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College of Health Sciences

School of Public Health

The association between medication adherence and cognitive function impairment among hypertensive patients a case-control study in Mekelle, northern Ethiopia

A research thesis submitted to the school of public health in partial fulfillment of the requirements for the Master's degree in Public Health

By: Senait Alemayehu (BSc)

Advisors: Dr. Negussie Deyessa (MD, Ph.D.)

Dr. Yared Mamusht (MD)

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Name of investigator	Senait Alemayehu
Name of Advisor(s)	1. Dr. Negussie Deyessa 2. Dr. Yared Mamushet
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Address of investigator	Tel: 0914197945 Gmail: senaitalemayohabrha@gmail.com

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Acronyms and Abbreviations

- AOR-----Adjusted Odds Ratio
- BP-----Blood Pressure
- CI-----Confidence Interval
- COR-----Crude Odds Ratio
- DBP-----Diastolic Blood Pressure
- DM-----Diabetes Mellitus
- HHs-----Households
- MMAS-----Morisky Medication Adherence Scale
- MMSE-----Mini-Mental State Examination
- NCDs-----Non-Communicable Diseases
- OR-----Odds Ratio
- SSA-----Sub-Saharan Africa
- SBP-----Systolic Blood Pressure
- SD-----Standard Deviation
- SPSS-----Statistical Package for Social Science
- VIF-----Variance Inflation Factor
- WHO-----World Health Organization

Abstract

Background: Hypertension is a global public health problem. In developing countries, the high prevalence of hypertension followed by poor hypertension control remains a significant public health challenge. The brain is one of the main target organs affected by hypertension, excluding age hypertension is the most important risk factor for cerebrovascular pathology leading to cognitive function impairment. However, the level of antihypertensive medication adherence among hypertension patients and the difference in the development of cognitive function impairment is not well studied.

Objective: This study aimed to assess the association between medication adherence and cognitive function impairment among hypertensive patients in Mekelle, northern Ethiopia from April to September 2020 G.C.

Method: An unmatched case-control study design was conducted in the selected health facilities in Mekelle, Ethiopia from April to September 2020. The study population was hypertensive patients, aged 60 years and above and who have been on antihypertensive medications for at least 6 months. A sample size of 106 cases and 106 controls were included in the study, participants with cognitive function impairment were considered as cases, and participants without cognitive function impairment were controls. The data collection was done twice and the data were collected by reviewing the medical chart of patients and interviewer-administered questionnaire, by trained data collectors. Mini-Mental State Examination was used to assess the cognition status of the study participants and to assess the antihypertensive medication adherence, Morisky Medication Adherence Scale was used. The collected questionnaires were entered into Epi data version 3.1 and exported to SPSS version 23 for cleaning and further analysis. Bivariable and multivariable logistic regression was used for analysis. An adjusted odds ratio along with a 95% confidence interval and a p-value of < 0.05 was used for declaring statistical significance.

Result: The prevalence of medication adherence was found to be 34(32.1%) among cases and 84(79.2%) among controls. Medication adherence was independently significantly associated to cognitive function impairment with [AOR =7.77, 95% CI: (3.44 -17.24)]. The odds of cognitive function impairment was 7.7 times more among antihypertensive medication non-adherent participants compared to those who were adherent. Marital status and educational status were also found to be significantly associated with cognitive function impairment

Conclusion and recommendation: There is an association between antihypertensive medication adherence and cognitive function impairment after controlling for possible confounders. Further work needs to be done by the health professionals on informing patients about the consequences of elevated and/ or uncontrolled BP and on the benefits of medication adherence and the consequences of non-adherence.

1. Introduction

1.1. Background

Hypertension, also known as high or raised blood pressure (BP) is when the systolic and/or the diastolic blood pressure is equal to or higher than the cutoff point (systolic greater than or equal to 140mmHg, diastolic greater than or equal to 90 mmHg) and/or taking antihypertensive medication. Hypertension is a global public health problem. It contributes to the burden of cardiovascular diseases, stroke, and chronic kidney disease which results in premature mortality and disability (1).

Chronic or non-communicable diseases (NCDs) alone are responsible for 71% (41 million) of global mortality, according to the World Health Organization (WHO) (2). The most common metabolic change predisposing to non-communicable diseases is elevated BP which alone attributes 19% of the global deaths related to non-communicable diseases. Each year 15 million people at the age of 30 - 69 years die from NCDs and over 85% of these premature deaths occur in low- and middle-income countries (2).

Globally, in 2015, 22% of the adult population aged 18 years and older i.e. one in four men, and one in five women had raised BP. Twenty-eight percent of the population in low-income countries had high BP, compared with 18% of the population in high-income countries. A review of current trends shows that the number of adults with raised BP increased from 594 million in 1975 to 1.13 billion in 2015, with the increase seen largely in low- and middle-income countries (3). There were approximately 80 million adults with hypertension in sub-Saharan Africa (SSA) in 2000 and projections based on current epidemiological data suggest that this figure will rise to 150 million by 2025 (4).

In Ethiopia, a national WHO step survey was conducted in the 9 regions and two city administrations (Addis Ababa and Dire Dawa). Accordingly, the overall prevalence of hypertension was 15.8% with a slightly higher prevalence in females 16.3% than 15.5% in males. The urban prevalence of raised BP was 19.7% and rural prevalence was 14.9%. There was a progressive increase in the prevalence of raised BP with increasing age of the participants (5). The highest prevalence of hypertension (30.2%) was reported in Addis Ababa and the lower prevalence of hypertension (9.3%) in Gilgel Gibe, southwest Ethiopia (6). In Tigray regional

state, the prevalence of hypertension increased significantly in magnitude (from 9257 in 2011/12 to 23,633 in 2014/15) (7).

Medication adherence is defined as the extent to which the medication-taking behavior of a patient corresponds with agreed recommendations from a health care provider. In developing countries, the high prevalence of hypertension followed by poor hypertension control remains a significant public health problem (8). WHO identifies poor adherence as the most important cause of uncontrolled BP and estimates that 50–70% of people do not take their antihypertensive medication as prescribed (9). In Ethiopia, studies done in Jimma and Gonder showed that the level of adherence to antihypertensive medication was 61.8% and 64.6% respectively (10, 11). Poor adherence to antihypertensive medication is associated with worse BP control and adverse outcomes including stroke, myocardial infarction, heart failure, and death (12).

Cognitive impairment is when a person has trouble remembering, learning new things, concentrating, or making decisions that affect their everyday life. Cognitive impairment ranges from mild to severe. With mild impairment, people may begin to notice changes in cognitive functions, but still be able to do their everyday activities. Severe levels of impairment can lead to losing the ability to understand the meaning or importance of something and the ability to talk or write, resulting in the inability to live independently (13).

In the United States (US) 22.2% (about 5.4 million) of individuals aged 71 years or older have cognitive impairment without dementia. This result suggests that the number of individuals with cognitive impairment without dementia in the US is about 70% higher than that of cognitive impairment with dementia which was 3.4 million individuals (14). According to a community-based study done in Cameron in 2019 the prevalence of cognitive impairment was 33.3% and being female, an increase in systolic BP, and being single were significantly associated factors affecting cognitive function (15). In Ethiopia, no data shows the overall-prevalence of cognitive impairment but there are some studies done in patients with a specific type of diseases like HIV/AIDS, DM, and hypertension. According to a study done in 2019 in Jimma, among hypertension patients, the proportion of respondents who had cognitive impairment was 30.8% (16).

For cognitive impairment age is the primary risk factor, other risk factors include family history, brain injury, exposure to pesticides or toxins, physical inactivity, and chronic conditions such as Parkinson's disease, heart disease, stroke, hypertension, and diabetes (13).

Developing countries are being affected with triple burden disease (i.e communicable disease, NCDs, and traffic accidents) due to this the prevention and control of hypertension have not received due attention although it is one of the most modifiable risk factors of cardiovascular diseases. Prevention, control, treatment of hypertension, and other NCDs are extremely low in those countries as health care resources are overwhelmed by other priorities i.e communicable diseases. There are also many other barriers to the health care system and health care providers (17). In developing countries, the level of adherence to prescribed antihypertensive medications is very low due to different reasons and because of the low adherence level, people are being affected with further complications of hypertension. Therefore, to prevent and control further damage studying the level of antihypertensive medication adherence among hypertensive patients and the difference in the development of further complications is very necessary.

1.2.Statement of the problem

The prevalence of age-related health problems is becoming an important public health concern as proportions of older individuals in populations worldwide grow due to the increase in life expectancy. Alzheimer's disease and cerebrovascular diseases are the two leading causes of cognitive impairment. Among vascular risk factors, chronic arterial hypertension is a major contributor to cognitive impairment. Hypertension is a highly prevalent disease affecting billions of individuals worldwide. It is the leading cause of global disease burden and overall health loss. The brain is one of the main target organs affected by hypertension. Thus, excluding age hypertension is the most important risk factor for cerebrovascular pathology leading to cognitive impairment. Hypertension has been associated with reduced abstract reasoning, slowing of mental processing speed, and memory deficits.

Data on the trends of prevalence of hypertension suggest that it has increased in economically developing countries in recent years while it remained stable or decreased in developed countries. In Ethiopia, the magnitude of hypertension is increasing from time to time as is in other developing countries and it is related to different modifiable and non-modifiable risk factors.

Hypertension is the most powerful modifiable risk factor of cerebrovascular damage and the increase in the prevalence of stroke, cognitive impairment and other cerebrovascular related diseases in the developing world including Ethiopia could be related to the increase in prevalence/magnitude of hypertension and the low level of adherence to antihypertensive medications among hypertensive patients. And, as stated in the background part the prevalence of cognitive impairment among hypertension patients in Jimma was 30.8%, this number is not small. Therefore, this study was aimed at assessing the association between the level of medication adherence and development of cognitive function impairment among hypertensive patients.

1.3. Rationale/ significance of the study

Hypertension is a metabolic risk factor of cardiovascular disease & other NCDs and it is a public health problem. Studies done in our country showed that its prevalence is increasing and the treatment and adherence to antihypertensive medications are not as high as expected to be. Since most hypertension is not controlled complications, and mortality due to those complications are increasing, as a result, focus needs to be given to the possible ways of minimizing complications of the disease.

Therefore, this study aimed at assessing the cognitive function of hypertension patients and the association between medication adherence and cognitive function impairment among hypertensive patients.

