PREVALENCE OF HYPERTENSION AND ASSOCIATED FACTORS AMONG TYPE 2 DIABETES MELLITUS PATIENTS AT DIABETES FOLLOW UP CLINIC OF JIMMA UNIVERSITY MEDICAL CENTER (JUMC):

A CROSS-SECTIONAL STUDY

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AUGUST, 2017

JIMMA, ETHIOPIA

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ABSTRACT

Objectives: This study aimed to assess the prevalence of hypertension among adult type 2 diabetic patients and to identify risk factors that may affect the development of hypertension in those patients.

Methods: A cross-sectional study was conducted from January 2017 to June 2016 in Jimma University Medical Center (JUMC) diabetes follow-up clinic in Jimma, Ethiopia. A total of 301 diabetic type 2 patients were included in this study .Data was obtained directly from patients through interview and review of their medical files. Simple random sampling was used for the selection of study participants. Data was checked for completeness and entered into SPSS 21 for descriptive and inferential statistical analysis.

Descriptive statistics were used to describe findings. A bivariate analysis was run to sort variables candidate for multiple logistic regression having value less or equals to 0.2. Multiple logistic regression analyses was conducted to identify factors independently associated with the dependent variable. Finally, association was declared with P-value less than 0.05.

Results: In our study, prevalence of hypertension was noted in 170 (56.5%) patients. Hypertension was present in 61 (53%) females and 109 (59%) males. Majority of hypertensive patients, 130(76.5%) were 50 to 69 years old. Family history of hypertension was present in 29(17.1%) of hypertensive patients and only in 6(4.6%) of non-hypertensive patients. Obesity was present 34(20%) of hypertensives whereas only 1(0.8%) of them was normotensive. Overweight on the other hand, was present in 50.6% of hypertensives and in 30.5% of non-hypertensives.

Conclusion: The prevalence of hypertension in patients with DM in this study very high. Abnormal BMI, reflected by both obesity and overweight was the most common modifiable risk factor identified along with age and family history of hypertension. Therefore, addressing obesity and overweight through life style modification, dietary advice and medical therapies should be undertaken. Enforcing measures for detecting and managing hypertension in patients with diabetes is the most effective things that can be done to prevent adverse events. Hence, intervention measures should be undertaken and earlier more aggressive blood pressure control are likely to offer the greatest promise for reducing the incidence of complications and its associated mortality.

Key words: Type 2 diabetes mellitus, Obesity, Overweight, family history of hypertension

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ACRONYMS AND ABBREVIATIONS

ACCORD	Action to Control Cardiovascular Risk in Diabetes
ALLHAT	Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack
ASCVD	Atherosclerotic Cardiovascular Disease
BPLTTC	Blood Pressure Lowering Treatment Trialists' Collaboration
BMI	Body Mass Index
CRF	Chronic Renal Failure
CVA	Cerebrovascular Accident
CVD	Cerebrovascular Disease
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
DPP	Diabetes Prevention Program
DVT	Deep Venous Thrombosis
ESRD	End-Stage Renal Disease
FBS	Fasting Blood Sugar
GFR	Glomerular Filtration Rate
HBP	High Blood Pressure
HDL-C	High Density Lipoprotein Cholesterol
HLA	Human Leukocyte Antigen
HOT	Hypertension Optimal Treatment
HR	Heart Rate
IDF	International Diabetic Federation
IGT	Impaired Glucose Tolerance
JUSH	Jimma University Specialized Hospital
LDL-C	Low Density Lipoprotein Cholesterol
PAD	Peripheral Arterial Disease
PPBG/PPG	Post Prandial Blood Glucose
RFT	Renal Function
SBP	Systolic Blood Pressure

TC	Total Cholesterol
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
UKPDS	United Kingdom Prospective Diabetes Study
WC	Waist Circumference
WHR	Waist to Hip Ratio
WHO	World Health Organization

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CHAPTER ONE: INTRODUCTION

1.1. Background

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. (1).

DM is classified on the basis of the pathogenic process that leads to hyperglycemia, as opposed to earlier criteria such as age of onset or type of therapy. There are two broad categories of DM, designated type 1 and type 2. However, there is increasing recognition of other forms of diabetes in which the pathogenesis is better understood. (1).

