

# The Magnitude of Diabetes Mellitus in Adult Hypertensive Patients in Northeast Ethiopia

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**Background:** Hypertension and diabetes mellitus are the most common comorbid non-communicable chronic diseases that threaten human beings worldwide. Hypertension is associated with an increased risk of diabetes mellitus and vis-a-vis. However, there is limited information on the magnitude of diabetes mellitus in hypertensive patients in sub-Saharan countries. Hence, this study assessed the magnitude of diabetes mellitus and its associated factors among adult hypertensive patients attending a hypertension clinic in Northeast Ethiopia.

**Methods:** Institution-based cross-sectional study conducted on 407 participants from April to June 2019. The participants were included in the study using systematic random sampling. Data were collected using the WHO STEPwise method. We run descriptive statistics to determine the magnitude of diabetes mellitus in hypertensive patients and logistic regression to identify factors associated with diabetes, and statistically significant associations were declared at a P-value of less than 0.05.

**Results:** The magnitude of diabetes mellitus among hypertensive patients was 29.1%, of whom 24% were newly diagnosed. Respondents with a family history of diabetes mellitus (AOR: 4.6, CI: 2.2, 9.48), increased waist-to-height ratio (AOR: 21.5, CI: 5.62, 43.67), increased waist circumference (AOR: 3.2, CI: 1.58, 6.53) and primary school educational status (AOR: 3.2, CI: 1.41, 7.25) were more likely to have diabetes. Similarly, respondents with longer hypertension duration (AOR: 4.09, CI: 1.22, 13.64), past daily smoking history (AOR: 10.46, CI: 1.59, 6.8), increased diastolic blood pressure (AOR: 4.15, CI: 1.51, 11.37), and increased waist circumference (AOR: 7.5, CI: 4.47, 14.95) were more likely to be diagnosed newly for diabetes.

**Conclusion:** Our study indicated around one-third of hypertensive patients had diabetes. Family history of diabetes mellitus, primary educational status and increased waist-to-height ratio and waist circumference were significant predictors of diabetes among hypertensive patients. The finding suggests the need for regular diabetic screening among hypertensive patients.

**Keywords:** magnitude, hypertension, diabetes mellitus, Ethiopia

## Background

Hypertension (HTN) and diabetes mellitus (DM) are among the non-communicable chronic diseases (NCD) that threaten human beings throughout the entire world.<sup>1</sup> According to the American College of Cardiology, hypertension refers to a persistent elevation of systolic blood pressure at or above 130 mmHg and/or diastolic blood pressure at or above 80 mmHg.<sup>2</sup> Diabetes mellitus refers to a metabolic disorder of carbohydrate, protein, and fat, which is associated with hyperglycemia and a broad range of clinical presentations. Type two DM is the

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most common type of diabetes, which can be prevented or delayed with lifestyle modifications, otherwise expressed as low glucose control or elevated plasma glucose.<sup>3</sup>

The 2019 international diabetes federation (IDF) report showed that the prevalence of diabetes was 8.3% globally, 4.7% in Africa and 5.2% in Ethiopia. Africa is the continent with a high burden of diabetes, where over 16 million adults 20 and 70 years lived with diabetes in the continent in 2017. This figure is projected to increase by 156%, reaching over 41 million in 2045. On the other hand, Ethiopia is one of the most populous countries in Africa and is among the top five countries with the highest numbers of people with diabetes.<sup>4,5</sup> Over two-third of diabetic cases in low-income countries like Ethiopia are undiagnosed, living without knowing that they have diabetes.<sup>5</sup>

Diabetes is the most common reported comorbid condition to hypertension. On the other hand, increased blood pressure is a risk factor for diabetes.<sup>6–8</sup> Office and masked hypertension are associated with long-term blood glucose abnormalities and an increased risk of developing diabetes.<sup>9</sup> Studies reported from Asia and Africa showed that diabetes prevalence among hypertensive patients ranges from 9.8% to 24%.<sup>10–14</sup> The prevalence of newly diagnosed diabetes among hypertensive patients varies by region. For example, it accounts for 3.4% to 20.8%<sup>15–17</sup> in China and 6.8% to 22.1% in Africa.<sup>13,14,18</sup>