This study will help the population, health professionals, and policy makers to focus on increasing medication adherence among patients and other important public health measures to reduce hypertension-related complications, morbidities, and mortalities

2. Literature review

2.1.Prevalence of hypertension

A Population-based Systematic Analysis study done in 90 countries stated that the estimated global age-standardized prevalence of hypertension in adults aged ≥ 20 years in 2010 was 31.1% (31.9% in men and 30.1% in women) and it was found to be 28.5% in high-income countries and 31.5% in low- and middle-income countries. In 2000, the global age-standardized prevalence of hypertension was 25.9% in adults aged ≥ 20 years, which shows an increase in hypertension prevalence of 5.2% over ten years, from 2000-2010. This increase was consistent in men and women, who had an age-standardized hypertension prevalence of 26.4% and 25.1% in 2000, respectively. But the difference was inconsistent by economic status, the hypertension prevalence decreased by 2.6% in high-income countries from 31.1% in 2000, whereas the prevalence increased by 7.7% in low- and middle-income countries from 23.8% in 2000.(17)

The study also found that; almost three times as many individuals with hypertension lived in low- and middle-income countries (1.04 billion) than in high-income countries (349 million). In high-income countries, the greatest absolute burden was found in old age groups (≥ 60), while in low- and middle-income countries the greatest absolute burden was in the middle-aged groups (40 - 59 years) (17).

According to a study done in four SSA, i.e, Nigeria, Namibia, Kenya, and Tanzania hypertension was the most frequently observed risk factor for CVD, and determinants for blood pressure were similar, in all four populations while they are very different in terms of socioeconomic status, living environment, and geographical location. The sample size used for all the countries was different the highest being from Namibia (2000HHs) and the lowest from Tanzania (800HHs). The study stated the majority of the hypertensive population had both systolic and diastolic hypertension. The crude prevalence of hypertension was 19.0% in Tanzania, 20.2% in Kenya, 21% in Nigeria, and 32.0% in Namibia. The prevalence of hypertension increased with age and the age-adjusted prevalence was found to be 19.3% in Nigeria, 21.4% in Kenya, 23.7% in Tanzania, and 38.0% in Namibia (18).

A study that was done in Ethiopia, in the 9 regions and two city administrations (Addis Ababa and Dire Dawa) based on the data of national WHO Steps survey, where the target population for

this survey included all men and women aged 15 - 69 years old who had lived at their current place of residence for at least six months, found that the overall prevalence of raised blood pressure (SBP 140 and/or DBP 90 mmHg) was 15.8% with slightly higher prevalence in females 16.3% than 15.5% in males. The urban prevalence of hypertension was found to be 19.7% and rural prevalence was 14.9%. Among the people with raised BP, 42.7% of them had both systolic and diastolic raised BP. On the other hand, 33.5% and 23.8% of the participants had raised BP on their diastolic and systolic BP respectively. Out of the participants who were previously diagnosed as hypertensive and who were on drug treatment, 53.4% of them had controlled BP (<140/90). In this study, a progressive increase in the prevalence of raised BP was also found with the increasing age of the participants (5).

2.2. Medication adherence among hypertensive patients

A study that was done in the northwestern region of China in 2019, where the data collection was done by trained pharmacists from three different departments (neurology, cardiology, and ophthalmology) using a standard questionnaire called therapeutic adherence scale for hypertensive patients (TASHP) which comprises 25 questions that are related to medication adherence and lifestyle intervention and which was designed according to the actual condition of Chinese hypertensive patients found that only 27.46% of the participants had satisfactory adherence behavior, while the remaining 72.54% hypertensive patients were non-adherent. The study also stated that the adherence rate found in this study was very low compared to other similar studies done in other regions (developed regions) of China (19).

In this study gender, residence, and duration of high BP were significantly associated factors with adherence. Females than males, urban residents than rural residents, and patients with longer duration of hypertension than with short duration of hypertension were found to be more adherent to their antihypertensive medications (19). The possible reasons for this difference could be the educational status of patients, the economic status of patients, differences in knowledge about the diseases, and awareness about the benefits of adherence to the medication.

A study that was done in Kerala, India in 2018, where the participants were above 30 years old, diagnosed with hypertension for at least 6 months, where the data collection was done by interview method using the Morisky Medication Adherence Scale (MMAS-4) to assess medication adherence found that 46% of the study participants were highly adherent while

41.3% and 12.7% of them were medium and low adherent respectively. In this study poor knowledge of complications, availing government pharmacy, and being asymptomatic at the time of diagnosis are the factors that were significantly associated with poor compliance (20).

A study that was done in 12 SSA countries (Benin, Cameroon, Congo (Brazzaville), the Democratic Republic of Congo, Gabon, Guinea, Cote d'Ivoire, Mauritania, Mozambique, Niger, Senegal, Togo) where the medication adherence was assessed by the 8-items Morisky Medication Adherence Scale (MMAS-8) and was scored from 0 to 8 with scores of <6, 6 to <8, and 8 reflecting low, medium, and high adherence, respectively found that out of the study participants 30.8% of them had low adherence while 33.6% and 35.6% of the participants had medium and high adherence to antihypertensive medications respectively (21).

According to this study, adherence level differed across countries, the proportion of low medication adherence ranged from 15.0% in Senegal to 55.2% in the Democratic Republic of Congo. The use of traditional medicine and poor individual wealth index were significantly and independently associated factors with low adherence to medication (21).

A study that was done in Sokoto, Nigeria in 2018, where the study participants were patients aged 18 years and above, with a primary diagnosis of hypertension and who were on antihypertensive medications for at least 3-months and where the medication adherence assessment was done using a 9-item modified Morisky Adherence Predictor Scale (MMAPS) found that out of the total participants 8.9% participants had optimal adherence to antihypertensive medications, while 91.1% were non-adherent. According to this study forgetfulness, dose omission, side effects of medications, expensiveness of medications, disliking the medication, intentional decision to take medicine when desired, preference of herbal medicine than prescribed drugs, and too many drugs to take were mentioned as factors affecting medication adherence (22).

A study done in Jimma, Ethiopia in 2018, where an eight-item Morisky's Medication Adherence Scale (MMAS-8) was employed to assess the study participant's medication adherence found that 61.8% of the participants were adherent to their antihypertensive medication whereas 38.2% of patients were non-adherent. The study also stated that the presence of co-morbidity, regular alcohol intake, self-purchasing of the medications, and combinations of antihypertensive

medications were found to be significantly associated factors affecting medication adherence (10).

Another similar study that was done in three referral hospitals found in Bahrdar, Gonder, and Debre Markos, Northwest of Ethiopia, in 2017 where adherence status was assessed using the Morisky Medication Adherence Scale – 8 (MMAS-8) found that the overall prevalence of good drug adherence to antihypertensive medications was 67.2% while the overall poor adherence to antihypertensive medications was 32.8%. The highest prevalence of 70.7% of good adherence was seen in Bahirdar (70.7%) whereas the highest prevalence of poor adherence was found in Gonder (37%). According to this study having co-morbidity, duration of treatment, medical cost, attitude, and patient-provider relationship were the factors significantly associated with low adherence to antihypertensive treatment (23).

2.3. Hypertension and cognitive function impairment

A study done in Indonesia, in 2019 by taking a sample from Karya Kasih Nursing Homes where the assessment of cognitive function was done using Mini-Mental State Examination (MMSE) found that out of older adults who had a history of hypertension for less than five years 53.8% of them had a normal cognitive function while 46.2% had impaired cognitive function. Whereas, out of older adults who had a history of hypertension for more than five years 16.1% of them had a normal cognitive function while 83.9% of them experienced impaired cognitive function. The longer someone has a history of hypertension (over 5 years), the greater the occurrence of cognitive impairment. The study also stated that out of the elderly with first-grade hypertension 57.1% of them had mild cognitive function impairment while another 42.9% had severe cognitive function impairment. Of the elderly with second-grade hypertension, it was found that 82.4% of them experienced severe cognitive function impairment and 17.6% of them experienced a decrease in mild cognitive function. A significant relationship was found between the degree of hypertension and the occurrence of decreased cognitive function in the elderly (24).

A study that was done in India in 2014 where the study participants were 60 years old & above and assessment of cognitive function was done using Mini-Mental State Examination (MMSE) found that the mean MMSE in hypertensive patients were significantly less than the mean MMSE in normotensives and pre-hypertensive whereas the mean MMSE score in normotensives and pre-hypertensive was not significantly different. They also stated that the

score of orientation, attention-calculation, immediate recall, and language was significantly less in hypertensive patients compared to normotensives and pre-hypertensive individuals (25).

From the above studies conducted in different countries, we can see that the prevalence of hypertension is increasing from time to time in developing countries while it is decreasing in the developed world and further attention needs to be given to the prevention, treatment, and control of the disease. As we can see from the adherence studies the adherence level among hypertension patients who are taking medication is low and as a result, they are being exposed to different complications of hypertension, and cognitive function impairment is one of the complications.

In Ethiopia, the exact prevalence of cognitive function impairment is not known. But according to a study done in Jimma, cognitive impairment among hypertensive patients was 30.8%, from this study we can understand that the prevalence of cognitive function impairment among hypertensive patients in Ethiopia is as high as many other countries. Therefore, attention needs to be given to decreasing the prevalence of hypertension and increasing medication adherence, since medication adherence is also very important to decrease complications and increase life expectancy among hypertensive patients.

Different studies are done on the association between cognitive impairment and medication adherence among hypertensive patients and most studies focused on the consequences of cognitive impairment i.e cognitive impairment can lead to non-adherence or poor adherence of medication among patients. But what if a patient has poor adherence to antihypertensive medication? Does it lead to the development of cognitive impairment? Or does adherence to antihypertensive medications decrease the occurrence of cognitive impairment among hypertensive patients? Therefore, in Ethiopia, since there is no study conducted regarding this issue, this study was aimed to assess the association between medication adherence and cognitive function impairment among hypertensive patients.

2.4. Conceptual framework

Cognitive function impairment can be related with different factors. It can be related with socio-demographic factors like age, chronic diseases like hypertension, injury, behavioral factors and non-adherence to medications (Figure 1).

