed and pretested to ensure the quality of the data. Additionally, interviewers and data extractors were trained properly, and the discussions were held among the principal investigators, supervisors, and data collectors as necessary.

Results

Socio-demographic characteristics of the study participants

A total of 159 participants in two groups of HHD patients (n=53 cases) and hypertensive patients (n=106 controls) with 96.4% response rate for each were included in this study. The majority of cases (n=38, 71.7%) and controls (n=57, 53.8%) aged 60 years and older.

A higher proportion of the cases (n=15, 28.3 %) had a family history of CVDs, compared to 13 (12.3%) patients in the control group (Table 1).

Behavioral risk factors among cases and controls

In this study, 15 (28.3%) and 19 (17.9 %) cases and controls had a history of stress, respectively. Similarly, 17(32.1%) cases and 36 (34 %) controls reported a history of excessive salt intake (Table 2).

Medical risk factors among cases and controls

With regard to medical risk factors, 67.9% (n=36) and 86.8% (n=92) of the cases and controls had less than a 10-year-period with hypertension, respectively (Table 3).

Predictors of hypertensive heart disease

Variables considered for multivariable logistic regression included age, educational status, family history, physical exercise, stress, lipid profile, and diabetes mellitus comorbidity, duration of hypertension, baseline blood pressure, and hypertension control.

Participants who had a family history of cardiovascular diseases were more likely to be cases than controls (AOR=4.7, 95% CI: 1.8, 11.9).

In addition, the hypertensive patients who were not engaged in physical exercise were more likely to develop hypertensive heart disease than physically active ones (AOR=3.2, 95% CI: 1.3, 7.8). Similarly, the odds of having hypertensive heart disease were also more likely to occur in patients with uncontrolled blood pressure (AOR=4, 95% CI: 1.8-9.0).

Additionally, the odds of having hypertensive heart disease were more likely to occur among patients with longer duration of hypertension, compared to their counterparts (≥10 years) (AOR=3, 95% CI: 1.1-8.7) (Table 4).

Table 1. Socio-demographic characteristics of study participants at Gondar University Referral Hospital during 2018

Variables	Categories	Control n=106 N (%)	Case n=53 N (%)	Total n=159 N (%)	COR (95%CI)	P-value
Age	18-39	17 (16)	6(11.3)	23(14.5)	1.0	
	40-59	32(30.2)	9(17)	41(25.8)	0.7(0.2-2.6)	0.7
	>=60	57 (53.8)	38(71.7)	95(59.7)	1.9(0.6-5.2)	0.2*
Gender	Male	38(35.8)	22(41.5)	64(38.8)	1.2(0.6-2.5)	0.4
	Female	68(64.2)	31(58.5)	101(61.2)	1.0	
Place of residence	Urban	67(63.2)	41(77.4)	108(67.9)	1.9(0.9-4.2)	0.07*
	Rural	39(36.8)	12(22.6)	51(32.5)	1.00	
Educational level	no formal education	38(35.8)	30(56.6)	68(42)	3.5(1.3-9.7)	0.014*
	Primary	19(17.9)	11(20.8)	30(18.9)	2.6(0.8-8.2)	0.1*
	Secondary	22(20.8)	6(11.3)	28(17.6)	1.2(0.3-4.3)	0.7
	higher education	27(25.5)	6(11.3)	33(20.8)	1.0	
Marital status	Single	9(8.5)	7(13.2)	16(10.5)	1.0	
	Married	59(55.7)	23(43.4)	82(51.6)	1.1(0.2-4.4)	0.8
	Widowed	28(26.4)	16(30.2)	44(27.7)	0.5(0.1-1.6)	0.28
	Divorced	10(9.4)	7(13.2)	17(10.7)	0.8(0.2-2.5)	0.7
Income	<1500 ETB	78(73.6)	42(79.2)	120(75.5)	1.3(0.6-3.6)	0.4
	>=1500 ETB	28(26.4)	11(20.8)	39(24.5)	1.0	
Family history	Yes	13(12.3)	15(28.3)	28(17.6)	5.4(2.4-12.1)	<0.001*
	No	93(87.7)	38(71.7)	131(82.4)	1.0	

Notes: ** Candidate variables for multiple logistic regressions*
Abbreviations: *COR: Crude odds ratio; CI: Confidence interval; ETB: Ethiopian birr*

Table 2. Behavioral risk factors among cases and controls at Gondar University Referral Hospital during 2018