If not well managed, the comorbidity of hypertension and T2DM is complex and associated with a high chance of complications.<sup>19</sup> Diabetes-related microvascular complications are higher in T2DM patients with hypertension than those without hypertension.<sup>20</sup> Thus, WHO recommends that hypertensive patients undergo diabetes screening with varying frequency based on their risk profile.<sup>21</sup>

The driving forces behind the two disease co-morbidity are family history, unhealthy eating, reduced physical activity, smoking, sedentary behavior, non-current smoking, and current alcohol drinking.<sup>11,12,14–17,22,23</sup> Overweight, obesity, elevated blood pressure, higher waists to height ratio above 0.5 have a significant association with DM,<sup>6,8,11,14,16,17,24</sup> whereas controlled blood pressure below 140/90 mmHg is protective against diabetes.<sup>11,13,15,25</sup> A combination of many factors like limited access to healthcare services, inadequate training among healthcare professionals, and lack of awareness of diabetes symptoms contributes to the highest proportion of undiagnosed diabetes in low-income countries.<sup>5</sup>

In 2019, half the 463 million adults living with diabetes were unaware that they had diabetes. This could also be

related to the alarmingly rising diabetes in Africa including Ethiopia, where over two-thirds of them do not know that they have diabetes. On the other hand, an upsurge in hypertension might lead to an upsurge in T1DM and related risk factors. In public hospitals of Ethiopia, diabetes screening among hypertensive patients has not been standard of care for hypertensive patients on follow-up in the hypertension clinics. To our knowledge, in Ethiopia, there has been limited evidence on the magnitude of diabetes among hypertensive patients. Therefore, this study aimed to determine the magnitude of diabetes and its associated risk factors among hypertensive patients attending Dessie comprehensive specialized hospital, Northeast Ethiopia.

## Methods and Materials

### Study Design and Setting

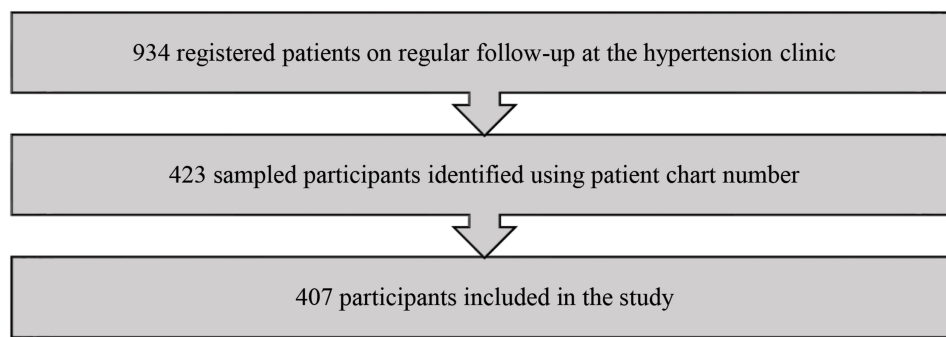
An institution-based cross-sectional study was conducted from April to June 2019 in Dessie comprehensive and specialized hospital (DCSH), North-East Ethiopia. The hospital serves around 7 million people with 240 beds capacity. The outpatient service hypertension clinic is one of the hospital's outpatient department providing follow-up services for 934 registered patients.

### Study Participants

Hypertensive patients aged 18 years and above who were on follow-up in the DCSH hypertension unit during the study period were included in the study. 1) Pregnant hypertensive women, 2) Patients who developed hypertension secondary to diabetes mellitus or who were diagnosed at the same time for both diseases, and 3) Hypertensive patients unable to respond due to severe illness were excluded from the study. Co-morbid patients for hypertension and diabetes were asked which disease was diagnosed first for inclusion and exclusion criteria before including in the study. Systematic random sampling was applied to select 423 study participants out of 934 registered patients on regular follow-up at the DCSH hypertension clinic, and the first patient on the list was identified using a lottery method (Figure 1).