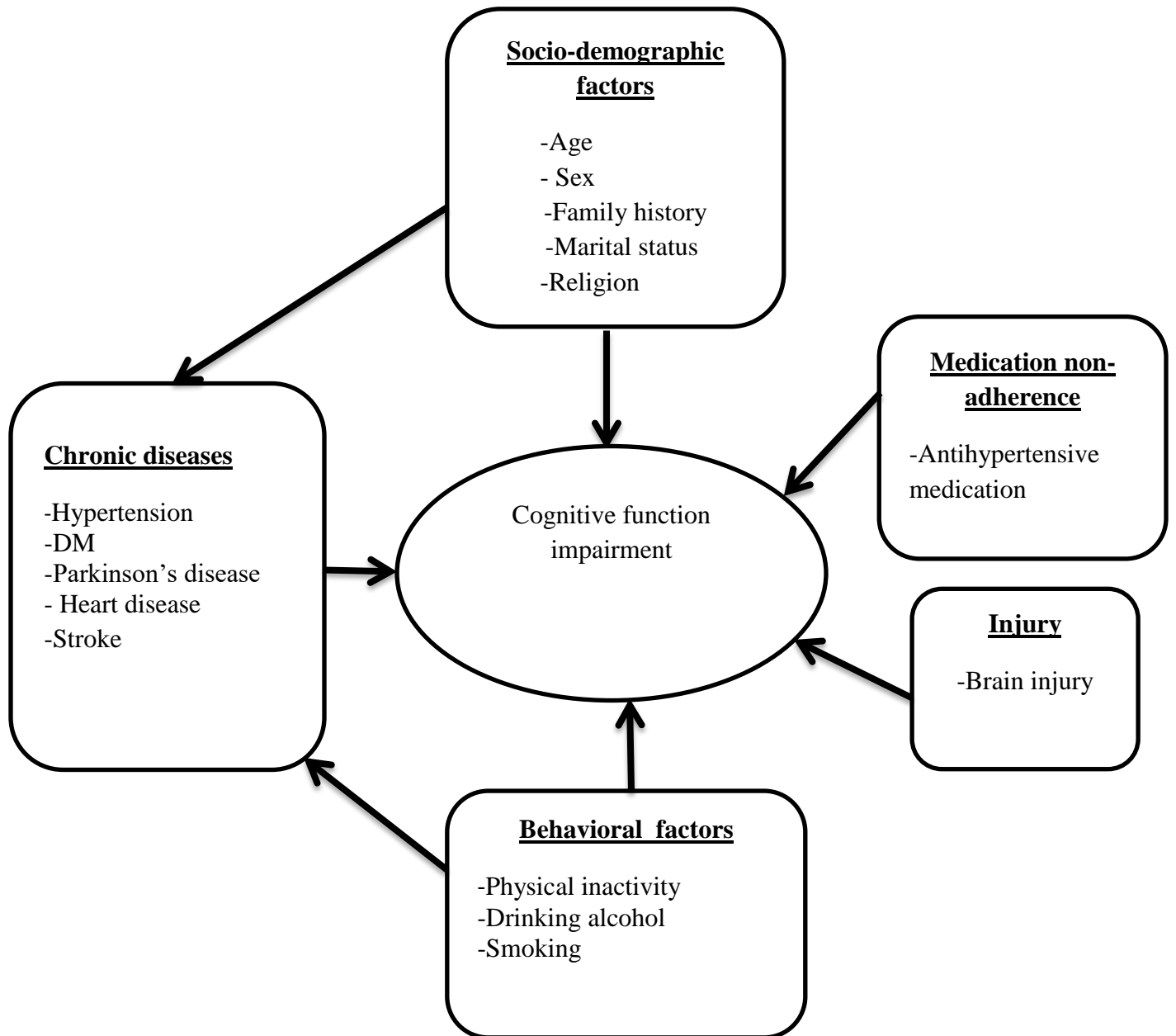


Figure 1: Conceptual framework on possible factors affecting cognitive function Mekelle, Ethiopia, 2020 G.C.

Hypothesis

H₀: There is no association between medication adherence and cognitive function impairment among hypertensive patients.

H₁: There is an association between medication adherence and cognitive function impairment among hypertensive patients.

3. Objective

3.1. General objective

- To assess the association between medication adherence and cognitive function impairment among hypertensive patients in Mekelle, northern Ethiopia from April to September 2020 G.C.

4. Methods

4.1. Study area and period

The study was conducted in Mekelle, the capital city of Tigray regional state which is located in the northern part of Ethiopia. There are seven sub-cities in Mekelle with a total population of 376,533. There are 76 health institutions in Mekelle out of which 13 are governmental health institutions i.e. 3 hospitals and 10 health centers while 63 are private health institutions i.e. 4 hospitals and 59 health centers. Two governmental hospitals i.e. Ayder comprehensive specialized hospital and Mekelle hospital were selected to be included in the study due to their high patient flow. There are around 2000 hypertensive patients per year in Ayder comprehensive specialized hospital and around 1000 hypertensive patients per year in Mekelle hospital. In both hospitals, hypertensive patients have appointments every two or three months based on their level of blood pressure, and the services that are given by the health professionals are measuring BP, prescribing medications, advice on lifestyle, anthropometric measurements, and further investigations for comorbidities like DM, cardiac disease, kidney disease, etc. are also being given if necessary.

The study was conducted from April to September 2020 G.C.

4.2. Study design

Facility-based unmatched case-control study design was used

4.3. Population

4.3.1. Source population

The source populations were hypertensive patients, who were on antihypertensive medications.

4.3.2. Study population

The study populations were hypertensive patients, aged 60 years and above, who have been on antihypertensive medications and who had follow-up in the selected health facilities. According to this study, cases were individuals who had cognitive function impairment while controls were individuals who had no cognitive function impairment.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

Hypertensive patients who were 60 years old and above and have been taking antihypertensive medications for at least 6 months and patients who had a follow-up in the selected health facilities were included in the study.

4.4.2. Exclusion criteria

Patients who were previously diagnosed with dementia, seriously ill patients who were unable to finish the interview, and unable communicate were excluded from the study.

4.5. Sample size determination

The sample size was calculated using double population proportion formula with the following assumptions: 95% confidence interval, 80% power, 43% proportion of cases & 24% proportion of controls from a case-control study done in Karachi, Pakistan in 2019 G.C and ratio of cases to controls of 1.

$$n_1 = \frac{\left[Z_{\alpha/2} \sqrt{\left(1 + \frac{1}{r}\right) P(1 - P)} + Z_{\beta} \sqrt{P_1(1 - P_1) + \frac{P_2(1 - P_2)}{r}} \right]^2}{(P_1 - P_2)^2}$$

Where,

- n_1 = sample size of cases or controls
- $Z_{\alpha/2}$ = Z score corresponding to 95% CI = 1.96
- Z_{β} = Z score corresponding to 80% of power = 0.84
- P_1 = Proportion of cases = 43%
- P_2 = Proportion of controls = 24%
- r = Ratio of cases to controls = 1
- $P = \frac{P_1 + rP_2}{1 + r}$

$$n_1 = \frac{\left[1.96 \sqrt{\left(1 + \frac{1}{1}\right) 0.335(1 - 0.335)} + 0.84 \sqrt{0.43(1 - 0.43) + \frac{0.24(1 - 0.24)}{1}} \right]^2}{(0.43 - 0.24)^2}$$

$$n_1 = 95.577 \cong 96$$

Therefore, the sample size required for this study was 96 cases and 96 controls, and using 10% of the non-response rate the final sample size required was 106 cases and 106 controls.

4.6. Sampling procedure

Out of the 3 governmental health facilities two hospitals, Ayder comprehensive specialized hospital and Mekelle hospital were selected to be included in the study due to high patient flow. The sample size required for this study was 106 cases and 106 controls, using proportional allocation 70 cases and 70 controls were taken from Ayder comprehensive specialized hospital and 36 cases and 36 controls were taken from Mekelle hospital. A consecutive sampling technique was used to select study subjects. Since cognitive function impairment (the outcome variable) is not regularly assessed in the selected hospitals it had to be assessed during the data collection. So, the data collection was done twice, in the first visit of the study participants they were asked about the outcome status and they were classified as cases and controls based on the score they had, and in their second visit they were asked about the exposure status. And, the same code was being given to the questionnaires and to the medical charts of patients to prevent mixing up and missing of the participants (Figure 2).

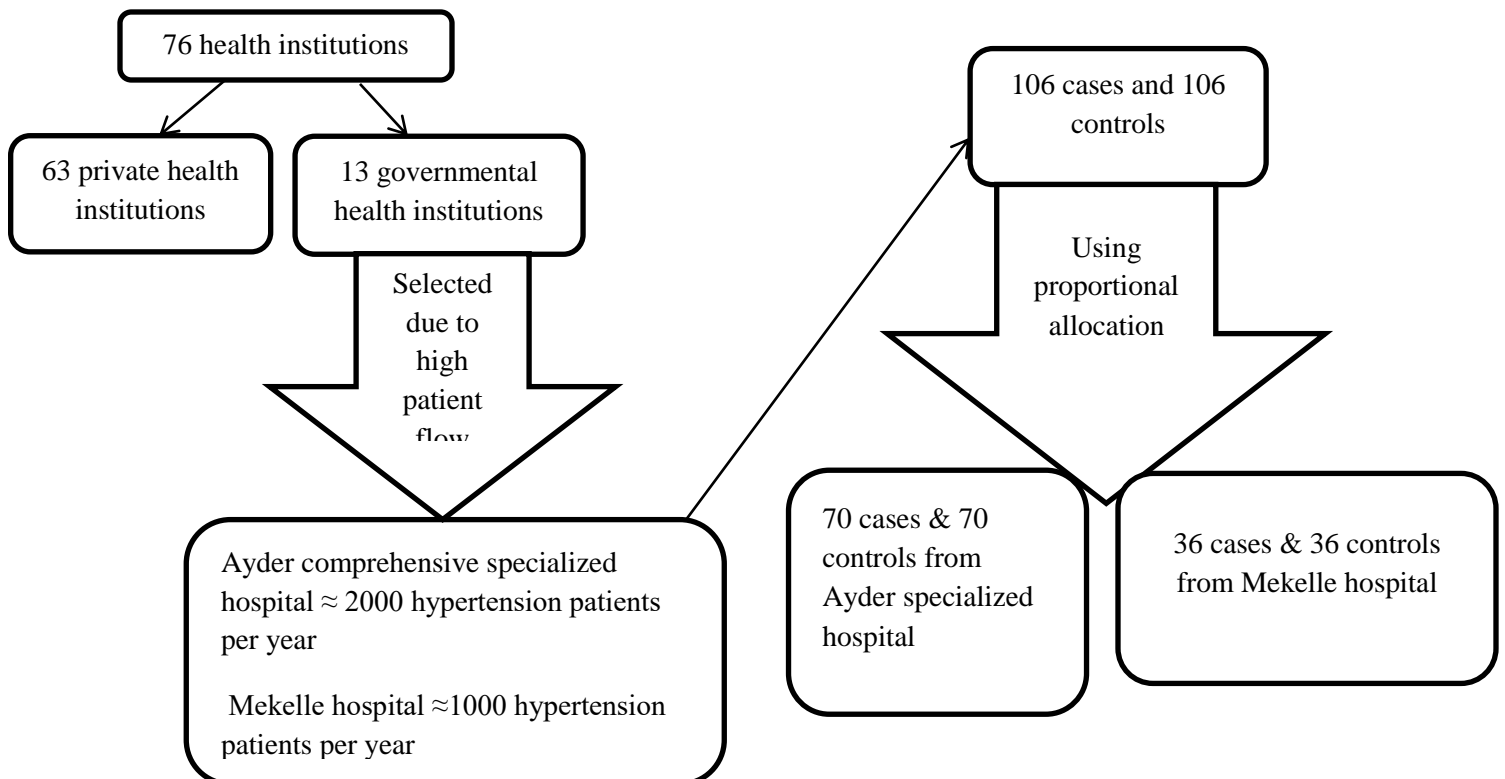


Figure 2: Schematic Sampling Procedure on the association between medication adherence and cognitive function impairment among hypertensive patients in Mekelle, Ethiopia, 2020

4.7. Dependent and independent variables

4.7.1 Dependent variable

The dependent variable in this study was cognitive function impairment

4.7.2 Independent variables

- Adherence to antihypertensive medication
- Presence of comorbidities (DM, stroke, heart diseases, etc)
- History of head injury
- Behavioral characteristics of patients (physical inactivity, drinking alcohol, etc)
- And socio-demographic characteristics (age, sex, occupation, etc) were the independent variables.