Though diabetes is a worldwide problem, there is considerable geographic variation in the incidence of both type 1 and type 2 DM. Scandinavia has the highest incidence of type 1DM; the lowest incidence is in the Pacific Rim where it is 20- to 30-fold lower. Northern Europe and the United States have an intermediate rate. Much of the increased risk of type 1 DM is believed to reflect the frequency of high-risk human leukocyte antigen (HLA) alleles among ethnic groups in different geographic locations. The prevalence of type 2 DM and its harbinger, Impaired Glucose Tolerance (IGT), is highest in certain Pacific islands and the Middle East and intermediate in countries such as India and the United States. This variability is likely due to genetic, behavioral, and environmental factors. DM prevalence also varies among different ethnic populations within a given country, with indigenous populations usually having a greater incidence of diabetes than the general population of the country. For example, the CDC estimated that the age-adjusted prevalence of DM in the United States (age >20 years; 2010–2012) was 8% in non-Hispanic whites, 9% in Asian Americans, 13% in Hispanics, 13% in non-Hispanic blacks, and 16% in American-Indian and Alaskan native populations. The onset of type 2 DM occurs, on average, at an earlier age in ethnic groups other than non-Hispanic whites. In Asia, the prevalence of diabetes is increasing rapidly, and the diabetes phenotype appears to be somewhat different from that in the United States and Europe, with an onset at a lower body mass index (BMI) and younger age, greater visceral adiposity, and reduced insulin secretory capacity (1).

Hypertension, which is defined as Systolic Blood Pressure (SBP) >140mmHg and/or Diastolic Blood Pressure (DBP) frequently coexist with diabetes mellitus (DM) (2). The prevalence rate of hypertension among type 2 diabetic patients is higher than that of age- and sex-matched patients without diabetes, ranging between 32% and 82% (3).

Though hypertension is a common problem in patients with both type 1 and type 2 diabetes, the time course in relation to the duration of diabetes is different. Whereas only 5% of type 1 DM patients develop hypertension in the first 10 years after diagnosis, many patients present with hypertension in type 2 DM at the time of their first diagnosis. In one of the studies, about 39% of type 2 DM patients first presented with hypertension. (4)

In addition to the development of diabetic nephropathy, at least three other factors have been proposed to contribute to hypertension in type 2 diabetes: hyperinsulinemia, extracellular fluid volume expansion, and increased arterial stiffness (5).

Hyperinsulinemia, due to insulin resistance in type 2 diabetes or to insulin administration, may increase systemic blood pressure since insulin can increase sympathetic activity and promote renal sodium retention (6). Sodium retention and volume expansion may be induced both by insulin and the hyperglycemia-induced increase in the filtered glucose load (7, 8). Patients with diabetes have also increased vascular stiffness, which is thought to be a consequence of increased protein glycation and, at a later stage, atheromatous disease. (9).

In Ethiopia, national data on prevalence and incidence of diabetes are lacking. However, patient attendance rates and medical admissions in major hospitals are rising (10). A population based study in northwestern Ethiopia (Gondar) showed an overall prevalence of diabetes and impaired glucose tolerance of 0.5%; a surprising low prevalence could be because most of the subjects were young (86%). Furthermore the prevalence of diabetes among older subjects (age >40 years) was higher (2.4%) (11). yet, there are no adequate studies on the prevalence of hypertension among type 2 DM and its associated factors.

Therefore, given a significant morbidity overlap between these two conditions, the aim of this study is to assess the prevalence of hypertension & associated factors among type 2 DM patients at diabetic follow up clinic of Jimma University Specialized Hospital (JUSH).

1.2. Statement of the Problem

The prevalence rate of hypertension among type 2 diabetic patients is higher than that of age- and sex-matched patients without diabetes, ranging between 32% and 82% (3).

Hypertension increases the risk of long-term vascular complications of type 2 diabetes mellitus (T2DM), including stroke, chronic kidney disease, heart disease, peripheral vascular disease, and death (14) and can delay complications (14). Blood pressure reduction has been associated with a decreased risk of T2DM-related complications, including death, stroke, and the need for retinal photocoagulation (15).

Within all countries, the poorest people are affected the most (15).In southwest Ethiopia, age >45 years, female sex, type 2 DM and obesity were found to be independently associated with hypertension while address, educational status, duration of diabetes, type of treatment for diabetes, physical activity, smoking, alcohol use and chat chewing were not significantly associated with hypertension (16).

1. Even though many studies conducted elsewhere in developed and developing countries has shown that the coexistence of type 2 DM and hypertension is very high and are associated with elevated risk of mortality and morbidities, paucity of domestic studies on DM, particularly on type 2 and hypertension comorbidities is there.
2. Many epidemiologic reports describe separate prevalence rates for hypertension, obesity, and diabetes among the general population (15) or present prevalence rates of hypertension or obesity in patients with diabetes but often without separating data for type 1 versus type 2 diabetes (17). As the majority of complications/ comorbidities can either be prevented or delayed, it would be very important to study prevalence of hypertension and its associated factors specifically in type 2 DM patients
3. Knowing the proportion of the T2DM population at additional risk of complications from hypertension is an important public health measure to determine public requirements to reduce these risk factors or to care for patients after cardiovascular events.