### Data Collection

A structured questionnaire adapted from the WHO STEPwise approach translated to Amharic by Jimma University Gilgel Gibe research project was used.<sup>26</sup> The questionnaire consists of 5 items, and information about



**Figure 1** Flow diagram of participant recruitment.

patient height, weight, waist circumference, blood pressure, fasting blood sugar level, and heart rate. The data were collected by two-degree level nurses and two laboratory technologists trained for one day on the objective and relevance of the study, confidentiality and right of participants and correct methods of anthropometric measurements. To reduce social desirability bias, nurses working in the hypertension clinic were not involved in data collection.

Blood pressure (BP) was measured with an Omron Hem-7121 digital sphygmomanometer with the BP machine cuff placed at the mid-arm. Three intermittent blood pressure readings were recorded with five minutes rest between each measurement and the average is used for this study similar to other international surveys.

Heart rate reading was taken from a digital BP measuring instrument. Height (cm) was measured using the vertical measuring board (stadiometer). For height measurement, each participant was asked to remove his/her shoes, cap/hat, and stand on both feet on a flat surface/board with heels together in an erect position and the value was read at the exact point and recorded to the nearest 0.5 cm.

Weight (kg) was measured using a standardized weight scale. The participant was asked to remove their footwear, take off coat or jacket and heavy clothing while standing in the center of the weighing scale with body weight evenly distributed between both feet.

Waist circumference (WC) in cm was determined by using a non-extensible/non-stretchable tape measure that was placed around the midway between the last rib and the superior iliac crest, and the recording was taken at the point of normal expiration to the nearest 0.5 cm. Venous blood was drawn after 8 or more hours of fasting. Then blood glucose was determined by using the chemistry machine model Dirru CST-240. For those first blood sugar

labels >125mg/dl, the test was repeated on the next day again in a fasting state by using a similar machine and test procedure.

Body-mass index (BMI) was calculated as weight (kg) divided by height (in meters) squared. Waist to height ratio (WHR) was calculated as waist circumference (cm) divided by height (cm). The questionnaire and physical measurement took 15–20 minutes on average to complete.

Besides, we have also collected information about socio-demographic characteristics (age, educational status, income, marital status, employment, sex and residence), behavioral measurements (tobacco use, alcohol consumption, physical activity label, diet, and sedentary behavior), biological variables (heart rate, diastolic blood pressure, systolic blood pressure, BMI, waist circumference, and waist to height ratio), family history of diabetes and hypertension-related variables (duration of hypertension, use of traditional healers, use of prescribed medication, or advice for hypertension). The dependent variables of this study were the magnitude of diabetes mellitus. Similarly, the independent variables were socio-demographic characteristics, behavioral measurements, biological variables, family-related variables, and hypertension-related variables.

To ensure data quality, a pre-test was conducted on 5% of the total sample size in another hospital, Boru hospital, before the actual data collection period. Based on the pre-test skip errors and few locally less understood wordings were modified. Moreover, the average time required for the interview and anthropometric measurements was determined.

## Measurements

Our primary outcome variable was the fasting plasma glucose (FPG) level. The response variables include socio-demographic characteristics (age, educational status,

income, marital status, employment, sex and residence), behavioral outcomes (tobacco use, alcohol consumption, physical activity and diet), biological (heart rate, diastolic BP, systolic BP, BMI, waist circumference and waist to height ratio), family history of diabetes and hypertension-related variables (duration and use of traditional healers, prescribed medication or advice).

