Teklu Abraham, Solomon Teferra, Tesfaye Yilma, Charlotte Hanlon. *Ethiop Med J, 2020, Vol. 58, No. 2*

ORIGINAL ARTICLE

TREATMENT GAP FOR CO-MORBID DEPRESSION IN MEDICAL OUTPATIENTS WITH HYPERTENSION: A CROSS-SECTIONAL HOSPITAL-BASED STUDY

Teklu Abraham, MD[1], Solomon Teferra, MD, PhD[1], Tesfaye Yilma, MD[2], Charlotte Hanlon, MRCPsych, PhD[1,3,4*]

ABSTRACT

Introduction: *Despite an increasing number of studies reporting high levels of co-morbidity between depression and hypertension in high-income countries, there is limited information on co-morbid depression among hypertensive patients in low- and middle-income countries.*

Objectives: *The aim of this study was to determine the prevalence of depression, associated factors and treatment gap among hypertensive patients attending outpatient follow-up at a referral hospital in Ethiopia.*

Methods*: A hospital-based cross-sectional study was conducted in 302 consecutive outpatient attendees with hypertension. Probable depression was measured using an interviewer administered depression scale (the Patient Health Questionnaire; PHQ-9) previously validated for the Ethiopian setting for a cut-off of 9 and above. Contextualised standardized measures of medication adherence, alcohol and khat use were used. Clinical information was extracted from medical notes, augmented by assessment of body mass index. Univariate and multivariable analyses were carried out to assess factors associated with depression.*

Results*: The prevalence of probable depression among participants was 22.2%. The treatment gap was 91%. Only 9% (n=6) had received any treatment for depression. Of these, all were prescribed an antidepressant. Female gender, adjusted odds ratio (aOR) 2.6, (95% confidence interval (CI) 1.2, 5.8), being unmarried (aOR 2.0; 95% CI 1.0, 3.7) and having two or more co-morbid medical illnesses (aOR 12.6; 95% CI 4.3, 37.0) were associated independently with depression. There was no association between depression and medication adherence, diet, physical activity or body mass index.*

Conclusions*: The prevalence of depression is high among hypertensive outpatients in Ethiopia. Most of the depressed hypertensive patients were not receiving treatment for depression. Larger, prospective studies are needed to further evaluate the impact of co-morbid depression on patient behaviours and hypertensive complications. Training general health workers to detect and treat co-morbid depression, as per recommendations from the World Health Organization is essential to decrease the treatment gap.*

Key words*: Depression, Hypertension, Prevalence, Co-morbid, Ethiopia, treatment gap*

INTRODUCTION

Depression and hypertension are among the leading causes of the global burden of disease (1, 2). Growing evidence suggests high levels of co-morbidity between hypertension and depression (3). The overall prevalence of depression in people with hypertension was estimated to be 26.8% (95% Confidence Interval (CI): 21.7%-32.3%) in a systematic review and meta-analysis of 41 observational studies from high-income countries (HICs) (4).

Several pathophysiological mechanisms have been proposed to explain the complex interaction between the two conditions, including autonomic nervous system dysfunction, shared genetic vulnerability, behavioral and psychosocial factors (5).

Depression has been found to increase the incidence of hypertension (6). In keeping with this, depression was found to be associated with subsequent diagnosis of hypertension in the World Mental Health Survey (WMHS), comprising 19 countries (7). Hypertension may also increase the risk of depression. There is now compelling evidence that the antihypertensive medications reserpine and methyldopa can induce or worsen depression, but the data supporting the link between beta-blockers and depression are not as certain (8, 9). The association between depression and hypertension has not been so clearly determined in studies from low- and middle-income countries (LMICs) to date. A population-based study from sub-Saharan Africa (3) and a prospective population-based study in Brazil (10) reported an absence of any association between hypertension and depression.