CHAPTER TWO

2.1. Literature Review

2.1.1. Prevalence of Hypertension

Many studies has shown that the Prevalence of hypertension in type 2 DM is very high and the resulting comorbidities to be higher than either conditions alone.

A cross-sectional study that was carried out on 300 type 2 diabetic patients who were admitted to medical ward of Moosabne Jafar hospital in Quchan, Iran, for follow-up from April 2011 to August 2012. Two hundred and ten out of 300 subjects had hypertension, thus giving a prevalence rate of 70%. One hundred males (47.6%) were hypertensive compared with 110 (52.4%) females, but this difference was not significant ($\chi 2=0.1$, df =1, $P>0.05$). The mean age of them was 62.9 years. One hundred and fifty subjects (50%) had reported at least one problem in past history like heart disease, CVA, DVT, CRF, retinopathy, diabetic foot and paresthesia. The most common problem in past history was heart disease (37%), supporting the fact that presence of hypertension and increased CVD morbidities (18).

Another study which was conducted in Benin also revealed the prevalence of HBP in type 2 diabetics to be 70%. The study didn't identify gender as risk factor for HBP in type 2 diabetes ($p = 0.059$), though the frequency of High Blood Pressure (HBP) in female was higher (73.1%) than in male (64%) while age was identified to be a risk factor associated to HBP in type 2 diabetes ($p = 0.000$) such that occurrence of HBP increased with age (19).

Other authors reported similar conclusion. In this way, Dibia reported that 67% of diabetics with hypertension had age range between 51 and 70 years (20); Aassri *et al.* found that HBP and diabetes association was significant between 66 and 69 years (21); Ralison *et al.* found a pic of HBP in type 2 diabetics above 50 years and particularly between 60 and 69 years (22); according to Khochtali *et al*. in Tunisia, 77% of diabetics above 65 years had hypertension (23). This fact would be due to modifications of vascular system observed with age. In effect, an alteration and a relative reduction of elastic fibers occur and are replaced by collagen tissue in arteries wall. This evolution induces more rigidity of arteries contributing to elevate blood pressure

2.1.2. Risk Factors for Hypertension in Type 2 DM

The duration of diabetes was a factor associated with hypertension in type 2 diabetes. Likewise, abdominal obesity was significantly associated with the occurrence of hypertension in type 2 diabetic patients ($p = 0.036$). Indeed in this study, the frequency of hypertension in type 2 diabetics with abdominal obesity was 71.9% against 57.1% among those who did not have abdominal obesity. Contrary, the study showed no correlation between dyslipidemia and hypertension in type 2 diabetics (19).

Conflicting results have been reported in Japan, where a significant correlation is found between the HDL hypocholesterolemia and the occurrence of hypertension in diabetic hypertensive by Miyagi *et al* (24). This same observation was made in Morocco by Diyane *et al*. (25).

History of stroke was found to be correlated with hypertension in type 2 diabetics because all diabetic patients with stroke had hypertension ($p = 0.013$). This observation corroborates those of Diyane *et al.* (25) and Tanguy *et al*. (26). In addition, a meta-analysis (27) published in 2011 showed that in diabetic type 2, reducing the risk of stroke was proportional to the reduction in SBP .they also identified the diabetic foot as a factor associated with hypertension in type 2 diabetics. Therefore, special monitoring of the feet will be indicated in diabetic patients with hypertension.

2.1.3. Impact of Hypertension on DM

Dozens of literatures highlighted well the impact of hypertension on diabetic microvascular and macrovascular complications.

The pathogenesis of macrovascular disease is multifactorial, with significant contributions from dyslipidemia, hypertension, hyperglycemia, insulin resistance, dysfibrinolysis, obesity and lifestyle factors, such as sedentary habits and smoking (28).The basic atherosclerosis processes leading to coronary, cerebrovascular or peripheral vascular disease is similar in all patients, but those with hypertension and diabetes appear to have accelerated development of advanced lesions (29).

Studies have shown that the benefit of early glycemic control to reduce the future risk of microvascular and cardiovascular complications is sustained beyond the period of good glycemic control ("metabolic memory") (30). The pathophysiologic link between hyperglycemia and macrovascular disease includes possibly direct effects of glucose, activation of protein kinase C,

endothelial dysfunction from oxidative stress, activation of athero-inflammatory cytokines and epigenetic changes, among others (31). The superimposition of hypertension on diabetes further aggravates microvascular and macrovascular complications through additive mechanisms that include arteriolar and capillary damage in retinal, renal, coronary, cerebral and peripheral vascular territories. These added lesions accelerate the progression to target-organ renal failure (32).