A participant can be considered pre-diabetic if his or her fasting plasma glucose (FPG) is 100–125 mg/dL;<sup>27</sup> newly diagnosed for diabetes mellitus, when he or she was not diagnosed for diabetes before this study and if two fasting plasma glucose (FPG) measurement with the same machine is  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L),<sup>4,27</sup> and Overweight when his or her BMI is between 25.0 and 29.9 kg/m<sup>2</sup>, otherwise obese if his or her BMI is greater than or equal to 30.0 kg/m<sup>2</sup> or more.<sup>27</sup> A waist circumference >94 cm for male and >80 cm for a female is considered as increased risk and a waist circumference >102 cm for male and >88 cm for a female is considered as substantially increased risk for cardio-metabolic diseases.<sup>27</sup> Optimal waist to height ratio (reduced risk of cardiometabolic diseases) was defined as less than 0.5 and above normal if it is above 0.5.<sup>24</sup>

A patient is considered a tobacco user if he or she daily uses smoked or smokeless tobacco in the form of cigarettes, cigars, pipes, snuff, and other local tobacco products.<sup>28</sup> A patient is considered as highly physically active when his or her metabolic equivalent (MET) is greater than or equal to 3000; physically active when his or her MET is in the range of equal to 600–2999; physically inactive when his or her MET is less than 600.<sup>29</sup> A patient consumes insufficient fruits and vegetables if he or she consumes less than the recommended five servings of fruits or vegetables daily.<sup>28</sup>

## Data Analysis

Data were coded and entered into the computer using an Epi Data entry client 4.2.1 and exported to SPSS version 23 for analysis. Variables observed in the bivariate analysis at P-value 0.25 and less were candidates for multi-variable logistic regression analysis. Logistic regression backward method was run to explore the level of association. The strength of statistical association was reported as adjusted odds ratios with 95% confidence intervals.

## Ethical Consideration

This study was conducted in accordance with the ethical standards of the institutional and/or national research

committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Before the commencement of data collection, ethical approval was secured from the institutional review board of Jimma University Institute of Health (JUIH). During data collection written informed consent was obtained from each of the study participants after explaining the study purpose, procedure, and duration of the study. Written informed consent taken from study participants was approved by the institutional review board of Jimma University Institute of Health. Participants were also informed that they have a full right to withdraw from the study without affecting their routine care. The blood sample taken for FPG was discarded immediately after blood sugar determination per the hospital sample discarding protocol. Based on the result, each patient was told their diabetic status. Those who were newly diagnosed and pre-diabetic were counseled on lifestyle modification and linked to the hospital chronic diabetic follow-up unit.

## Results

### Socio-Demographic Characteristics

Four hundred seven (407) adult hypertensive patients were included in this study with a response rate of 96.2%. The result includes socio-demographic characteristics, behavioral measurements, the magnitude of diabetes and factors associated with diabetes. Out of 407 participants, around half (50.6%) of them were males. The mean ( $\pm$ SD) age of the participants was 60.4 ( $\pm 12.1$ ) years, with around one-third (33.4%) of them above the age of 65 years, and over half (55.8%) of them had no formal education. Most (71%) of them married, 84.5% of them were urban residents, and 43.5% of them had a monthly income of less than 1000 ETB [Ethiopian Birr] (Table 1).

### Behavioral Measurements

Around 4% of the study participants had a history of smoking. Around 9% of the study participants had a history of alcohol intake for at least a year, among which 45.7% of them consumed alcohol in the last month. Of all the participants, 57.1% were physically inactive, 62.9% used semi-solid oil at room temperature, and almost all of them (99.7%) had less than the recommended amount of fruit/vegetable intake (Table 2).

**Table 1** Socio-Demographic Characteristics of the Study Participants (n = 407)

Variables		Frequency	Percent
Gender	Male	206	50.6
	Female	201	49.4
Age	18–40	32	7.9
	41–65	239	58.7
	Above 65	136	33.4
Educational status	No formal schooling	227	55.8
	Primary school completed	38	9.3
	Secondary school completed	45	11.1
	College and above	97	23.8
Residence	Urban	344	84.5
	Rural	63	15.5
Marital status	Not married	8	2.0
	Married	289	71.0
	Divorced	30	7.4
	Widowed	80	19.7
Occupation	Farmer	71	17.4
	Government employed	70	17.2
	Privately employed	15	3.7
	Merchant	19	4.7
	Housewife	155	38.1
	Retired	57	14.0
	Unemployed	20	4.9
Monthly income	Less than 1000 Birr	177	43.5
	1000–5000 Birr	192	47.2
	Above 5000 Birr	38	9.3

**Abbreviation:** DCSH, Dessie Comprehensive Specialized Hospital.

## Magnitude of Diabetes Mellitus and Associated Factors

The magnitude of diabetes mellitus among DCSH hypertensive patients was 29%, of which 23.5% of them were newly diagnosed. Out of all the participants, the proportion of patients diagnosed newly for diabetes was 6.9%. On the other hand, 21.4% (87) of the study participants were pre-diabetics (Figure 2).