4.8. Data collection procedure and tools

The data collection was done by reviewing the medical chart of patients and interviewer-administered questionnaires. The medical chart was used to check and confirm hypertension by the blood pressure (BP) of patients, the type of medication the patients are taking, the presence of comorbidities, etc. The questionnaire has five parts: the first part contains socio-demographic characteristics of patients followed by clinical characteristics. Then, the cognitive function of patients was assessed using Mini-Mental State Examination (MMSE), each correct response had one mark which makes the total assessment out of 30. Based on the correct responses the participants gave they were classified into two groups as no cognitive function impairment and having cognitive function impairment. Following this, an eight-item Morisky Medication Adherence Scale (MMAS-8) was used to assess medication adherence of study participants. It has a total of 8 items and each of them has ‘one’ score when mentioned ‘yes’ and ‘zero’ when answered ‘no’, which makes the assessment out of eight. The final part of the questionnaire assesses the behavioral characteristics of participants.

Mini-Mental State Examination is a validated and standardized questioner, which was used to assess the cognitive function of patients. It has five parts including orientation, language and praxis, registration, attention and calculation, and recall with scores of 10,9,3,5, and 3 respectively. This makes the total score out of 30. MMSE has been validated and used by many developing and developed countries i.e. Malaysia India, China, USA, etc. and according to a cross-sectional study done on population norms for mini-mental state examination in Ethiopia in

2011, they found that it can be used in Ethiopia, but since the educational status was independent predictor it needs to be considered (26). Morisky Medication Adherence Scale is also a validated assessment tool used to measure non-adherence in a variety of patients. It has been used and verified by many studies on the globe. In Ethiopia, MMAS is a commonly used adherence assessment scale for different diseases, it is also a commonly used assessment tool for adherence to antihypertensive medications. Studies that were done in Jimma in 2018, Northwest part of Ethiopia (Bahrdar, Gonder and Debre Markos) in 2017 and Gonder in 2012 are some of the many articles which used MMAS to assess the adherence level of hypertension patients to their prescribed medications (10, 11, 23).

In this study, there were five data collectors and two supervisors and they had two days of training on how to do the data collection and supervision. The data collection was done twice, first (in the participant's first appointment during the data collection) the socio-demographic and MMSE parts of the questionnaire were covered to classify the participants into two groups as cases and controls, and during the second appointment of the study participants the clinical characteristics, medication adherence (MMAS) and the behavioral characteristics parts of the questionnaire were covered.

During the first data collection, in order to get the required number of cases which was 106, all participants who fulfilled the inclusion criteria were being interviewed on the socio-demographic characteristics and the MMSE parts of the questionnaire. A total of 681 participants i.e. 194 from Mekelle hospital and 487 from Ayder comprehensive specialized hospital were interviewed, the first 106 participants who had no cognitive function impairment were included in the study as controls and the 106 participants who had cognitive function impairment were cases.

As we can see from the table below, those who got included in the study and those who didn't had almost similar socio-demographic characteristics. So, the sample can be representative to the elderly hypertensive patients.

Table 1: Socio-demographic characteristics of participants in Mekelle, Ethiopia, 2020G.C. (681)

Variables	Category	Participants who get included in the study (106 cases and 106 controls)		Participants who didn't get included in the study (469)	
		Freq.	%	Freq.	%
Age	60 – 69	147	69.3	348	74.2
	70 – 79	50	23.6	67	14.3
	80 – 89	15	7.1	54	11.5
Sex	Male	101	47.6	191	40.7
	Female	111	52.4	278	59.3
Religion	Orthodox Christian	192	90.6	374	79.7
	Muslim	20	9.4	87	18.6
	Protestant			8	1.7
Marital status	Married	140	66	297	63.3
	Divorced	14	6.6	63	13.4
	Widowed	58	27.4	109	23.3
Educational status	No formal education	52	24.5	123	26.2
	Primary education	72	34	142	30.3
	Secondary education	51	24.1	113	24.1
	College and above	37	17.5	91	19.4
Occupation	Unemployed	32	15.1	46	9.8
	Employed	55	25.9	136	29
	Merchant	19	9	39	8.3
	Farmer	16	7.5	34	7.3
	House wife	22	10.4	67	14.3
	Retired	68	32.1	147	31.3

4.9.Data quality control

To ensure the data quality, four psychiatry nurses and three medical students were recruited for the data collection & supervision and two days of training was given on how to approach participants, how to take informed consent, about ethical procedures, and general information was given on the objective of the study, the questionnaires, data collection procedures and

interview techniques to have a common understanding. The questionnaire was prepared in English and translated in-to Tigrigna and then translated back into English to check for consistency. Before the actual data collection, a pre-test was done on five individuals in Quiha hospital to check for accuracy, completeness, and consistency of the questionnaire and to check whether the data collectors and supervisors are working according to the training given or not. And, the problems observed in the questionnaire and/or data collectors and supervisors during the pre-test were corrected accordingly. During the data collection, supervisors were checking each questionnaire, and incomplete and unclearly filled questionnaires were given back to the interviewers and get completed. The principal investigator was also strictly controlling the data collection procedures by supporting the supervisors and data collectors.

To decrease selection bias, cases and controls were selected using similar criteria (from the same health facilities, and their age was 60 and above) except for their cognitive function status and to decrease the non-response rate detailed explanation was given on the purpose of the study to the selected individuals.

4.10. Operational/ standard definitions

- **Cognitive function impairment**, based on the score of the Mini-Mental State Examination was classified as
 - No cognitive function impairment, if the score is 24-30, and
 - cognitive function impairment, if the score is 0-23
- But, according to studies done in Ethiopia and Cameron MMSE score was affected by the educational status of the participants (15, 26). And, the cut-off point should consider the educational status of participants. So, for this study, cognitive function impairment was defined as having an MMSE score below the cut-off value of 22 for participants with no or primary level education (< 8 years of education), 24 for those with secondary level education (9–12 years of education) and 26 for those with college-level education and above (>13 years of education).
- **Medication adherence:** Patients were considered as non-adherent when the Morisky Medication Adherence Scale (MMAS-8) score is less than six and when the score is greater than or equal to six patients were considered adherent to antihypertensive medications.

4.11. Data processing and analysis

The collected questionnaires were checked manually, coded, and then entered into Epi data version 3.1 software and exported to SPSS version 23 for cleaning and further analysis. Descriptive statistics was done for each study variable and data were presented using tables, and figures. Normality for the distribution of continuous variables was checked with histogram and for normally distributed data, the mean and standard deviation (SD) was reported.

Binary logistic regression analysis was carried out using the bivariable analysis to assess the association between the dependent (cognitive function impairment) and independent variable (medication adherence) and, to see the effect of the other independent variables a bivariable analysis was done for the other variables against both the outcome and the exposure variables. Independent variables that were mutually associated with both, the outcome and exposure variables, at a P-value of less than 0.25 in the bivariable analysis were entered into multivariable analysis to control the possible effect of confounders and to assess the real association between cognitive impairment and medication adherence. In multivariable logistic regression analysis adjusted odds ratio (AOR) with a corresponding 95% confidence interval was computed to show the strength of association and a P-value of < 0.05 was used to declare the statistical significance. Multicollinearity was checked using variance inflation factor (VIF) and the VIF lied between 1 up to 10. Hosmer and-Lemeshow test (0.42) was used to check the fitness of the model to the data.

4.12. Ethical considerations

Ethical approval was taken from the ethical committee of the School of Public Health, College of Health Sciences, Addis Ababa University, and permission was asked from each health institution that was included in the study. The participation was based on informed consent and only volunteers were part of the study and to help them understand; the aim or purpose of the study, benefits, and risks was clearly explained to the study participants. They were free to withdraw from the study at any time and they were allowed to skip any question they were not comfortable answering, and this didn't have any impact on their subsequent management. The confidentiality and privacy of the study participants were kept. They were not expected to give their names, address, and signature. And, everyone had a non-zero chance of being included in the study as long as they fulfilled the requirements.

5. Result

5.1 Socio-demographic characteristics of the participants

A sample of 106 cases and 106 controls participated in this study. More than half of cases 59(55.7) and 52(49.1%) of controls were females. The mean (\pm SD) age was 68.9(\pm 7.26) years among cases and 66.2(\pm 4.97) years among controls respectively. Most of the participants, 97(91.5%) cases, and 95(89.6%) controls were orthodox Christian religion followers. Among cases, 51(48.1%) were married and 42 (39.6%) had primary education and among controls, 89(84%) were married and 30(28.3%) had primary education (Table 2).

Table 2: Socio-demographic characteristics of participants in Mekelle, Ethiopia, 2020 G.C. (106 cases and 106 controls)

Variables	Category	Cognitive function impairment				Chi-square	p-value
		Cases		Controls			
		Freq.	%	Freq.	%		
Sex	Male	47	44.3	54	50.9	0.93	0.34
	Female	59	55.7	52	49.1		
Age	60 – 69	64	60.4	83	78.3	9.86	0.01
	70 – 79	30	28.3	20	18.9		
	80 – 89	12	11.3	3	2.8		
Religion	Orthodox Christian	97	91.5	95	89.6	0.22	0.64
	Muslim	9	8.5	11	10.4		
Marital status	Married	51	48.1	89	84	35.2	0.00
	Divorced	7	6.6	7	6.6		
	Widowed	48	45.3	10	9.4		
Educational status	No formal education	33	31.1	19	17.9	18.18	0.00
	Primary education	42	39.6	30	28.3		
	Secondary education	23	21.7	28	26.4		
	College and above	8	7.5	29	27.4		
Occupation	Unemployed	23	21.7	9	8.5	9.86	0.079
	Employed	23	21.7	32	30.2		
	Merchant	8	7.5	11	10.4		
	Farmer	10	9.4	6	5.7		
	House wife	9	8.5	13	12.3		
	Retired	33	31.1	35	33		

5.2 Clinical characteristics of participants

The mean (\pm SD) duration of hypertension in years was 9.02(\pm 6.7) among cases and 6.65(\pm 5.7) among controls. And the mean (\pm SD) duration of use of anti-hypertension medication in years was 7.89(\pm 6.3) & 5.69(\pm 4.5) among cases and controls respectively. Only 32 (30.2%) of cases achieved normal BP whereas 54 (50.9%) achieved normal BP among controls. Out of the participants, 8(7.5%) among the cases and 17(16%) among controls had comorbidities other than hypertension, and more than half of the participants 63(59.4%) cases and 64(60.4%) controls use HCT as antihypertensive medication. None of the participants had a history of recent head injury and none had admitted to having cognitive dysfunction in their family (Table 3).