One of the most common microvascular complication is diabetic retinopathy.it is responsible for 12,000 to 24,000 new cases of vision loss each year (33). Coexistence of hypertensive retinopathy and diabetic retinopathy further magnifies the risk of vision loss (34). In the Wisconsin Epidemiologic study of Diabetic Retinopathy, within 5 years of diagnosis of diabetes 14% of patients with type 1 and 33% with type 2 diabetes had developed diabetic retinopathy (35).

Diabetic nephropathy occurs in as many as 40% of patients with diabetes, and hypertension magnifies the risk of this microvascular complication. Diabetic nephropathy differs from other causes of renal disease at the histopathological level. Initially the glomerular basement membrane thickens, followed by an increase in the amount of mesangial matrix that in some patients can progress to increasingly more severe diffuse or nodular glomerulosclerosis (36). The basement membrane may be gradually lost in diabetes mellitus, leading to loss of its sieve like permselectivity and progressive proteinuria. This change in the basement membrane permselectivity appears to be caused by non-enzymatic glycosylation of long-lived proteins (37). In addition, advanced glycosylation end products bind to mesangial cells and cause increased formation of fibronectin and basement membrane collagen (38). Overt diabetic nephropathy is characterized by urine albumin excretion greater than 300mg/24hrs, and is associated with a 1ml/min/1.73m^2 decline in glomerular filtration rate (GFR) per month. Microalbuminuria is an early indicator of diabetic nephropathy, and is also associated with an increased risk of CVD (39)

Diabetic peripheral neuropathy affects approximately 70% of diabetic patients and is the leading cause of foot amputation (40).The pathogenesis of peripheral neuropathy is poorly understood, but felt to be related to impaired blood flow, demylelinization of nerves, and inflammation. However, it is also known that peripheral neuropathy develops in the background of long-standing hyperglycemia and its associated metabolic derangements: increased polyol flux, accumulation of advanced glycosylation end products, lipid derangements, and oxidative stress. Hyperglycemic

exposure appears to be the most important risk covariate, and rigorous glycemic control is recommend to stabilize and sometimes improve symptoms (41).

Autonomic neuropathy typically manifests as orthostatic hypotension, decline in vasomotor tone, anhidrosis, and pupillary abnormalities. However, patients may also have impairment in cardiovascular, gastrointestinal, and urogenital function. Cardiovascular autonomic neuropathy can manifest as orthostatic hypotension, lack of normal heart rate variation with breathing, resting tachycardia, and even sudden death. The presence of autonomic neuropathy identifies patients at high risk of CVD and can be used for risk stratification independently of other CVD risk markers. Risk factors associated with development of cardiovascular autonomic neuropathy include hyperglycemia, diabetic peripheral neuropathy, nephropathy and retinopathy, hypertension, obesity, smoking, and dyslipidemia (41).

The impact of hypertension on type 2 DM was also studied with respect to the occurrence of specific comorbidities.

In a prospective study conducted in Finland, the risk of coronary artery disease-related death was comparable in patients with diabetes and no history of prior myocardial infarction to those without diabetes and prior myocardial infarction (42).

In the Hypertension in Diabetes Study, patients with hypertension and concomitant diabetes compared to nonhypertensive diabetics were found to have higher rates of cardiovascular death, myocardial infarction, angina pectoris, amputation, and stroke independent of other risk factors (3).Despite a decline in the rate of mortality from heart disease in the United States, there has been a less marked decline seen in the diabetic persons, especially in women Furthermore, the contribution of peripheral vascular disease to the risk of lower extremity amputation in patients with diabetic neuropathy is well known (41).

The metabolic syndrome, often present for years before diabetes is diagnosed, clearly predispose patients with type 2 diabetes to increased risk of CVD. Components of the metabolic syndrome include insulin resistance, upper body obesity, hyperinsulinemia, hypertriglyceridemia, increased small dense LDL decreased HDL-cholesterol levels, hypertension, hyperuricemia, and a procoagulant state, among others (42). Endothelial dysfunction also tracks the severity of insulin resistance. Indeed, as demonstrated in the EPIC-Norfolk study, cardiometabolic risk factors can

be associated with increased CVD events and mortality even during the prediabetes stage (43).Although insulin resistance is not a characteristic feature of type 1 diabetes, a phenotype of insulin resistance can be superimposed on pre-existing type 1 diabetes, particularly in persons with a family history of type 2 diabetes and those who develop abdominal obesity (44)