Our multiple logistic regression model showed educational status, past daily smoking history, family history of diabetes; hypertension duration, diastolic blood pressure, and waist circumference were significantly associated with diabetes mellitus among hypertensive patients. The odds of developing diabetes in patients with hypertension patients was higher 4.6 (AOR 4.6, 95% CI 2.2, 9.48) for

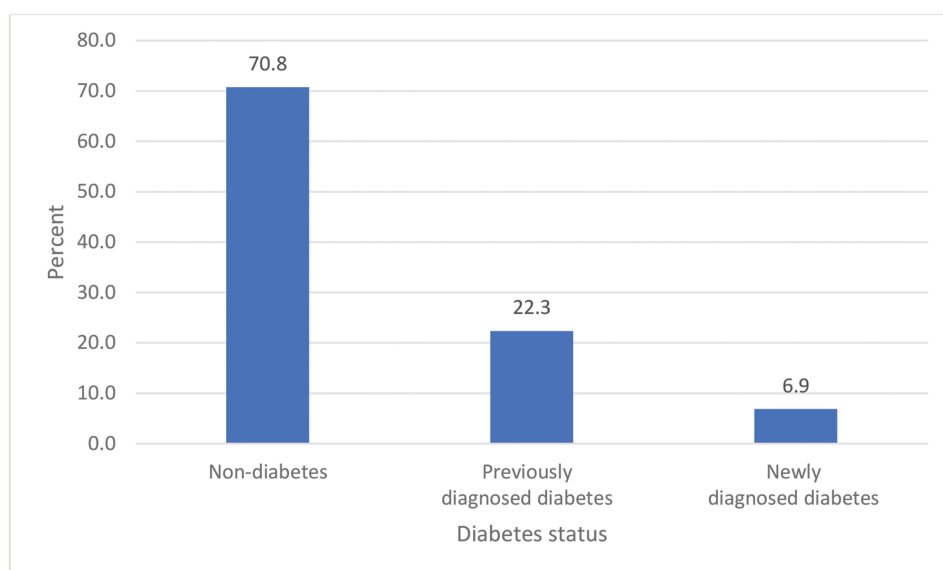
**Table 2** Behavioral Characteristics of the Study Participants (n = 407)

Variables		Frequency	Percent
Current smokers	Yes	4	1.0
	No	403	99.0
Past smokers	Yes	16	3.9
	No	391	96.1
Last year alcohol use	Yes	35	8.5
	No	372	91.5
Last month alcohol use (n = 35)	Yes	16	45.7
	No	19	54.3
Physical activity label	Physically inactive	232	57.0
	Physically moderately active	155	38.1
	Physically highly active	20	4.9
Fruit/vegetable use	Adequate	1	0.2
	Inadequate	406	99.8
Oil type used	Semi-solid at room temperature	256	62.9
	Liquid at room temperature	141	34.6
	Non in particular	10	2.45

**Abbreviation:** DCSH, Dessie Comprehensive Specialized Hospital.

those having a family history of diabetes. On the other hand, participants with a waist-to-hip ratio above 0.5 were around 22 times (AOR: 21.55, 95% CI: 5.62, 43.67) more likely to develop diabetes than those with less than 0.5. Similarly, male hypertensive patients with a waist circumference above 102cm and female participants with a waist circumference above 88cm were 3 times more likely (AOR: 3.2, 95% CI: 1.58, 6.53) to develop diabetes compared to their counterparts (Table 3).