[1]Addis Ababa University, College of Health Sciences, School of Medicine, Department of Psychiatry, WHO collaborating center for mental health research and capacity building, Addis Ababa, Ethiopia. [2]Zewditu Memorial Hospital, Department of Internal Medicine, Addis Ababa University, Addis Ababa, Ethiopia. [3]King's College London, Institute of Psychiatry, Psychology and Neuroscience, Centre for Global Mental Health, London, UK. [4]Center for innovative Drug development therapeutic Trail for Africa (CDT-Africa), College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia.
*Corresponding author: charlotte.hanlon@kcl.ac.uk

Depression in people with hypertension has been associated with various socio-demographic characteristics (older age, female sex (11), low education (11,12), unemployment, being unmarried (12,13), clinical characteristics (having multiple co-morbid chronic diseases (3), potentially detrimental behaviours (cigarette smoking (5,11), alcohol intake (5), poor adherence to antihypertensive medications (11,13) and physical inactivity) and possible adverse clinical consequences, for example, uncontrolled hypertension (14). Despite this, the burden of depression in clinical settings in LMICs has been little-investigated. Recent global movements to expand access to mental health care integrated within general healthcare settings (15) offer great potential to address the burden of untreated depression in medical settings, including people with hypertension.

In Ethiopia, the prevalence of depression was estimated to be 9.1% in a nationally representative survey (16) and it was in the top 10 causes of disease burden (17). In a recent meta-analysis, hypertension was estimated to affect 19.6% of Ethiopians aged 15 years and older (18). Early detection and provision of effective treatment for co-morbid depression would be expected to bring about better clinical outcomes for both disorders (7). However, as a prerequisite to integrating depression care, it is imperative to understand the current burden of depression in such settings and the level of unmet need for mental health care.

This study aimed at determining the prevalence of co-morbid depression, associated factors and the treatment gap among people with hypertension attending medical outpatient clinics at a government referral hospital in Addis Ababa, Ethiopia.

PATIENTS AND METHODS

Study design: A hospital-based cross-sectional study was conducted in July 2016 at Zewditu Memorial Hospital (ZMH), a general referral hospital located in the capital city Addis Ababa, Ethiopia. ZMH has 188 in-patient beds and serves 9,171 inpatients and 89,540 outpatients per year (19). People with hypertension are seen by a case team consisting of an internist and three nurses at a hypertension clinic twice a week. The clinic provides outpatient follow up services for adults diagnosed with hypertension who have been referred from the different departments of the hospital and nearby health centers. Currently there are around 720 patients under regular follow up at the clinic, with an average of 30 patients seen on each clinic day.

Sample Size: The sample size was estimated using the single population proportion formula with 95% confidence level and 80% power.

As the prevalence of depression among hypertensive patients is not known in Ethiopia, the 26.8% prevalence reported in a meta-analysis of observational studies (7) was used. With these assumptions, a sample size of 302 was required.

Sampling: The study included all consenting patients aged 18 years and above with an established diagnosis of hypertension who attended for follow up at ZMH hypertension clinic during the study period. Acutely unwell patients, those with cognitive impairment and patients who were unable to communicate in the language of the interview (Amharic) were excluded from the study. Consecutive hypertensive patients who fulfilled inclusion criteria were included until the target sample size was obtained.

Measures: The data were collected by a trained nurse and a psychiatric resident using a structured questionnaire. Participants were interviewed and information regarding socio-demographic characteristics, behavioral factors and clinical characteristics were collected.

Depression was assessed using the PHQ-9 (20). The PHQ-9 is a nine-item instrument with four response options. It assesses various domains of depressive symptoms and quantifies their severity in the past two weeks. PHQ-9 has been validated in Ethiopia and was found to be a reliable and valid instrument to assess depression among adults in an outpatient health care setting. An optimal cut -off score of ≥9 to define probable depression in medical out-patients in Ethiopia has been proposed (21).

Clinical measures: Height and weight were measured by a nurse. Body mass index (BMI) was calculated and categorized as normal (<25 kg/m^2), overweight (25-29.9kg/m^2) and obese (≥30 kg/m^2) according to the WHO classification (22).