Gang Hu et al in their study on the impact of history of hypertension and type 2 diabetes at baseline on the incidence of stroke and stroke mortality found that hypertension and type 2 diabetes increase stroke risk independently, and their combination increases the risk drastically. A significant proportion of the risk of stroke assumed to be related to hypertension may be attributable to concomitant diabetes. During a mean follow-up of 19.1 years, 2978 incident stroke events were recorded, of which 924 were fatal. Age-, sex-, and study year-adjusted HRs of stroke incidence were 1.35 (95% CI, 1.21 to 1.51), 1.98 (95% CI, 1.79 to 2.19), 2.54 (95% CI, 1.61 to 4.01), 3.51 (95% CI, 2.40 to 5.14), and 4.50 (95% CI, 3.60 to 5.61), respectively, among subjects with hypertension I (blood pressure 140 to 159/90 to 94 mm Hg) only, with hypertension II (blood pressure 160/95 mm Hg, or using antihypertensive drugs) only, with diabetes only, with both hypertension I and diabetes, and with both hypertension II and diabetes compared with the subjects without either of the diseases. The corresponding HRs of stroke mortality were 1.47, 2.62, 3.06, 5.59, and 9.27, respectively. Additional adjustments for body mass index, cholesterol, education, smoking, alcohol consumption, and physical activity did not appreciably change these risk estimates. Blood pressure affected the risk of stroke similarly in diabetic and nondiabetic subjects (45).

2.2. Significance of the Study

There is a considerable evidence for an increased prevalence of hypertension in diabetic persons.

Whereas there are many studies conducted elsewhere regarding the burden of hypertension among type 2, in our country such studies are done in a few centers only. Majority of studies conducted in Ethiopia describe the prevalence of hypertension in general diabetic society than specifically in type 2. The same is true regarding specific risk factors that may be attributed for the occurrence of hypertension in this group of patients.

This study will try to elucidate the burden and associated risk factors, look for any peculiar pattern in this group of patients in this setting, if any. Hence specific recommendations may follow that improve the overall care provided at follow-up clinic in order to prevent/delay morbidities &

mortalities ascribed to the complications of Hypertension. Therefore, it is important to determine whether the prevalence of hypertension is significant as to the global estimates and the major traditional risk factors that are associated with the development of hypertension exist in this setup like in the other developed nations.

The findings of the study are going to be useful for all practicing personnel including medical interns, residents and senior physicians working at the diabetic follow-up clinic in order to make improvement of the comprehensive care, for early diagnosis and intensive management of hypertension. The study is also will be useful as a reference tool for further studies regarding cardiovascular complications in type 2 DM patients. Furthermore, the study could be an entry for large scale studies in the country regarding the burden of hypertension in diabetic population and for community based preventive programs.