Variables		Control n=106 N (%)	Case n=53 N (%)	COR(95%CI)	P-Value
Stress Yes		19(17.9)	15(28.3)	1.8 (0.8-3.9)	0.13*
No		87(82.1)	38(71.7)	1.00	
Excessive salt intake Yes		36(34)	17(32.1)	0.91(0.45-1.85)	0.81
No		70(66)	36(67.9)	1.00	
Heavy alcohol consumption	Yes	16(15.1)	10(18.9)	1.4 (0.6-3.4)	0.374
	No	90(84.9)	43(81.1)	1.00	
Smoking status	Yes	9(8.5)	7(13.2)	1.4 (0.5-4)	0.471
No		97(91.5)	46(86.8)	1.00	
Physical exercise Sedentary lifestyle		16(15.1)	22(41.5)	3.9 (1.8-8.2)	<0.001*
Physically active		90(84.9)	31(58.5)	1.00	

Notes: ** Candidate variables for multiple logistic regressions*
Abbreviations: *COR: Crude odds ratio; CI: Confidence interval*

Table 3. Medical factors among cases and controls at Gondar University Referral Hospital during 2018

Variables		Control n=106 N (%)	Case n=53 N (%)	COR (95%CI)	P-value
Duration of hypertension	<10 years	92(86.8)	36(67.9)	1.00	
	≥ 10 years	14(13.2)	17(32.1)	3.1(1.4-6.9)	0.006*
Baseline BP	<140/90 mmHg	30(28.3)	6(11.3)		
	≥140 mmHg	76(71.7)	47(88.7)	3 (1.2 - 8.0)	0.02*
Hypertension control	Uncontrolled	28(26.4)	34(64.2)	4..9 (2.4-10.1)	<0.001*
	Controlled	78(73.6)	19(35.8)	1.00	
Diabetes mellitus	Yes	7(6.6)	7(13.2)	0.46(0.2 - 1.4)	0.17*
	No	99(93.4)	46(86.8)	1.00	
Lipid profile	Normal Profile	86(81.1)	35(66)	1.00	
	Abnormal lipid profile	20(18.9)	18(34)	2.2 (1.1-4.7)	0.038*

Notes: ** Candidate variables for multiple logistic regressions*
Abbreviations: *COR: Crude odds ratio; CI: Confidence interval*

Table 4. Multivariable logistic regression output of predictors of hypertensive heart disease at Gondar University Referral Hospital during 2018

Variables	Category	Case n=53 N (%)	Control n=106 N (%)	COR (95%CI)	AOR(95%CI)	P-value
Duration of hypertension	10 years and above	17 (32.1)	14(13.2)	3.1(1.38-6.94)	3(1.1-8.7)	0.03
	less than 10 years	36(67.9)	92 (86.8)	1.00	1.00	
Blood pressure control	Uncontrolled BP	34 (64.2)	28(26.4)	4..9 (2.4-10.1)	4(1.8-9.0)	0.001
	Controlled BP	19(35.8)	78(73.6)	1.00	1.00	
Physical exercise	Sedentary lifestyle	22(41.5)	16(15.1)	3.9 (1.8-8.2)	3.2(1.3-7.8)	0.01
	Physically active	31(58.5)	90(84.9)	1.00	1.00	
Family history	Yes	23(43.4)	13(12.3)	5.4(2.4-12.1)	4.7(1.8-11.9)	0.001
	No	30(56.6)	93(87.7)	1.00	1.00	

Abbreviations: *COR: Crude odds ratio; CI: Confidence interval; AOR: Adjusted odds ratio Ethiopian birr*