Blood Pressure was extracted from the medical notes for the current clinic attendance. Participants with a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg were classified as having uncontrolled blood pressure. All medications being taken at the time of data collection were recorded from the medical records and categorized according to their number and pharmacological class. Adherence was assessed using a 4-item measure of medication adherence (23) which has been adapted for Ethiopia previously (24). The total score was classified as high (0), medium (1-2) and low (3-4) adherence.

Participants were asked for any previous diagnosis of chronic medical conditions, including diabetes mellitus, heart disease, chronic respiratory diseases/ asthma, HIV/AIDS, cancer and epilepsy.

Lifestyle measures: Physical activity was classified as regular activities carried out at least twice a week during leisure time or as a part of work. Three or more servings of fruit and vegetable per week were classified as a high fruit and vegetable diet (25). Participants using any tobacco product at the time of data collection were classified as smokers. Frequency of khat use (amphetamine-like stimulant) was recorded.

Alcohol use was assessed using the FAST Alcohol Screening Test (26). The FAST has been adapted for use in Ethiopia (27) and an overall total score of 3 and above was classified as hazardous use.

Data analysis: Data were entered and analyzed using SPSS software version 20. Descriptive statistics was computed for socio-demographic, clinical and behavioral characteristics of participants. Chi-squared and Fisher's exact test were used for the purpose of statistical comparisons. Univariate and multivariable regression analysis were carried out for effect estimation. A priori explanatory variables to be included in the multivariable model were: sex, age, marital status, educational status, number of co-morbid chronic illnesses, taking beta blocker medication, alcohol use, BMI, physical activity, adherence with medication, duration of diagnosed hypertension and uncontrolled diastolic blood pressure. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. A value of $p < 0.05$ was considered statistically significant.

Ethics, consent and permissions: Ethical approval was obtained from the Scientific Review Committee, Department of Psychiatry, Addis Ababa University and Addis Ababa City Administration Health Bureau before conducting the study. Written, informed consent was obtained and confidentiality was maintained. Any person identified with depression was referred to the hospital psychiatric out-patient clinic for further assessment treatment. Adherence counseling was given for patients with poor treatment adherence.

RESULTS

Socio-demographic characteristics: A total of 302 participants were included in this study. The majority of participants (57.0%) were female. The age ranged between 18 and 96 years, with a mean of 55.8±12.9 years. More than a third (34.1%) of participants belonged to the age group 50-59 years.

Over a quarter (25.2%) of participants had at least college level education, but 60 (19.9%) had no formal education. More than two thirds (67.5%) were married. Around half of the participants (44.0%) were either employed or merchants and 36 (11.9%) were unemployed (Table 1).

Table 1: Socio-demographic characteristics of patients on treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	Percent
Sex		
Male	130	43.0
Female	172	57.0
Age group (years)		
18-29	7	2.3
30-39	24	7.9
40-49	50	16.6
50-59	103	34.1
60-69	72	23.8
≥70	46	15.2
Educational level		
No Formal education	60	19.9
Grade 1-6	52	17.2
Grade 7-12	114	37.7
College/above	76	25.2
Marital status		
Unmarried	98	32.5
Married	204	67.5
Job status		
Unemployed	36	11.9
Employed/merchant	133	44.0
Housewife	50	16.6
Other	83	27.5

Clinical and behavioral characteristics: The mean systolic and diastolic blood pressures were 142.7 (Standard Deviation (SD) 22.9) mmHg and 83.3 (SD 12.4) mmHg, respectively. Diastolic blood pressure was uncontrolled (≥90 mmHg) among 42.4% (n=128) and systolic blood pressure was uncontrolled (≥140 mmHg) among 56.6% (n=171) of the participants. The mean duration of diagnosed hypertension among the participants was 10.1 (SD 8.7) years. Enalapril 162 (53.6%), nifedipine 153 (50.7%) and atenolol 118 (39.1%) were the commonest antihypertensive medications prescribed to participants.