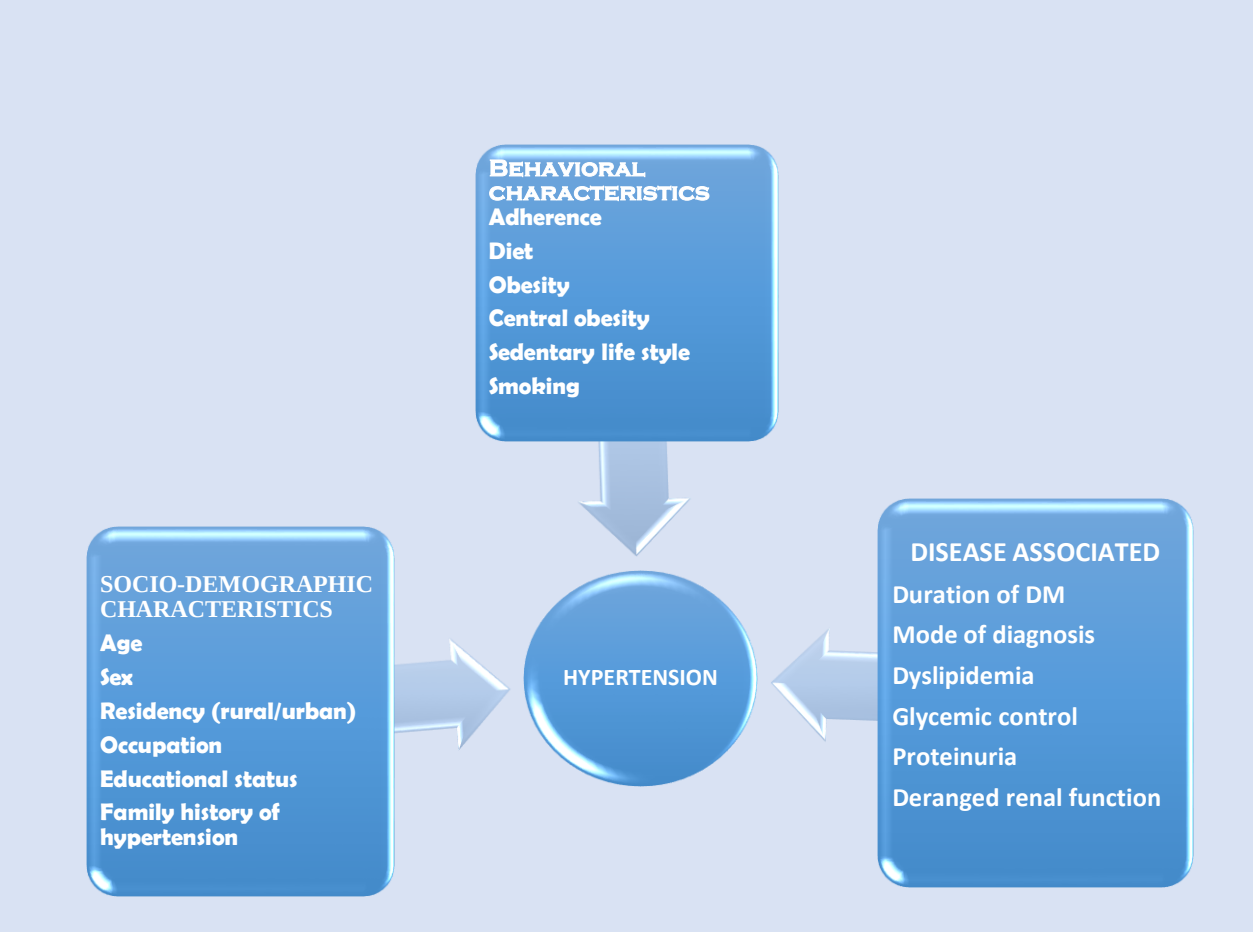

Figure 1 Conceptual framework for factors associated with Hypertension among DM patients

CHAPTER THREE: OBJECTIVE

3.1. General Objective:

- To determine the prevalence of hypertension and identify associated factors among type 2 DM patients on follow-up at Jimma Universality Medical Center from December 1, 2016 to march 30, 2017.

3.2. Specific objectives:

- To determine the prevalence of hypertension among DM patients
- To identify factors associated with hypertension among DM patients

CHAPTER FOUR: METHODOS AND MATERIALS

4.1. Study Area

The study was conducted at Diabetic follow-up clinic of Jimma University Medical Centre (JUMC). JUMC is located in Jimma town, which is 356km southwest of the Addis Ababa, capital city of Ethiopia.

JUSH is one of the teaching hospitals in the country. The hospital gives health service at inpatient and outpatient level as a referral Hospital for 15 million population in the South West of the country. It has one diabetic follow-up clinic. The number of diabetic patients enrolled in the clinic are about 2456. The clinic provides comprehensive care with regular follow-up for drug dose adjustments, evaluation for side effects of the drugs, detection of comorbidities and detection of acute and chronic complications by trained nurses, medical interns, residents, and specialists on monthly or two basis, even more frequently for patients with complications and poor glycemic control two days a week.

4.2. Study period

This study was conducted from January 1, 2017- June 30, 2017.

4.3. Study design

An institution based cross sectional quantitative, study was conducted.

4.4. Population

4.4.1 Source population

All patients with clinical diagnosis of type 2 Diabetes Mellitus who are on follow-up at JUMC including newly enrolled patients

4.4.2. Study population

Adult type 2 DM enrolled in diabetic care with age >30 years who are having regular follow-up (both newly enrolled and existing type 2 DM patients)

4.5. Inclusion and exclusion criteria

4.5.1. Inclusion criteria

- Patients with clinical diagnosis of type 2 DM and age >30 years without any condition listed in exclusion criteria.
- Those diabetic patients < 30 years with type 2 clinical phenotype and family history of diabetes.

4.5.2. Exclusion criteria

- Those patients with indeterminate clinical diabetes phenotype
- Those who are taking long-term steroid therapy
- Pregnant women
- OCP users
- HIV patients who are receiving HAART (1st or 2nd line)
- Those with known other endocrine disorders (e.g. thyrotoxicosis, pheochromocytoma, GH overproduction)

The above conditions are excluded for the following reasons (1)

- Patients with indeterminate clinical features of type 1 or 2 could potentially affect the association between hypertension and diabetes as one cannot clearly eliminate their effect in the study.
- Long term steroid treatment is associated with occurrence of hypertension and impaired glucose tolerance or sometimes even full blown diabetes mellitus.
- Pregnant women, as part of physiologic adaptation, they develop relative insulin resistance and sometimes gestational diabetes mellitus which later can progress to type 2 DM. On the other hand, few pregnant women may develop gestational diabetes or develop preeclampsia, a phenomena of pregnancy induced hypertension with evidence of end organ damage after 20 weeks of pregnancy.
- Oral Contraceptive Pills (OCPs) frequently cause a mild elevation in blood pressure within the normal range; however, overt hypertension can occur.
- Abnormal fasting lipid profiles and impaired glucose tolerance are common among patients on ART
- Most endocrine disorders are associated either with hypertension or diabetes mellitus.