Regarding, factors associated with newly diagnosed diabetes, participants with past daily smoking history were ten times more likely (AOR: 10.46, 95% CI: 5.1, 16.8) to be diagnosed newly for diabetes compared to those with no history of daily smoking. Similarly, the odds of being diagnosed newly for diabetes was 4 times higher (AOR: 4.09, 95% CI: 1.22, 13.64) among participants who lived with hypertension for 5 to 10 years compared to those who lived with hypertension for less than five years. Participants with a diastolic blood pressure of 90 mmHg and above (AOR: 4.15, 95% CI: 1.51, 11.37) were more likely to be diagnosed newly for diabetes compared to those with less than 90 mmHg. Similarly,



**Figure 2** Magnitude of diabetes mellitus among hypertensive patients.

waist circumference above 102cm for males and above 88cm for females (AOR: 13.7, 95% CI: 4.47, 14.95) was also associated with increased risk of newly diagnosed diabetes (Table 3).

## Discussion

The findings of this study showed the magnitude of diabetes mellitus among hypertensive patients was high (29%), which indicates a significant number of hypertensive patients are at the greatest risk of developing unnoticed complications. This finding is comparable with the magnitude reported (32%) by the study conducted in China.<sup>16</sup> However, our finding was greater than the prevalence of diabetes reported by the study conducted among newly diagnosed hypertensive patients in Cameroon 7.7%,<sup>13</sup> Algeria 21.8%,<sup>30</sup> and China 24.3%.<sup>15</sup> The possible reason for the greater prevalence in our study would be due to the fact that the study subjects in Cameroon study participants were newly diagnosed hypertensive patients. In addition, the mean age of the study participants of the study conducted in Cameroon was less than (50.8±11) our study participants' mean age of (60.39±12) which be associated with higher diabetes prevalence.<sup>13</sup> On the other hand, our study showed that the prevalence of previously diagnosed diabetes among hypertensive patients (22.35%) was slightly higher than the finding of the studies reported from China, which ranged from 3.4% to 15.86%.<sup>15–17</sup> This may be due to a lack of engagement in the prevention of diabetes and less

health-seeking behavior among hypertensive patients in Ethiopia that could lead to a higher chance of developing diabetes.<sup>31</sup>

The current study showed the magnitude of newly diagnosed diabetes mellitus among adult hypertensive patients was 6.9%, which is in line with the finding of a study reported from Cameroon (6.8%) and China (8.0%).<sup>13,15</sup> However, it is less than the finding of the studies conducted in the US, Minnesota that reported 19.6%,<sup>32</sup> Kenya 14.0%,<sup>11</sup> and China 9.8% and 20.8%.<sup>16,17</sup> These discrepancies might be related to using different glucose measurement methods like glycated hemoglobin (HbA1C), fasting plasma glucose, or oral glucose tolerance test (OGTT) to determine diabetes status. The other reason could be the significant socioeconomic differences of Ethiopia, China, and the US study participants.

The current study findings showed the magnitude of diabetic mellitus among hypertensive patients varies by educational status, past daily smoking history, family history of diabetes, duration of hypertension, diastolic blood pressure, and increased waist circumference. Those hypertensive patients at odds of having these variables are at the most significant risk of diabetes mellitus. For example, those who had a family history of diabetes mellitus have an increased chance of developing diabetes. This is supported by other studies conducted in Ethiopia, Kenya, Uganda, China, and Japan.<sup>11,14–17,22,23</sup> This could be related to the overlapping genetic predisposition linked to

**Table 3** Univariate and Multivariate Logistic Regression Analyses Showing Factors Associated with Diabetes Mellitus Among Hypertensive Patients