Nearly a quarter of participants (23.2%; n=68) were taking three or more antihypertensive medications.

The most commonly used classes of antihypertensive medications were calcium channel blockers (56%; n= 169), angiotensin converting enzyme inhibitors (54.6%; n=165), beta-blockers (42.4%; n=128)) and diuretics (26.8%; n=81).

Half (50.0%) of the participants had at least one other chronic medical illness. Twenty-three (7.7%) had two or more co-morbid medical conditions. (Table 2).

Table 2: Clinical characteristics of people receiving treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	percent
Duration of diagnosed hypertension		
<2 years	39	12.9
2-5 years	76	25.2
>5 years	187	61.9
BP (mmHg)		
<140/90	104	34.4
Diastolic Blood Pressure ≥90	128	42.4
Systolic Blood Pressure ≥140	171	56.6
Medications		
Propranolol	8	2.6
Atenolol	118	39.1
Metoprolol	3	1.0
Amlodipine	17	5.6
Nifedipine	153	50.7
Hydrochlorothiazide	81	26.8
Enalapril	162	53.6
Captopril	3	1.0
Medications for diabetes mellitus	81	26.8
Aspirin	11	3.6
Statins	18	6.0
Antihypertensive medication class		
Diuretics	81	26.8
Beta blockers	128	42.4
ACE inhibitors	165	54.6
Calcium channel blockers	169	56.0
Number of antihypertensive medications		
0	31	10.3
1	71	23.5
2	130	43.0
3	66	21.9
4	4	1.3
Chronic medical conditions		
Diabetes mellitus	82	27.2
Heart diseases	21	7.0
Respiratory system diseases	22	7.3
HIV/AIDS	6	2.0
Cancer	1	.3
Renal diseases	35	11.6
Others	9	3.0
Number of chronic diseases		
0	151	50.0
1	128	42.4
2	21	7.0
3	2	.7

Two thirds (66.6%) of the participants had high adherence (MMAS-4 score=0) with their antihypertensive medications. The mean (SD) Body Mass Index of participants was 26.6 (4.9) kg/m^2. More than a third (35.8%) of participants were overweight and 24.5% were obese. Only a quarter (23.5%) of participants had three or more servings of fruits and vegetables a week.

The majority (64.6%) reported doing regular physical activity. Very few (3.0%) of the participants were current smokers and 37 (12.3%) had hazardous use of alcohol (FAST score ≥3). Ten (3.3%) reported current khat use and 187 (61.9%) reported current coffee consumption. (Table 3).

Table 3: Behavioural characteristics of participants, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	Percent
Adherence to medication		
Low (MMAS-4 ≥3)	3	1.0
Medium (MMAS-4 =1 or 2)	98	32.5
High (MMAS-4 =0)	201	66.6
BMI (kg/m2)		
<25	120	39.7
≥25 and <30	108	35.8
≥30	74	24.5
Physical activity		
No	112	37.1
Yes	190	62.9
Fruits/vegetables ≥3servings/week		
No	231	76.5
Yes	71	23.5
Coffee consumption		
No	115	38.1
Yes	187	61.9
Hazardous alcohol use (FAST ≥3)		
No	265	87.7
Yes	37	12.3
Smoking		
No	293	97.0
Yes	9	3.0
Khat chewing		
No	292	96.7
Yes	10	3.3

Prevalence of depression and treatment gap among participants: The mean (SD) PHQ-9 score for all participants was 4.5 (4.9). The prevalence of depression (PHQ-9 score ≥9) among participants was 22.2% (n=67).

Only six participants (8.9%) were receiving treatment for depression, of whom all were receiving pharmacological treatment and none had received a psychosocial intervention. Four were treated for depression in public hospitals, one in a health center, and the other in a private general clinic.