4.6. Sample size and sampling procedure

4.6.1 Sample size

The sample was calculated using a formula for estimation of single population proportion taking prevalence of hypertension among type 2 DM patients to be p=50%(because there is no similar study done in relatively similar facilities in Ethiopia) , margin of error 5%, and using 95% confidence level.

$$\mathbf{n = (Z\alpha/2)^2\ p\ (1\text{-}p) / d^2}$$

P = 50%, assuming 50% prevalence as there is no similar reference study in the country

Zα/2 = standard normal variable at 95% confidence level (1.96).

d= precision (tolerable margin of error)

$$\mathbf{n = (Z\alpha/2)^2\ p\ (1\text{-}p)/d^2 = (1.96)^2\ x\ 0.5(1\text{-}0.5)/(.05)^2 = 384}\ \text{patients}$$

As the population size is <10,000 (1756), corrected sample size will be

$$\mathbf{Nf=n/\ ((1+n/N)=384/\ (1+384/1756)\ \sim 314.}$$

Considering the 10% non-respondent, the total sample size would be ;

$$\mathbf{314+31 = \underline{345}}$$

4.6.2. Procedure

The study involved primarily review of the medical records & interview of patients enrolled in the chronic care at the JUMC Diabetic clinic

4.7. Variables

4.7.1. Dependent variables

- Prevalence of Hypertension

4.7.2. Independent variables

Patient related factors

Socio-demographic characteristics

- Age
- Sex
- Residency (rural/urban)
- Occupation
- Educational status
- Family history of hypertension
- Adherence
- Obesity
- Central obesity
- Smoking

Disease associated

- Type 2 DM
- Mode of diagnosis (for routine checkup or after illness)
- Glycemic level
- Duration of diabetes
- Dyslipidemia

- FBS
- eGFR
- Proteinuria

4.8. Data collection

Data was collected by face to face interview and record review using semi-structured questionnaire and checklist respectively. Data collectors were Residents and Medical intern whereas supervisor is BSc clinical nurse. Data regarding treatment, level of glycaemic control (pattern of FBS/RBS), other laboratory results including renal function tests, urinalysis, fasting lipid profile were all collected from medical records and data regarding patient's adherence to drugs, dietary history, smoking, family history of DM/hypertension was collected from the patients themselves.

4.9. Data compilation & analysis

Collected data was rechecked for completeness by principal investigator. Finally, the data was entered in to SPSS 21 version for descriptive analysis and inferential statistics. Descriptive statistics: percentages, means, medians, standard deviations and ranges were used to describe findings. A bivariate analysis was done to sort variables candidate for multiple logistic regression having value less or equals to 0.2. Model adequacy was checked by running Hosmen's goodness of fit test, which showed that the model is acceptably adequate (total percent was about73%). Then, multivariate logistic regression analyses was conducted to generate factors strongly associated with the dependent variable after checking for multicollinearity by stepwise independent variable evaluation using logistic regression analysis and looking for their **tolerance and Variance Inflation Factor(VIF)**. All the independent variables were checked and all the 9 variables were having no collinearity having tolerance of >0.1 and VIF < 3.0, which both show absence of collinearity. Finally, multiple logistic regression was run and association was declared for those variables with p-value less than 0.05.

4.10. Data Quality Assurance

During preparatory stage, the questionnaires was carefully designed by WHO pillars of health and pre-coded and pretested to minimize errors. Instructional manual on the procedures of data collection, handling, operational definitions, roles of data collectors and ethical issues was prepared. The data collectors and assistant were trained with demonstrations on the questionnaires/checklists by principal investigator for 5 days on the instructional manual of data collection ahead of the data collection schedule. The necessary tools for the data collections were

given to the data collectors before the time of data collection and data collection was being supervised daily. The data assistant was arranging the medical records of the patients, cross check the collected data for completeness and arranged calls for the patients with incomplete medical records so that data completeness is ensured. The collected data was checked for completeness by data assistant during collection and finally by principal investigator before entry in to the computer. During data entry and clearance, error was minimized by using trained persons, mainly trained resident. During data analysis and report writing, appropriate statistical technique for appropriate data was used.