Table 3: Clinical characteristics of participants in Mekelle, Ethiopia, 2020 G.C. (106 cases and 106 controls)

Variables	Category	Cognitive function impairment				Chi-square	p-value
		Cases		Controls			
		Freq.	%	Freq.	%		
Duration of HTN in years	<5 years	34	32.1	43	40.6	1.65	0.19
	\geq 5 years	72	67.9	63	59.4		
Duration of anti-HTN medication in years	<5 years	41	38.7	50	47.2	1.56	0.21
	\geq 5 years	65	61.3	56	52.8		
Anti HTN medication	HCT	63	59.4	64	60.4	2.69	0.85
	Enalapril	7	6.6	6	5.7		
	Nifedipine	9	8.5	7	6.6		
	HCT & enalapril	16	15.1	12	11.3		
	HCT & nifedipine	5	4.7	8	7.5		
	Enalapril & nifedipine	1	0.9	3	2.8		
	Other	5	4.7	6	5.7		
Achieve normal BP	Yes	32	30.2	54	50.9	9.47	0.00
	No	74	69.8	52	49.1		
Know anti-HTN medication is life long	Yes	89	84	97	91.5	2.81	0.09
	No	17	16	9	8.5		
Presence of comorbidity	Yes	8	7.5	17	16	3.67	0.06
	No	98	92.5	89	84		

Table 3: continued

Type of comorbidity	DM	2	25	6	35.3	1.04	0.79
	HIV/AIDS	1	12.5	4	3.3		
	Kidney disease	3	37.5	4	23.5		
	Other	2	25	3	17.6		

5.3 Behavioral characteristics of participants

According to this study, all cases and 104(98.1%) controls had no history of smoking. On the other hand, 55(51.9%) cases and 50(47.2%) controls had a rare history of drinking alcohol. Among cases, 40(37.7%) of them do physical exercise rarely and 50(47.2%) controls do physical exercise usually (Table 4).

Table 4: Behavioral characteristics of participants in Mekelle, Ethiopia, 2020 G.C. (106 cases and 106 controls)

Variables	Category	Cognitive function impairment				Chi-square	p-value
		Cases		Controls			
		Freq.	%	Freq.	%		
Smoking	Yes			2	1.9	2.02	0.16
	No	106	100	104	98.1		
Alcohol	Never	34	32.1	33	31.1	1.15	0.56
	Rarely	55	51.9	50	47.2		
	Sometimes	19	16	23	21.7		
Physical exercise	Never	10	9.4	5	4.7	23.33	0.00
	Rarely	40	37.7	24	22.6		
	Sometimes	28	26.4	15	14.2		
	Usually	25	23.6	50	47.2		
	All the time	3	2.8	12	11.3		

5.4 Prevalence of anti-hypertensive medication adherence

The prevalence of adherence to antihypertensive medications were 84(79.2%) among controls and 34(32.1%) among cases. Out of the total participants, 94(44.9%) were non-adherent to their anti-hypertensive medications and fear of adverse effects 1(1.1%), forgetting to take medication 93(98.9%), feeling better 10(10.6%), feeling worse when taking medications 13(13.8%), expensiveness of the drug product 12(12.8%) and

availability of the drug product 3(3.2%) were some of the reasons for non-adherence (Figure 3).

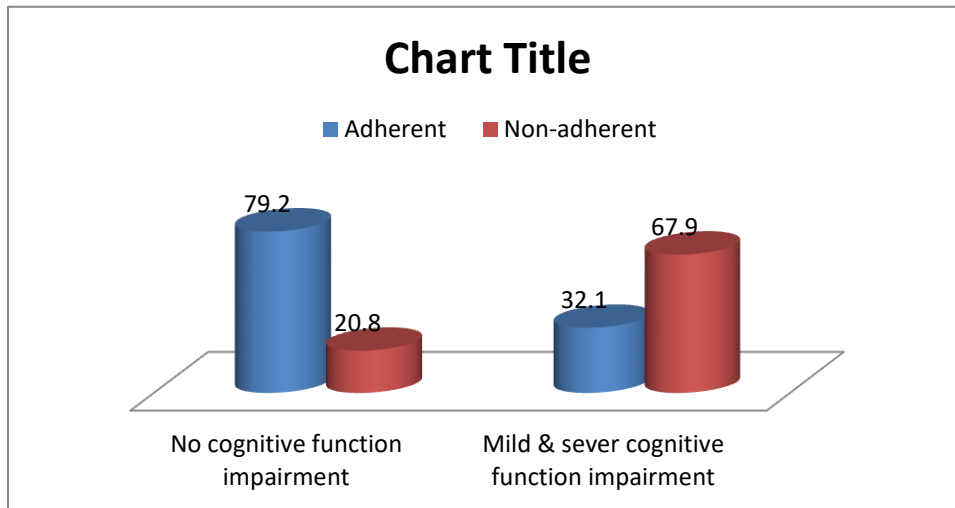


Figure 3: Anti-hypertensive medication adherence among participants in Mekelle, Ethiopia, 2020 G.C (106 cases and 106 controls)

5.5 The effect of Anti-hypertensive medication adherence on cognitive function impairment

The bivariable analysis revealed that cognitive function impairment was associated with medication adherence [COR= 8.09, 95% CI: (4.31-15.06)]. .

Since the association of medication adherence with cognitive function impairment may be related to other covariates, or to make sure the association between the outcome variable and the exposure variable is not confounded by other independent variables multivariable analysis had to be done. But, before that to get the confounding variables i.e. variables which were associated both with the outcome and the exposure variables, bivariable analysis was done for the outcome variable against all the independent variables.

In the bivariable analysis, the factors that were found to have a p-value of < 0.25 were age, marital status, educational status, occupation, achieving normal BP, duration of hypertension, duration of antihypertensive medications, know antihypertensive medications are life long, comorbidity, and exercise.

Table 5: Bivariable analysis on the effect of medication adherence and other factors on cognitive function impairment, Mekelle, Ethiopia, 2020 G.C. (106 cases and 106 controls)

Variables	Category	Cases (n=106)	Controls (n=106)	COR (95% CI)
Medication adherence	Adherent	34 (32.1%)	84 (79.2%)	1
	Non adherent	72 (67.9%)	22 (20.8%)	8.09 (4.34, 15.06)**
Age	60 – 69	64 (60.4%)	83 (78.3%)	1
	70 – 79	30 (28.3%)	20 (18.9%)	1.95 (1.01, 3.74)*
	80 – 89	12 (11.3%)	3 (2.8%)	5.19 (1.41, 19.15)*
Marital status	Married	51 (48.1%)	89 (84%)	1
	Divorced	7 (6.6%)	7 (6.6%)	1.75 (0.58, 5.26)
	Widowed	48 (45.3%)	10 (9.4%)	8.38 (3.9, 17.97)**
Educational status	No formal education	33 (31.1%)	19 (17.9%)	6.29 (2.39, 16.53)**
	Primary education	42 (39.6%)	30 (28.3%)	5.06 (2.04, 12.64)**
	Secondary education	23 (21.7%)	28 (26.4%)	2.98 (1.14, 7.76)*
	Collage and above	8 (7.5%)	29 (27.4%)	1
Occupation	Unemployed	23 (21.7%)	9 (8.5%)	1
	Employed	23 (21.7%)	32 (30.2%)	0.28 (0.11, 0.72)*
	Merchant	8 (7.5%)	11 (10.4%)	0.29 (0.08, 0.94)*
	Farmer	10 (9.4%)	6 (5.7%)	0.65 (0.18, 2.33)
	House wife	9 (8.5%)	13 (12.3%)	0.27 (0.08, 0.85)*
	Retired	33 (31.1%)	35 (33%)	0.37 (0.15, 0.91)*
Achieve normal BP	Yes	32 (30.2%)	54 (50.9%)	1
	No	74 (69.8%)	52 (49.1%)	2.4 (1.37, 4.22)*
Duration of hypertension	<5 years	34 (32.1%)	43 (40.6%)	1
	≥5 years	72 (67.9%)	63 (59.4%)	1.44 (0.82, 2.54)
Duration of antihypertensive medication	<5 years	41 (38.7%)	50 (47.2%)	1
	≥5 years	65 (61.3%)	56 (52.8%)	1.42 (0.82, 2.44)
Know antihypertensive medications are life long	Yes	89 (84%)	97 (91.5%)	1
	No	17 (16%)	9 (8.5%)	2.06 (0.87, 4.85)
Comorbidity	Yes	8 (7.5%)	17 (16%)	1
	No	98 (92.5%)	89 (84%)	2.34 (0.96, 5.69)

Table 5: continued

Exercise	Never	10 (9.4%)	5 (4.7%)	8 (1.52, 42)*
	Rarely	40 (37.7%)	24 (22.6%)	6.6 (1.7, 26)*
	Sometimes	28 (26.4%)	15 (14.2%)	7.5 (1.8, 30.6)*
	Usually	25 (23.6%)	50 (47.2%)	2 (0.5, 7.74)
	All the time	3 (2.8%)	12 (11.3%)	1

- * = p-value < 0.05, ** = p-value < 0.001, COR = crude odds ratio

On the other hand, a bivariable analysis done between the exposure variable which is medication adherence and the other independent variables showed that age, marital status, educational status, occupation, duration of hypertension, duration of antihypertensive medications, drinking alcohol, and exercise were associated with medication adherence at a p-value of < 0.25.