Univariate associations with depression: In the univariate analyses, female gender (OR 2.1, 95% CI 1.2, 3.7), being unmarried (OR 2.0, 95% CI 1.1, 3.5), taking a beta blocker antihypertensive (OR 1.8, 95% CI 1.1, 3.1), physical inactivity (OR 1.9, 95% CI 1.1, 3.3) and having two or more co-morbid medical illnesses (OR 8.2, 95% CI 3.2, 21.2) were associated with depression. (Table 4)

Table 2: Clinical characteristics of people receiving treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	percent
Duration of diagnosed hypertension		
<2 years	39	12.9
2-5 years	76	25.2
>5 years	187	61.9
BP (mmHg)		
<140/90	104	34.4
Diastolic Blood Pressure ≥90	128	42.4
Systolic Blood Pressure ≥140	171	56.6
Medications		
Propranolol	8	2.6
Atenolol	118	39.1
Metoprolol	3	1.0
Amlodipine	17	5.6
Nifedipine	153	50.7
Hydrochlorothiazide	81	26.8
Enalapril	162	53.6
Captopril	3	1.0
Medications for diabetes mellitus	81	26.8
Aspirin	11	3.6
Statins	18	6.0
Antihypertensive medication class		
Diuretics	81	26.8
Beta blockers	128	42.4
ACE inhibitors	165	54.6
Calcium channel blockers	169	56.0
Number of antihypertensive medications		
0	31	10.3
1	71	23.5
2	130	43.0
3	66	21.9
4	4	1.3
Chronic medical conditions		
Diabetes mellitus	82	27.2
Heart diseases	21	7.0
Respiratory system diseases	22	7.3
HIV/AIDS	6	2.0
Cancer	1	.3
Renal diseases	35	11.6
Others	9	3.0
Number of chronic diseases		
0	151	50.0
1	128	42.4
2	21	7.0
3	2	.7

In the multivariable model, female gender (adjusted odds ratio (aOR) 2.6, 95% CI 1.2, 5.8), being unmarried (aOR 2.0, 95% CI 1.0, 3.7) and having two or more co-morbid medical illnesses (aOR 12.6, 95% CI 4.3, 37.0) were associated independently with increased odds of depression among participants.

Taking beta blocker became marginally non-significant in the multivariable analysis but with the strength of association unchanged. Age, level of education, medication adherence, alcohol abuse, BMI, duration of diagnosed hypertension and blood pressure control showed no association with depression (Table 5).

Table 5: Multiple logistic regression analysis of factors associated with depression among people on treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Association with PHQ score ≥ 9	
	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Sex (female)	2.07 (1.16-3.70)	2.63 (1.20-5.80)
Age (years)	1.01 (0.99-1.03)	1.01 (0.98-1.04)
Education level (years of schooling)	0.99 (0.94-1.04)	1.03 (0.97-1.10)
Marital status (unmarried)	1.99 (1.14-3.48)	1.95 (1.02-3.71)
Number of co-morbid chronic diseases		
0	Reference	Reference
1	1.55 (0.85-2.83)	1.68 (0.87-3.22)
≥2	8.23 (3.20-21.16)	12.58 (4.28-36.97)
Beta blockers (present vs. absent)	1.81 (1.05-3.12)	1.88 (1.00-3.56)*
Hazardous alcohol use (FAST ≥3)	1.35 (0.62-2.96)	2.70 (1.00-7.30)±
BMI (kg/m2)		
<25	Reference	Reference
25-29.9	1.34 (0.71-2.55)	1.30 (0.62-2.74)
≥30	1.65 (0.83-3.29)	1.23 (0.55-2.72)
Physical inactivity	1.92 (1.12-3.32)	1.73 (0.91-3.31)
Adherence (low/medium)	1.73 (0.99-3.02)	1.66 (0.89-3.12)
Duration of diagnosed hypertension (years)	1.03 (1.00-1.06)	1.03 (0.99-1.07)
Uncontrolled DBP	1.13 (0.66-1.96)	1.04 (0.56-1.93)

*p = 0.05; ±p = 0.05; PHQ = Patient Health Questionnaire; FAST = FAST Alcohol Screening Test; BMI = Body Mass Index; DBP = Diastolic Blood Pressure; SBP = Systolic Blood Pressure