Variables		All Cases of DM AOR (CI)	Newly Diagnosed DM AOR (CI)
Education	No formal schooling	1	1
	Primary school completed	3.2(1.41, 7.25)*	3.4(0.98, 11.8)
	Secondary school completed	0.93(0.39, 2.23)	1.19(0.24, 5.24)
	College and above	1.658(0.88, 3.11)	3.64(1.49, 8.85)
Past daily smokers	No	1	1
	Yes	4.3(1.53, 12.05)	10.46(1.59, 6.8)*
DM family history	No	1	1
	Yes	4.6 (2.2, 9.48)**	3.31(1.25, 9.05)
WHR	0.5 and below	1	Not candidate at binary
	Above 0.5	21.5(5.62, 43.67)***	
HTN duration	Below 5 years	1	1
	5–10 year	2.07(1.13, 3.78)	4.09(1.22, 13.64)*
	Above 10 years	2.5(1.39, 4.52)	2.082(0.56, 7.75)
Diastolic BP	Below 90 mmHg	1	1
	90 mmHg and above		4.15(1.51, 11.37)**
Waist circumference	102 and below for male and 88 and below for female	1	1
	Above 102 for male and above 88 for female	3.2 (1.58, 6.53)**	7.5(4.47, 14.95)**

**Notes:** \*P value<0.05; \*\*P value<0.01; \*\*\*P value<0.001; 1, reference; overall statistics, 0.76.

**Abbreviations:** AOR, adjusted odds ratio; BMI, body mass index; BP, blood pressure; CI, confidence interval; DM, diabetes mellitus; ETB, Ethiopian birr; HTN, hypertension; WHR, waist-to-height ratio.

both hypertension and diabetes. On the other hand, the current study revealed that history of previous daily smoking was significantly associated with an increased risk of new diabetes mellitus diagnosis. This finding is supported by findings of studies conducted in China and Ethiopia.<sup>17,23</sup> Smoking has been reported as an independent risk factor of diabetes mellitus related to insulin resistance, low production of insulin and increased abdominal obesity.<sup>33,34</sup> The probability of developing newly diagnosed diabetes mellitus among hypertension patients was significantly associated with hypertension duration. The possible reason for this would be longer duration hypertension can lead to insulin resistance. Our study showed that diastolic blood pressure of 90 mmHg and above was significantly associated with newly diagnosed diabetes mellitus. This finding is in line with the finding study conducted in the United Kingdom.<sup>6,8</sup> Uncontrolled high blood pressure over a longer period is associated with an increased risk of diabetes-related complications and other cardiovascular diseases.<sup>35</sup>

Increased waist circumference was also significantly associated with the risk of developing diabetes mellitus. This result was in line with the findings of studies

conducted in China.<sup>16,17</sup> Waist circumference is a better indicator of metabolic syndrome risk than body mass index and waist to hip circumference ratio.<sup>12,36</sup> Similarly, those who had a waist-to-height ratio above 0.5 were more likely to develop diabetes compared to those who had a waist-to-height ratio of 0.5 and below. This finding is supported by the finding of the study conducted in China.<sup>24</sup> In obese individuals, adipose tissue may release an increased amount of non-esterified fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors that are involved in the development of insulin resistance that increases the risk of diabetes.<sup>37</sup>

Overall, our study showed that 1 in 3 of hypertensive patients had diabetes. Having family histories of diabetes, a history of daily smoking, increased waist-to-height ratio and waist circumference, longer hypertension duration and increased diastolic blood pressure were significantly associated with an increased chance of developing diabetes mellitus. We, therefore, recommend screening of hypertensive patients for diabetes as part of routine hypertensive care.

The interpretation of the findings of our study can be affected by several limitations. The study finding cannot

be generalized to the general population as this was a hospital-based cross-sectional study. Obesity parameters such as WC and BMI cutoff sizes may be different for low-income countries like Ethiopia. Moreover, the fasting blood glucose test that we used for diagnoses of diabetes is weak compared to glycated hemoglobin in identifying diabetes mellitus.

## Abbreviations

BMI, body mass index; CVD, cardiovascular disease; CI, confidence interval; DBP, diastolic blood pressure; DM, diabetes mellitus; DCSH, Dessie Comprehensive Specialized Hospital; FPG, fasting plasma glucose; HPN, hypertension; IDF, International Diabetes Federation; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NCD, non-communicable disease; PI, principal investigator; STEPS, STEPwise Approach to Surveillance; SBP, systolic blood pressure; WC, waist circumference; WHO, World Health Organization.

## Data Sharing Statement

The data can be accessed from the corresponding author on request.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no conflicts of interest for this work.

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