Table 6: Bivariable analysis on the effect of independent variables on medication adherence, Mekelle, Ethiopia, 2020 G.C. (106 cases and 106 controls)

Variables	Category	Medication adherence		COR (95% CI)
		Yes (n=118)	No (n=94)	
Age	60 – 69	93 (78.8%)	54 (57.4%)	1
	70 – 79	21 (17.8%)	29 (30.9%)	2.38 (1.24, 4.57)*
	80 – 89	4 (3.4%)	11 (11.7%)	4.74 (1.44, 15.61)*
Religion	Orthodox Christian	104 (88.1%)	88 (93.6%)	1.97 (0.73, 5.35)
	Muslim	14 (11.9%)	6 (6.4%)	1
Marital status	Married	86 (72.9%)	54 (57.4%)	1
	Divorced	10 (8.5%)	4 (4.3%)	0.64 (0.19, 2.13)
	Widowed	22 (18.6%)	36 (38.3%)	2.61 (1.39, 4.89)*
Educational status	No formal education	24 (20.3%)	28 (29.8%)	3.15 (1.27, 7.81)*
	Primary education	35 (29.7%)	37 (39.4%)	2.85 (1.21, 6.75)*
	Secondary education	32 (27.1%)	19 (20.2%)	1.6 (0.64, 4.03)
	Collage and above	27 (22.9%)	10 (10.6%)	1
Occupation	Unemployed	18 (15.3%)	14 (14.9%)	0.65 (0.28, 1.52)
	Employed	37 (31.4%)	18 (19.1%)	0.41 (0.19, 0.85)*
	Merchant	15 (12.7%)	4 (4.3%)	0.22 (0.07, 0.74)*
	Farmer	7 (5.9%)	9 (9.6%)	1.08 (0.36, 3.23)
	House wife	10 (8.5%)	12 (12.8%)	1.01 (0.38, 2.64)
	Retired	31 (26.3%)	37 (39.4%)	1
Duration of hypertension	<5 years	49 (41.5%)	28 (29.8%)	1
	≥5 years	69 (58.5%)	66 (70.2%)	1.67 (0.94, 2.97)
Duration of antihypertensive medication	<5 years	55 (46.6%)	36 (38.3%)	1
	≥5 years	63 (53.4%)	58 (61.7%)	1.41 (0.81, 2.44)

Table 6: continued

Alcohol	Never	44 (37.3%)	23 (24.5%)	1
	Rarely	56 (47.5%)	49 (52.1%)	1.67 (0.89, 3.15)
	Sometimes	18 (15.3%)	22 (23.4%)	2.34 (1.05, 5.21)*
Exercise	Never	7 (5.9%)	8 (8.5%)	4.57 (0.90, 23.14)
	Rarely	30 (25.4%)	34 (36.2%)	4.53 (1.17, 17.61)*
	Sometimes	15 (12.7%)	28 (29.8%)	7.47 (1.82, 30.65)*
	Usually	54 (45.8%)	21 (22.3%)	1.56 (0.39, 6.07)
	All the time	12 (10.2%)	3 (3.2%)	1

- * = p-value < 0.05, ** = p-value < 0.001, COR = crude odds ratio

The confounding variables i.e. variables that were mutually associated with both the outcome and the exposure variables in the bivariable logistic regression model were entered into the final model for further analysis, which is multivariable logistic regression. After controlling for possible confounders there was still significant association (p-value < 0.001) between medication adherence and cognitive impairment with [AOR =7.7, 95% CI: (3.44-17.24)]. This shows that the alternative hypothesis was correct and the null hypothesis needs to be rejected.

The odds of cognitive impairment was 7.7 times [AOR =7.7, 95% CI: (3.44-17.24)] more among those who were non-adherent to their antihypertensive medications compared to those who were adherent. And, the odds of cognitive impairment was 7.39 times [AOR=7.39, 95% CI: (2.72-20.09)] higher among widowed compared to married participants.

Those who had no formal education were 5.73 times [AOR=5.73, 95% CI: (1.21-27)] more likely to develop cognitive impairment compared to those who had a college education and above. Similarly, participants who had primary education were 4.09 times [AOR=4.09, 95% CI: (1.17-14.24)] more likely to develop cognitive impairment compared to participants who had a college education & above and the odds of cognitive impairment was 4.67 times [AOR=4.67, 95% CI: (1.28-17.01)] higher among participants who had secondary education than those who had a college education and above (Table 7).

Table 7: Multivariable analysis on the effect of medication adherence on cognitive function impairment, Mekelle, Ethiopia, 2020 G.C. (106 cases and 106 controls)

Variables	Category	COR (95% CI)	AOR(95% CI)
Medication adherence	Adherent	1	1
	Non adherent	8.09 (4.34, 15.06)**	7.7 (3.44, 17.24)**
Age	60 – 69	1	1
	70 – 79	1.95 (1.01, 3.74)*	1.06 (0.43, 2.64)
	80 – 89	5.19 (1.41, 19.15)*	0.67 (0.11, 4.04)
Marital status	Married	1	1
	Divorced	1.75 (0.58, 5.26)	1.83 (0.50, 6.68)
	Widowed	8.38 (3.9, 17.97)**	7.39 (2.72, 20.09)**
Educational status	No formal education	6.29 (2.39, 16.53)**	5.73 (1.21, 27)*
	Primary education	5.06 (2.04, 12.64)**	4.09 (1.17, 14.24)*
	Secondary education	2.98 (1.14, 7.76)*	4.67 (1.28, 17.01)*
	Collage and above	1	1
Occupation	Unemployed	1	1
	Employed	0.28 (0.11, 0.72)*	1.52 (0.37, 6.28)
	Merchant	0.29 (0.08, 0.94)*	0.97 (0.20, 4.60)
	Farmer	0.65 (0.18, 2.33)	1.12 (0.18, 7.04)
	House wife	0.27 (0.08, 0.85)*	0.58 (0.12, 2.81)
	Retired	0.37 (0.15, 0.91)*	0.67 (0.18, 2.56)
Duration of hypertension	<5 years	1	1
	≥5 years	1.44(0.82, 2.54)	1.01 (0.21, 4.93)
Duration of antihypertensive medication	<5 years	1	1
	≥5 years	1.42(0.82, 2.44)	1.13 (0.24, 5.33)
Exercise	Never	8 (1.52, 42)*	5.27 (0.68, 40.62)
	Rarely	6.6 (1.7, 26)*	3.11 (0.56, 17.16)
	Sometimes	7.5 (1.8, 30.6)*	3.24 (0.54, 19.29)
	Usually	2 (0.5, 7.74)	1.66 (0.32, 8.50)
	All the time	1	1

- * = p-value < 0.05, ** = p-value < 0.001, COR = crude odds ratio, AOR= adjusted odds ratio

6. Discussion

This case-control study aimed at determining the effect of medication adherence on cognitive function impairment among hypertensive patients who have been taking antihypertensive medications for at least six months or more. The magnitude of medication adherence was 34(32.1%) among cases and 84(79.2%) among controls and, the odds of cognitive impairment was more among medication non-adherent participants than those who were adherent. This study also found that marital status and educational status to be significantly associated with cognitive impairment.

Reasons for cognitive impairment is not limited to one disease or condition nor is limited to a specific age group, even though it is more common in old age groups. Cognitive impairment can be related to age, family history, brain injury, developmental disabilities and, chronic diseases like hypertension, DM, stroke, and heart diseases (13).

Both hypertension and hypotension are associated with disruptions in neurovascular coupling, which lead to a decrease in vascular reserve capacity and can cause micro vascular disease, stroke, cognitive decline, and dementia(27). Neurovascular coupling is a concept that refers to the interactions between neurons, vessels and other cells of the nervous system (such as astrocytes and other glial cells). This coupling controls the blood flow and gives these neurons the energy to send and receive messages. (28)

Hypertension exerts deleterious actions on the brain and its circulation. It alters the structure of cerebral blood vessels by producing vascular hypertrophy and remodeling and by promoting atherosclerosis in large cerebral arteries. These structural alterations facilitate vascular occlusions and compromise cerebral perfusion. Hypertension also impairs the function of cerebral blood vessels. (28)

According to this study, poor medication adherence was significantly associated with cognitive impairment in which, anti-hypertensive medication non-adherent participants were 7.7 times more likely to develop cognitive dysfunction compared with medication adherent participants. Different studies showed that hypertension in the elderly increases the risk of cognitive impairment (16, 24, 25). And, if a person is non-adherent to the prescribed antihypertensive

medications the probability of achieving normal BP decreases which might lead to development of cognitive impairment.

To the best of the researcher's knowledge, this study is the first study in its kind in our country Ethiopia and in Africa to assess, whether non-adherence to anti-hypertensive medications can lead to cognitive function impairment or not. But there are few similar studies done on this topic in other continents. Secondary longitudinal data analysis done in Canada in 2019 showed that adherence to antihypertensive agents had a positive and preserving effect on cognition. This study also found improved cognitive status in participants with comorbid hypertension and diabetes adhering to both oral antihypertensive and hypoglycemic agents (29). Another study also indicated that effective antihypertensive therapy may reduce cognitive decline in the elderly with mild cognitive impairment (30).

There are studies done in different countries which stated that the other way is also true i.e. cognitive function impairment can lead to poor medication adherence. A retrospective cohort study done in Korea in 2018 stated that in patients without over dementia medication adherence worsens with a decline in cognitive function (31). Another cross-sectional study done in 2018 also stated that cognitive impairment was associated with low treatment compliance (32).

This study also showed that marital status was significantly associated with cognitive function. Those who were widowed were 7.39 times more likely to develop cognitive impairment compared to those who were married. A similar finding was reported in studies done in Cameron, Finland, and FINE (Finland, Italy, and the Netherlands) (15, 33, 34). The elderly might have a difficulty of remembering to take their medications due to their age-related cognitive decline but if they are married, their partner might remind them or help them take their medications on time, which results in increasing the level of medication adherence and the occurrence of cognitive impairment might decrease. A cross-sectional study that was done in Brazil in 2015 also found that the presence of a caregiver at home who could assist with the use of medications was significantly associated with improved mini-mental state examination score of hypertensive older adults (35).

Different studies done in developed countries stated that greater educational attainment was related to better performance on cognitive measures. Also, educational experiences may provide

the necessary knowledge, understanding, skills, and competencies which might result in better cognition (36, 37). Studies done in Cameron and Ethiopia classified the MMSE score according to the educational status of study participants and this study used this classification system to assign cases and controls. Statistically significant association was found between educational status and cognitive impairment; those who had no formal education were 5.73 times more likely to develop cognitive impairment than those who had a college education and above. On the other hand, the likelihood of developing cognitive impairment was 4.09 times higher among participants who had primary education and 4.67 times higher among participants who had secondary education compared to those who had a college education and above. This result was similar to a study done in Cameron which stated that lack of formal education was independently associated with cognitive impairment (15).

7. Strengths and limitation

The strengths of this study were that the data were collected with high response rate, and this study was the first study in its kind in Ethiopia as well as in Africa that tried to assess the association between anti-hypertensive medication adherence and cognitive function impairment. The limitation of this study was that since this study was a case-control study recall bias could be a problem.

8. Conclusion

In this study it is indicted that there is an association between antihypertensive medication adherence and cognitive function impairment in elderly above the age of 60 after controlling for possible confounders. On the other hand, cognitive impairment was lower among married and well educated participants.