DISCUSSION

Prevalence of depression: In this hospital-based study from Ethiopia, the prevalence of depression was high at 22.2%. Although we did not have a comparison group in our study, this is substantially higher than the 9.1% 12-month prevalence reported among the general population in the 2012 Ethiopian National Health Survey (16). Increased prevalence of depression in hypertensive patients has been described in previous studies (12, 28). In a hospital-based study from Nigeria, the prevalence of depression among participants with essential hypertension was 26.7% (12). In another study that compared prevalence of depression among hypertensive patients and their age matched healthy controls, hypertension had a significant positive relationship with depression (28). The prevalence of depression in our study is also comparable to the 26.8% (95% CI 21.7, 32.3) overall prevalence of depression among people with hypertension reported in a recent meta-analysis from HICs (4).

Despite affecting nearly one quarter of hypertensive out-patients in our study, 91% were not receiving treatment for co-morbid depression. In a study that reviewed community-based psychiatric epidemiological studies that used standardized diagnostic instruments, the median treatment gap was 56.3% for depression, but data were lacking from LMICs (29). The treatment gap in this study is as high as the treatment gap for mental disorders observed in a rural Ethiopian population with limited access to mental health care (30).This is surprising given the presence of an on-site psychiatric clinic and the skilled levels of clinicians, including general and specialist physicians, present in this referral hospital. This might be due to low patient and provider awareness about depression and its treatment.

Factors associated with depression: In this study, having two or more co-morbid chronic medical illnesses was associated with increased odds of depression, both in univariate and multivariable analyses. This may be due to increased disability and decreased quality of life caused by additive effect of multiple co-morbid illnesses. Treatment of co-morbid chronic medical conditions could be considered as a potential target to reduce depression among hypertensive patients.

Despite the majority of patients taking two or more antihypertensive medications, nearly half of the participants in this study had uncontrolled blood pressure which might have contributed to increased risk of co-morbidities, caused by complications of high blood pressure, and disability. It might also reflect the quality of chronic disease care in the Ethiopian setting, where the health system and patient and provider expectations are orientated to acute, curable infectious conditions rather than long-term care.

Taking beta blocker antihypertensive medication was associated significantly with depression in univariate analysis. The association became marginally non-significant in the multivariable analysis (aOR=1.88, 95% CI= 1.00-3.56). This finding may reflect a true association between beta blockade and depression that was not evident due to small sample size. The association between beta blockers and depression has been supported in previous studies. Luijendijk et al. conducted a cohort study that included 5104 elderly persons to examine the relationship between beta-blockers and incident depression. They found that lipophilic beta blockers were associated with an increased risk of depressive symptoms (9).

Depression and behaviors: Medication adherence was not significantly associated with depression in this study. This finding was in agreement with a previous study that reported no significant association between poor treatment adherence and presence of depression among subjects with hypertension (13). However, the same study found significant association between poor treatment adherence and severity of depression which was not assessed in the present study. Contrary to our finding, a meta-analysis of twelve studies reported that depression is significantly associated with poor treatment adherence in patients with chronic medical illnesses (31). This difference may be due to methodological factors. In this study, we relied on self-report of medication adherence and the percentage of participants reporting poor adherence was low. The sample itself is biased towards people who have continued to engage with treatment, and were relatively well-educated, which may mean that this finding is not generalizable to the rest of the population.

Sedentary lifestyle has been previously reported to be associated with depression among hypertensive patients (13). We found that physical inactivity was associated with depression in univariate but not in multivariable analysis. The heterogeneity of the population attending ZMH might have contributed to this finding. Some of the attendees were from Addis Ababa, well-educated and not in manual jobs, while others were farmers referred for refractory blood pressure from outside of the city.

The association between depression and exercise is only really relevant for the people from Addis Ababa, but we did not have an adequate sample size to explore this hypothesis in our dataset. Other factors known to affect the beneficial effects of exercise on depression such as intensity of exercise (32), social support and resilience (33) need to be explored.