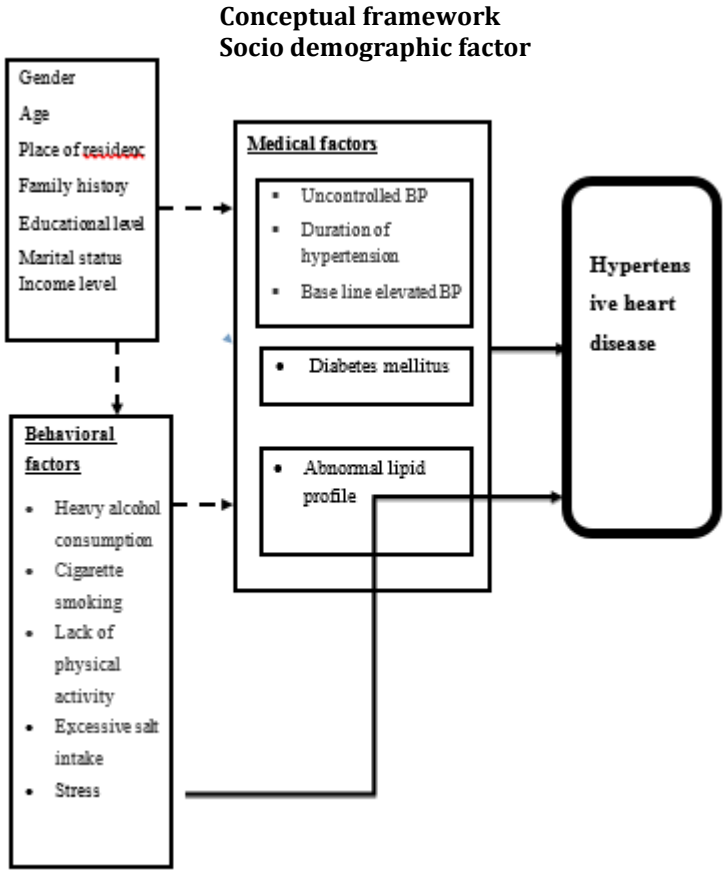

Figure 1: Conceptual frame work for studying determinants of hypertensive heart disease among adult hypertensive patients in university of Gondar referral hospital, Gondar North West Ethiopia, a case-control study

Discussion

Currently, the HHD as a cardiac complication of hypertension is the single most important contributor to death across the world. The analysis of major factors in this study indicated that a family history of cardiovascular disease, sedentary lifestyle, uncontrolled hypertension, and long duration of hypertension were predictors of hypertensive heart disease.

In this study, a longer duration of hypertension was significantly associated with hypertensive heart disease. Accordingly, the odds of hypertensive heart disease were more likely to occur in hypertensive patients with a 10-year duration of hypertension and longer, compared to those with a duration less than a 10-year period. However, this duration is higher, compared to that in the results of a study conducted in Ethiopia (19). The observed discrepancy can be attributed to the differences in the sample size and design.

In this study, the odds of hypertensive heart disease were more likely to occur in patients with uncontrolled blood pressure, compared to those with controlled blood pressure. This finding is in line with the results of a study conducted in Poland (25), South Africa (26), and Ethiopia (27). However, this rate was higher than that found in a study conducted in Ghana and Kenya (28). The association between uncontrolled blood pressure and hypertensive heart disease might be explained by the fact that uncontrolled blood pressure or continuously sustained high blood pressure cause structural and functional changes on the myocardium. This includes cellular permeability changes, intracellular and extracellular matrix protein synthesis, ventricular remodeling, hypertrophy, and fibrosis (29).

The odds of hypertensive heart disease are more likely to occur among patients with a family history of cardiovascular diseases, compared to their counterparts. This finding was consistent with a similar finding in a study performed in a multi-ethnic population which showed that a family history of CVDs was five and two times more likely to occur in patients with hypertensive heart disease in Amsterdam and South Asia, respectively (25). The relationship between a positive family history of cardiovascular disease and hypertensive heart disease might be explained by an underlined genetic predisposition related to CVDs (25). A number of genes, such as D alleles of the *ACE* gene and others are identified that contribute to the development of hypertensive heart disease which targets mostly angiotensin-aldosterone system.

Certain variants of these genes promote LVH and affect myocardial contractility in hypertensive individual (26). The odds of hypertensive heart disease were higher among those with a sedentary lifestyle, compared to those engaged in physical activities. This finding is in line with the results obtained from a study conducted in India and Nigeria (29, 30) in which 71.7% of the cases were 60 years and older leading a sedentary lifestyle. The reason for that is the effect of physical exercise on the improvement of endothelial function which enhances the vasodilation in the blood vessel and reduces insulin resistance. Additionally, physical exercise enhances blood coagulation and fibrinolysis, which in turn improves cardiac function, and therefore, reduces the development of cardiac complication of hypertension (30).

Unlike other studies conducted so far (29), age, gender, the place of residence, diabetes mellitus comorbidity, dyslipidemia, baseline blood pressure, stress, cigarette smoking, and heavy alcohol consumption were not independently associated with hypertensive heart disease in this study. The observed differences can be attributed to the varieties in the study setting, sample size, study design, and definitions.

Conclusion

A family history of cardiovascular disease, sedentary lifestyles, longer duration of hypertension, and uncontrolled hypertension were the possible predictors for developing HHD. It is highly recommended to monitor closely and improve the follow-ups of CVD patients with a history of CVD. In addition, preventive interventions, such as physical activity and controlling baseline glucose should be scaled up in a manner that all CVD patients get this counseling and professional advice.

Limitations of the study

The limitations in this study included the recall bias due to the incomplete information which was inevitable in this case-control study. Moreover, the way the outcome variable was defined in this study might cease comparison across different studies. Eventually, the non-adequacy of the sample size might have introduced imprecise results with wide confidence intervals while categorizing variables.

Conflict of interest

The authors declare that they have no competing interest

Ethical considerations

The study protocol was approved by the Research and Ethical Review Board of Jimma University, Jimma, Ethiopia. In addition, the required permission was obtained from Gondar University, Gondar, Ethiopia. Moreover, informed consent was obtained from each study participants. The patients were also informed of the confidentiality of the information regarding the use of codes instead of any personal identifiers.

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