9. Recommendations

- Further work needs to be done by the health professionals on informing patients about the consequences of elevated and/ or uncontrolled BP and on the benefits of medication adherence and the consequences of non-adherence.
- It could be better if regular assessment of cognitive function status of the elderly hypertensive patients is started to be given in hospitals.
- Elderly hypertensive patients better be not left alone, they need to be active and they have to participate in different social activities.
- Further work needs to be done by ministry of education and other responsible bodies on providing educational programs for the elderly who had no formal education and to those who want further education to help them improve their intellectual activities.

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Annexes

Annex I: English version questioner

- Study information sheet and consent form

Study information sheet

Good morning/ good afternoon

My name is_____.I'm a member of the study that is being carried out at Mekelle, Ethiopia which is entitled as, "The association between medication adherence and cognitive function impairment among hypertension patients". The study is being conducted by Senait Alemayehu from Addis Ababa University, school of public health, department of epidemiology and biostatistics, post graduate program.

The aim of this study is to assess the association between medication adherence and cognitive function impairment among hypertension patients in Mekell, Tigray, Ethiopia. It is expected that the study will identify drug adherence level among hypertension patients and its effect on cognitive function and at the end of the study, recommendations will be provided according to the study findings.

The study will be conducted through interviewing and recording medical findings from your medical chart. If you are voluntary to participate in this study, we will stay together for about----- minutes and you are expected to answer the questions found in this questioner. The information that you will provide will be kept confidential. It will be kept in secret and coded. You are free to answer only what you understand, to ask any question, and to withdraw from the interview at any time. And, you are not expected to give your name, address and signature.

Date: ___/___/___

Signature of the interviewer: _____

Address of the investigator: Senait Alemayehu

Cell phone: 0914197945

E-mail: senaitalemayohabrha@gmail.com

Consent form

I have been given information about the research titled as “The association between medication adherence and cognitive function impairment among hypertension patients”. Which is being conducted by Senait Alemayehu from Addis Ababa University, school of public health, department of epidemiology and biostatistics, post graduate program.

I have been advised of the potential risks and burdens associated with this research, which includes spending with the data collectors for about _____ minutes and have had an opportunity to ask any questions I may have about the research and my participation.

I understand that my participation in this research is voluntary, I am free to refuse to participate and I am free to withdraw from the research at any time. My refusal to participate or withdrawal of consent will not affect my treatment in any way.

If I have any question about the research, I can contact the investigator using her phone number or Email address.

Address of the investigator: Senait Alemayehu

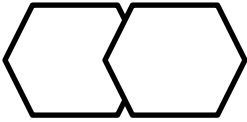
Cell phone: 0914197945

E-mail: senaitalemayohabrha@gmail.com

I’m showing my agreement by making “X” sign below in the box which says ‘Yes I’m voluntary to participate’.

Are you voluntary to participate? Yes No

If the interviewee responds “Yes” please thank him/her and proceed and if the interviewee responds “No” thank him/her and quit the interview.

10	Make up and write a sentence about anything.	
11	Please copy this picture 	
	Total	

Part IV assessment of medication adherence using Morisky Medication Adherence Scale (MMAS-8)

No	Questions	Yes	No
1	Do you sometimes forget to take your antihypertensive pills?	1	0
2	Over the past two weeks, were there any days when you did not take your antihypertensive medicine?	1	0
3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	1	0
4	When you travel or leave home, do you sometimes forget to bring along your medicine?	1	0
5	Did you take your antihypertensive medicine yesterday?	0	1
6	When you feel like your blood pressure under control, do you sometimes stop taking your medicine?	1	0
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	1	0
8	How often do you have difficulty remembering to take your antihypertensive medicine? 1 Never 2 Rarely 3 Once in a while 4 Sometimes 5 Usually 6 All the time		
	Total score		

If you have any problems that challenges your medication adherence please select your reason (more than one answer is possible)

1. Fear of adverse events
2. Disbelief in drug effectiveness
3. Directions not understood
4. Patient forgets to take
5. Patient felt better
6. Patient felt worse
7. Drug product too expensive
8. Patient cannot swallow/ administer
9. Drug product not available
10. Regimen complexity

If others, specify-----

Part V: assessment of behavioral characteristics

1. Do you have history of smoking? 1 Yes 2 No

If yes, for how long _____

If you are smoking currently how many cigarettes do u smoke per day? _____

2. Do you have history of drinking alcohol?

- 1 Never
- 2 Rarely
- 3 Once in a while
- 4 Sometimes
- 5 Usually
- 6 All the time

If you are drinking alcohol currently how much do you drink per day or week? _____

3. Do you do physical exercise?

1 Never

2 Rarely

3 Once in a while

4 Sometimes

5 Usually

6 All the time

Annex II: tigrigna version questioner

ናይ ትግርኛ መጠይቕ

ናይ መፅናዕቲ ሓበሬታ ወረቐትን ናይ ፍቓደኝነት ፎርምን

ሽመይ _____ ኣብ ናይ መቐለ፣ ኢትዮጵያ ዝካየድ ዘሎ መፅናዕቲ ኣባል እዩ። ኣርእስቲ እዚ መፅናዕቲ ድማ “ርክብ ኣብ መንጎ ኣወሳስዳ መድሓኒትን ተገንዝቦኣዊ ድኽመትን ኣብ መንጎ ሕሙማት ድፍኢት ደም” ይብል። እዚ መፅናዕቲ ኣዲስ ኣበባ ዩኒቨርሲቲ ማሕበራዊ ጥዕና ክፍሊ ትምህርቲ ሕማም ለበዳን ስነ-በዝሕን፣ ድሕረ ምረቓ ፕሮግራም ብሰናይት ኣለማየሁ ዝካየድ እዩ።

ዕላማ ናይዚ መፅናዕቲ ድማ ርክብ ኣብ መንጎ ኣወሳስዳ መድሓኒትን ተገንዝቦኣዊ ድኽመትን ሕሙማት ድፍኢት ደም ኣብ መቐለ፣ ትግራይ፣ ኢትዮጵያ ግምገማ ምክያድ እዩ። እዚ መፅናዕቲ ድማ ናይ መድሓኒት ተኸታሊ መጠን ኣብ ድፍኢት ደም ዘለዎም ተሓከምትን ኣብ ተገንዝቦኣዊ ስራሕ ዘለዎ ጉድኣት ክፈልግልና እዩ ተባሂሉ ትፅቢት ይግበረሉ። ኣብ መወዳእታ እዚ መፅናዕቲ ድማ ኣብ ዝተረኸበ ውፅኢታት መፅናዕቲ ተደራሽ ሓበሬታ ክወሃብ እዩ።

እዚ መፅናዕቲ ብ ቃለ መሕትትን ኣብ ናይ ጥዕና ቻርትኻ ብዝረኽብናዮ ውፅኢት ዝካየድ እዩ። ኣብዚ መፅናዕቲ ክትሳተፍ ፍቓደኛ እንተኾይንካ _____ ደቓይቕ ብሓባር ክንፀንሕ ኢና፣ ኣብዚ ቃለ መሕትት ዘለዉ ሕቶታት ክትምልስ ድማ ትፅቢት ይግበረልካ። እቲ እትህበና ሓበሬታ ሚስጥራዊ ኮይኑ ይቕመጥ፣ ብሚስጠርን ብኮድን ድማ ይተሓዝ። ዝተረደአካ ጥራሕ ናይ ምምላስ፣ ዝኾነ ሕቶ ናይ ምሕታት፣ እዚ መጠይቕ ኣብ ደስ ዝበለካ ግዜ ናይ ምቁራፅ መሰልካ ዝተሓለወ እዩ። ብተወሳኺ ሸምካ፣ ኣድራሻኻ ኮነ ክታምኻ ናይ ምሃብ ግዴታ የብልኻን።

ዕለት ___/___/___ ክታም ኣታቲ _____

ኣድራሻ ናይ መፅንዒት፡ ሰናይት ኣለማየሁ

ቁፅሪ ሞባይል፡ 0914197945

ኢ- ሜይል፡ senaitalemayohabr@gmail.com

ናይ ስምምዕነት ፎርም

“ርክብ ኣብ መንጎ ተኸታሊ ጥዕናን ተገንዝቦአዊ ድኽመት ሕሙማት ድፍኢት ደምን” ኣብ ዝብል ርእሲ ብሰናይት ኣለማየሁ ኣዲስ ኣበባ ዩኒቨርሲቲዮ ማሕበራዊ ጥዕና ክፍሊ ትምህርቲ ሕማም ለበዳን ስነ-ብዝሕን ድሕረ ምርቓ ፕሮግራም ኣብ ዝካየድ ዘሎ መፅናዕቲ እኹል ሓበሬታ ተዋሂቦ እዩ።

ምስ እዚ መፅናዕቲ ተተሓሔዞም ዝመፅእ ጉድኣትን ሓላፍነትን ብዝግባእ ተገሊፁለይ እዩ። ምስ መፅናዕቲ/ዒት ን _____ ደቓይቕ ብሓባር ከም እንፀንሕን ዝደለኸዎ ሕቶ ብዛዕባ እዚ መፅናዕቲ ወይ ናተይ ተሳትፎ ክሓትት ከም ዝኸእልን ተገሊፁለይ እዩ።

ኣብዚ መፅናዕቲ ዘለኒ ተሳትፎ ኣብ ፍቓደኝነት ዝተመስረተ እዩ። ኣብዚ መጠይቕ ናይ ዘይምስታፍ ከምኡ እውን ኣብ ዝኾነ እዋን እዚ መጠይቕ ናይ ምቁራፅ መሰለይ ዝተሓለወ እዩ። ኣብዚ መጠይቕ ዘይምስታፊይ ወይ ካብዚ መጠይቕ ኣቋሪፀ ምውፅኣይ ብምንም ዓይነት መልክዑ ንሕክምናይ ከምዘይገባእ ተረዲኦ እዩ።

ብዛዕባ እዚ መፅናዕቲ ዝኾነ ሕቶ እንተገልጻኒ ንመፅንዒት ብስልኪ ቐፅራ ወይ ብኢ-ሜይል ኣድራሻኦ ክሓታ ይኸእል እዩ።

ኣድራሻ መፅንዒት: ሰናይት ኣለማየሁ

ስልኪ ቐፅራ: 0914197945

ኢ-ሜይል: senaitalemayohabrha@gmail.com

ፍቓደኛ ምኺነይ ኣብ ታሕቲ ኣብ ዘሎ ሰደቓ ናይ “X” ምልክት ብምቕማጥ ገሊፀ ኣለኹ።

ንክትሰተፍ ፍቓደኛ ዲኻ? እወ ኣይ

ቅዳማይ ክፋል፡- ናይ ተሓከምቲ ማሕበረ ህዝባዊ ባህርያት (ብዝተረኸበ መልሲ ተደሪኽካ ነቲ መልሲ ዝሓዘ ቁፅሪ ኣኸብብ)