Contrary to previous studies (11,33), hazardous alcohol use was not associated with depression in our study. This might be due to under-reporting of alcohol use by participants.

Limitations: This study was a cross-sectional hospital-based study. Its findings may not be generalizable to the entire population of hypertensive patients. No causal links or directions can be inferred in a cross-sectional survey of this nature. The study used a sample size calculated for measurement of prevalence. A larger sample size would be preferable for measures of association and adjusting for confounders. Additionally, khat and tobacco use were not included in the final logistic analysis because of the small proportion of users in the current sample.

Conclusions: The findings of this study suggest a need to equip general health workers to detect, assess and treat co-morbid depression in people with hypertension in Ethiopia. A prospective study with a larger sample size is needed for future studies to establish more definitive link between depression and hypertension and consequences of co-morbid depression on patient behaviours and hypertension complications. Furthermore, future studies looking at the effect of physical activity and beta-blockers on depression are needed to understand the nature of their relationship.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the participants for giving their time to contribute to the study. We are also grateful for the staff at the hypertension clinic at Zewditu Memorial Hospital for facilitating the data collection. The study was funded by Addis Ababa University as part of a research study conducted to fulfill requirements for a Certificate in Psychiatry for TA.

Competing of interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

Funding: CH is supported by the National Institute of Health Research (NIHR) Global Health research unite on health system strengthen in sub-Saharan Africa, Kings college London (GHRU 16/136/54). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the department of health and social care.
CH Additionally receives support from AMARI as part of the DELTAS Africa initiative (DEL-15-01).

REFERENCES

1. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet 2012;380(9859):2197-223.
2. Whiteford HA, Degenhardt L, Rehm J, Baxter AJ, Ferrari AJ, Erskine HE, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. The Lancet 2013;382(9904):1575-86.
3. Grimsrud A, Stein DJ, Seedat S, Williams D, Myer L. The Association between Hypertension and Depression and Anxiety Disorders: Results from a Nationally-Representative Sample of South African Adults. PLOS ONE 2009;4(5):e5552.
4. Li Z, Li Y, Chen L, Chen P, Hu Y. Prevalence of Depression in Patients With Hypertension: A Systematic Review and Meta-Analysis. Medicine 2015;94(31):e1317.
5. Goldstein BI, Carnethon MR, Matthews KA, McIntyre RS, Miller GE, Raghuveer G, et al. Major Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis and Early Cardiovascular Disease. Circulation 2015;132(10):965.
6. Meng L, Chen D, Yang Y, Zheng Y, Hui R. Depression increases the risk of hypertension incidence: a meta-analysis of prospective cohort studies. Journal of Hypertension 2012;30(5):842-51.
7. Stein DJ, Aguilar-Gaxiola S, Alonso J, Bruffaerts R, de Jonge P, Liu Z, et al. Associations between mental disorders and subsequent onset of hypertension. General Hospital Psychiatry 2014;36(2):142-9.
8. Bant WP. Antihypertensive drugs and depression: a reappraisal. Psychological Medicine. 2009;8(2):275-83.
9. Luijendijk HJ, van den Berg JF, Hofman A, Tiemeier H, Stricker BH. β-blockers and the risk of incident depression in the elderly. Journal of Clinical Psychopharmacology 2011;31(1):45-50.
10. Wiehe M, Fuchs SC, Moreira LB, Moraes RS, Pereira GM, Gus M, et al. Absence of association between depression and hypertension: results of a prospectively designed population-based study. J Hum Hypertens 2006;20(6):434-9.
11. Neupane D, Panthi B, McLachlan CS, Mishra SR, Kohrt BA, Kallestrup P. Prevalence of Undiagnosed Depression among Persons with Hypertension and Associated Risk Factors: A Cross-Sectional Study in Urban Nepal. PLOS ONE 2015;10(2):e0117329.
12. Igwe MN, Uwakwe R, Ahanotu CA, Onyeama GM, Bakare MO, Ndukuba AC. Factors associated with depression and suicide among patients with diabetes mellitus and essential hypertension in a Nigerian teaching hospital. African Health Sciences 2013;13(1):68-77.
13. Zakaria Z, Baharudin A, Razali R. The effect of depressive disorders on compliance among hypertensive patients undergoing pharmacotherapy. ASEAN Journal of Psychiatry 2009;10(1):89-99.
14. Rubio-Guerra AF, Rodriguez-Lopez L, Vargas-Ayala G, Huerta-Ramirez S, Serna DC, Lozano-Nuevo JJ. Depression increases the risk for uncontrolled hypertension. Experimental & Clinical Cardiology 2013;18 (1):10-2.
15. World Health Organization. Mental health action plan 2013-2020. Geneva: WHO; 2013.
16. Hailemariam S, Tessema F, Asefa M, Tadesse H, Tenkolu G. The prevalence of depression and associated factors in Ethiopia: findings from the National Health Survey. International Journal of Mental Health Systems 2012;6(1):23.
17. Abdulahi H, Haile-Mariam D, Kebede D. Burden of disease analysis in rural Ethiopia. Ethiopian Medical Journal 2001;39:271-81.
18. Kibret KT, Mesfin YM. Prevalence of hypertension in Ethiopia: a systematic meta-analysis. Public Health Reviews 2015;36(1):14.
19. Zewditu Memorial Hospital. Health Management Information System annual report. Addis Ababa, Ethiopia: Zewditu Memorial Hospital; 2015.

20. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. Journal of General internal Medicine.2001;16(9):606-13.
21. Gelaye B, Williams MA, Lemma S, Deyessa N, Bahretibeb Y, Shibre T, et al. Validity of the Patient Health Questionnaire-9 for depression screening and diagnosis in East Africa. Psychiatry Research 2013;210:653-61.
22. World Health Organization. Physical status: the use and interpretation of anthropometry: report of a WHO expert committee. Geneva: WHO; 1995.
23. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive Validity of A Medication Adherence Measure in an Outpatient Setting. Journal of Clinical Hypertension 2008;10(5):348-54.
24. Mayston R, Habtamu K, Medhin G, Alem A, Fekadu A, Habtamu A, et al. Developing a measure of mental health service satisfaction for use in low income countries: a mixed methods study. BMC Health Services Research 2017;17:183.
25. Ethiopian Public Health Institute. Ethiopia STEPS survey 2015 Fact Sheet. Addis Ababa, Ethiopia: EPHI; 2015.
26. Hodgson R, Alwyn T, John B, Thom B, Smith A. The FAST Alcohol Screening Test. Alcohol. 2002;37.
27. Fekadu A, Medhin G, Selamu M, Hailemariam M, Alem A, Giorgis TW, et al. Population level mental distress in rural Ethiopia. BMC Psychiatry 2014;14(1):194.
28. Mushtaq M, Najam N. Depression, Anxiety, Stress and Demographic Determinants of Hypertension Disease. Pakistan Journal of Medical Sciences 2014;30(6):1293-8.
29. Kohn R, Saxena S, Levav I, Saraceno B. The treatment gap in mental health care. Bull WHO 2004;82 (11):858-66.
30. Alem A, Kebede D, Fekadu A, Shibre T, Fekadu D, Beyero T, et al. Clinical course and outcome of schizophrenia in a predominantly treatment-naive cohort in rural Ethiopia. Schizophrenia Bulletin 2009;35(3):646-54.
31. DiMatteo M, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. Arch Inter Med 2000;160 (14):2101-7.
32. Callaghan P, Khalil E, Morres I, Carter T. Pragmatic randomised controlled trial of preferred intensity exercise in women living with depression. BMC Public Health 2011;11(1):465.
33. Yoshikawa E, Nishi D, Matsuoka YJ. Association between regular physical exercise and depressive symptoms mediated through social support and resilience in Japanese company workers: a cross-sectional study. BMC Public Health 2016;16(1):553.