ኮድ _____				
1. ዕድመ _____				
2. ምታ	1 ተባ		2 ኣን	
3. ኩነታት ሓዳር	1 ሓዳር ዘይብሉ/ላ	2 በዓል ሓዳር	3 ዝተፋተሐ/ት	4 በዓል ሓዳር/ራ ብሞት ዝተፈለየቶ/ያ
4. ሃይማኖት	1 ኦርቶዶክስ	2 ሙስሊም	3 ፕሮቴስታንት	4 ካቶሊክ ካልእ _____
5. ኩነታት ትምህርቲ	1 ስሩዕ ትምህርቲ ዘይወሰደ/ት	2 ቅዳማይ ብርኪ	3 ካልኣይ ብርኪ	4 ኮሌጅ ወይ ልዕሊኡ
6. ስራሕ	1 ስራሕ ዘይብሉ/ላ	2 ናይ መንግስቲ ስራሕተኛ	3 ነጋዴ	4 ሓረስታይ
	1 መራሒት ስድራ	2 ኣብ ናይ ውልቀ ተቆፃሪ/ት	3 መዓልታዊ ስራሕተኛ	4 ካልእ _____

ካልኣይ ክፋል፡- ናይ ተሓካማይ ክለኒካዊ ባህሪ (እዚ ዝምላእ ካብ ናይ ጥዕና ቻርት ወይ ካብ ቃለ መሕትት ክኸውን ይኸእል እዩ።)

1. ድፍኢት ደም ከም ዘለካ/ኪ መዓዝ ፈለጥካ/ኪ? _____
2. እንታይ ዓይነት ፀረ ድፍኢት ደም መድሓኒት ትጥቀም? _____
3. ኣብ መዓልቲ ክንደይ ክኒን ትወስድ? _____
4. ፀረ ድፍኢት ደም መድሓኒት ምውሳድ ካብ እትጅምር ክንደይ ግዘ ጌረካ?

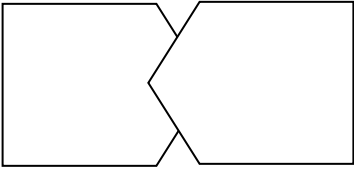
5. ኣብ ትክክለኛ መጠን (normal) ድፍኢት ደም በዓሕካ 'ዶ? 1 እወ 2 ኣይ
6. ፀረድፍኢት ደም መድሓኒት ሂወት ሙሉእ ዝውሰድ መድሓኒት ምኳኑ ትፈልጥ 'ዶ?
1 እወ 2 ኣይ
7. ካብ ድፍኢት ደም ብተወሳኺ ካልእ ሕማም ኣለካ 'ዶ? 1 እወ 2 ኣይ
መልስኻ/ኺ እወ እነተኾይኑ ዘርዘር _____

8. አብ ቀረባ እዋን ናይ ርእሲ ሓደጋ ኢጋጢ.ሙካ ይፈልጥ 'ዶ? 1 እወ 2 አይ መልስኻ/ኸ እወ እነተኾይኑ ግለፆ። _____

9. አብ ውሽጢ ቤተሰብካ ናይ ምምሃር፣ ምሕሳብ፣ ምኽንያታውነት፣ ምስትዋስ፣ ፀገም ምፍታሕ፣ ምውሳኔን ምሙካርን ድኽመት ዘለዎ አሎ 'ዶ? 1 እወ 2 አይ መልስኻ/ኸ እወ እነተኾይኑ እቲ ድኽመት ዘለዎ ሰብ ምሳኻ/ኸ ዘለዎ ዝምድና እንታይ እዩ (አብነት አይ፣ አቦ፣ ወዘተ.) _____

ሳልሳይ ክፋል፡- ፈተኻ ተገንዝቦአዊ ኩነታት ተሓካማይ

ተ.ቁፅሪ	ሕቶታት	ናይ ተሓካማይ ውፅኢት
1	አብ አየናይ ዓመት _____ ወቕቲ _____ ዕለት _____ መዓልቲ _____ ወርሒ _____ ንርኩብ?"	
2	ሕዚ አባይ ንርኩብ? ሃገር _____ ክልል _____ ከተማ _____ ሆስፒታል _____ ደብሪ _____	
3	ነዘን ቐፂሊ ዝነግረካ ነገራት ደጊምካ ንገረኒ መፅሓፍ፣ መኪና፣ ሓኪም፡፡ _____ ፣ _____ ፣ _____	
4	ካብ 100 ጀሚርካ 7 ^ተ አፈላላይ ንድሕሪት ቐፀር" (93፣ 86፣ 79፣ 72፣ 65...) _____ ፣ _____ ፣ _____ ፣ _____ ፣ _____	
5	ኸኛድም ክብል ናይ ሰለስተ ነገራት ስም ነገረካ ነይረ፡፡ እንታይ ምዃኖም ክትንግረኒ ትኽእል 'ዶ? _____ ፣ _____ ፣ _____	
6	ነቲ ተሓካማይ እርሳስን ወረቐትን አርእዮ እንታይ ምዃኖም ድማ ሕተቶ፡፡ _____ ፣ _____	
7	እዞም ዝሰዕቡ ሓረጎት ደጊምካ በል	

8	ሓደ ወረቆት ኣብ የማናይ ኢድካ ሓዘ፤ ኣብ ክልተ ማዕረ ዕፀፎ፤ ኣብ መሬት ኣቐምጦ። ነቲ ተሓካማይ ነቲ ተግባር ንክደግሞ ሕተቶ። _____ ፣ _____ ፣ _____	
9	ነዚ ፅሑፍ ኣንቢብኻ ኣተግብር። (እቲ ዝተፅሓፈ መምርሒ “ዓይንኻ ተዓመት” ዝብል እዩ።) _____	
10	ብዛዕባ ደስ ዝበለካ ርእሰ ጉዳይ ሓደ ሙሉእ ሓሳብ ህነፅ። _____	
11	ነዚ ስዒቡ ዘሎ ምስሊ ደጊምኩም ሰኣልዎ። 	
	ድምር	

ራብዓይ ክፋል፡- ኣወሳስዳ መድሓኒት ዝምልከት

ተ.ቁፅ	ሕቶታት	እወ	አይ
1	ሓልሓሊካ ናይ ፀረ ድፍኢት ደም መድሓኒትካ ምውሳድ ትርስዎ 'ዶ?	1	0
2	ኣብ ዝሓለፉ ክልተ ሰሙናት ናይ ፀረ ድፍኢት ደም መድሓኒትካ ዘይወሰድካሉ መዓልቲ ኣሎ 'ዶ?	1	0
3	መድሓኒት ብምውሳድካ ሕማቕ ስምዒት ስለዝተሰምዐካ ንይክተርኻ ከየማኸርካ መድሓኒት ካብ እቲ ክትወስዶ ዝግበአካ ቐኒስካ ወይ ምውሳድ ምሉእ ብምሉእ ኣቋሪፅካ ትፈልጥ 'ዶ?	1	0
4	ጉዕዞ እንትትጉዓዝ ወይ ካብ ገዛኻ ኣብ እትወፀሉ ግዜ መድሓኒትካ ረሲዐኻ ዝወፃኻሉ ግዜ ኣሎ 'ዶ?	1	0
5	ትማሊ ፀረ ድፍኢት ደም መድሓኒትካ ወሲድካ 'ዶ?	0	1
6	ድፍኢት ደምካ ፅቡቕ ኣብ ዝኾነሉ ግዜ መድሓኒትካ ምውሳድ ኣቋሪፅኻ ትፈልጥ 'ዶ?	1	0
7	መዓልቲ መዓልቲ መድሓኒት ምውሳድ ንሓደ ሓደ ሰባት ብጣዕሚ	1	0

	የፀግመሎም እዩ። ናይ ሕክምና ክትትልኻ ናይ ምቁራፅ ሓሳብ እናመፀ የፀግመልካ 'ዶ?		
8	ናይ ፀረ ድፍኢት ደም መድሓኒትካ እንትትወስድ ብብኸንደይ ግዘ ናይ ምስትዋስ ፀገም ከጋጥመካ ይኸእል? 1 ፊዒሙ 2 ሓልሓሊፉ 3 ኣብ ወረሒ ሓደ ግዘ 4 ኣብ ሰሙን ሓደ ግዘ 5 መብሃሕትኡ ግዘ 6 ኩሉ ግዘ		
	ጠቕላላ ድምር		

መድሓኒትካ ብኣግባቡ ከይትወስድ ዝገብረካ ምክንያት እንታይ እዩ? (ካብ ሓደ ንላዕሊ መልሲ ምሃብ ይከኣል እዩ)

1. ካልእ ጉድኣት ከይህልዎ ስለዝፈርሕ
2. የድሕነኒ እዩ ኢሊ ስለዘይኣምን
3. ብሃዕባ ኣጠቓቕማ እቲ መድሓኒት እኩል ግንዛብ ስለዘይብለይ
4. መድሓኒት ምውሳድ ስለዝርስዕ
5. ዝሓሸኒ ክመስለኒ ከሎ
6. እቲ መድሓኒት ሕማመይ ስለዘበኣእሶ
7. እቲ መድሓኒት ክባር ስለዝኾነ
8. እቲ መድሓኒት ምውሓጥ ስለዘፀግመለይ
9. መድሓኒት ክረክብ ስለዘይከኣልኩ
10. ዝወስደም መድሓኒታት ብዙሓትን ዘደናግሩን ስለዝኾኑ
ካልእ ምክንያት (ዘርዝር) _____

ሓምሻይ ክፋል፡- ልምድታት ተሓካሚ ዝምልከት

1. ሲጋራ ኣትኪኸካ/ኪ ትፈልጥ/ጠ. 'ዶ? 1 እወ 2 ኣይ
መልሲኻ/ኸ. እወ እነተኾይኑ ንኸንደይ ግዘ? _____

ኣብዚ ሕዚ እዋን ሲጋራ ተትክኽ እነተኾይንካ ኣብ መዓልቲ ክንደይ ዝኣክል ሲጋራ ተትክኽ? _____

2. ኣልኮላዊ መሰተ ትሰቲ 'ዶ?

- 1 ፈጊመ
- 2 ሓልሓሊፉ
- 3 ኣብ ወረሒ ሓደ ግዘ
- 4 ኣብ ሰሙን ሓደ ግዘ
- 5 መብዛሕትኡ ግዘ
- 6 ከሉ ግዘ

3. ኣካላዊ ምንቅስቃስ ትሰርሕ 'ዶ?

- 1 ፈጊመ
- 2 ሓልሓሊፉ
- 3 ኣብ ወረሒ ሓደ ግዘ
- 4 ኣብ ሰሙን ሓደ ግዘ
- 5 መብዛሕትኡ ግዘ
- 6 ከሉ ግዘ