4.11. Ethical Consideration

Ethical clearance was obtained first from Institutional Review Board (IRB) of Jimma University Institute of Health. Then, letter of cooperation from department of Internal Medicine was submitted to hospital director and then to diabetes follow-up clinic prior to data collection. Purpose & significance of the study was explained by the data collector during the interview verbally. Patient's confidentiality, equity of services and interests of patients was ensured during the study period by informing the data collectors on ethical issues. This study didn't involve any potentially harmful intervention to the patient. The interview scripts were coded and personal identifying details were not collected.

4.12. Operational Definition & Measurements

4.12.1. Operational definitions

Comorbidities; Co-existence of other disease with DM

BMI: Weight of a person divided to the square of ones height in meters.

Overweight: a relative state of adiposity where the BMI of an individual falls between 25-30 kg/m^2

PPBG: a blood glucose level determined 2hours after meal was taken

Obesity: A state of adiposity where a person's Body Mass Index (BMI) exceeds $30kg/m^2$.

Central obesity: A waist circumference >102cm in men and >88cm in women when measured with a flexible tape placed on a horizontal plane at the level of the iliac crest as seen from the anterior viewpredominant abdominal adiposity that waist circumference exceeds the 99^{th} centile of the normal population

Adherence to diabetic treatment: A patient with type 2 DM who takes the antidiabetic and/or other co-administered prescribed drugs as per recommended by his/her physician with the right drug, dose and time without missing any of the drugs.

Smoker: A person who smoked at least 100 cigarettes.

Family history of hypertension: Presence of hypertension in one or more of his/her first degree relative.

Hypertension: an SBP ≥140mmHg and/or DBP ≥90mmHg and or patient taking specific antihypertensive drugs

Poor glycaemic control: the level of blood glucose that exceeds the target, FBS >130mg/dl and /or RBS >180mg/dl in diabetic patient.

Microvascular complications: The occurrence of renal, eye or nervous system damage in DM patients evidenced by abnormal RFTs, proteinuria, funduscopic examination or subjective/objective evidences of peripheral neuropathy.

Macrovascular complications: The occurrence of CVA, CVA, PAD in diabetic patient

Dyslipidemia: A biochemical disturbance of serum lipids where HDL decreases and /or elevated TC and/or LDL

Deranged renal function tests: Elevated urea and /or creatinine above the reference upper normal limit for a given laboratory

Proteinuria: Detection of protein in a urine sample with qualitative dipstick assays.

Active urinary sediments: Presence of cellular casts (RBC, epithelial casts or other forms of cast (granular, waxy, broad casts) that suggest renal parenchymal injury.

Fasting Blood Sugar: Capillary blood sugar level determined after 8 hours of fasting

Fasting lipid profiles: Serum lipid measurements in order to know the different serum lipid component level, determined after 8-12hour fasting.

4.12.2. Anthropometric Parameters

Anthropometric measurements of waist circumferences were taken. Waist circumference (WC) was measured midway between the inferior angle of the ribs and the suprailiac crest (16). The measurement were measured to the nearest 1 cm using a non-stretchable fiber-glass measuring tape (Butterfly, China). During measurement, participants stood in an upright position, with arms relaxed at the side, feet evenly spread apart, and body weight evenly distributed in accordance with the WHO expert consultation report on waist

circumference (23). Abdominal obesity was determined as a waist circumference >102 cm in men and >88 cm in women according to the World Health Organization cut-off points and risk of metabolic complications for waist circumference (16).

4.12.3. Clinical Parameters

Clinical variables such as systolic blood pressure (SBP) and diastolic blood pressure (DBP) and fasting plasma glucose (FPG) values were taken from the personal health record files of the diabetic patients. Elevated blood pressure denoted a mean BP ≥ 140/90 mmHg and/or documented antihypertensive treatment [24]. Poor glycemic control was determined by a FBG >130mg/dl according to ADA guideline (**16**). Sociodemographic data such as gender, age, and duration of diabetes were also obtained from the patients.

4.13. Dissemination Plan

After approval by the advisors, the findings of the study will be disseminated to all relevant stakeholders through presentation and publication. Copies of the research will be given to Jimma University, College of Health Science postgraduate library, and the department of Internal Medicine.

CHAPTER FIVE: RESULT

5.1. Sociodemographic Characteristics

The total sample size calculated was 345 including the 10% estimated non-respondent, of whom only 301 were included in the study making the response rate of about 87%. The remaining 44 patients were excluded from the study for the following reasons. Nine of the subjects were T1DM patients who mistakenly interviewed, 15 were interviewed for the second time while 5 of them were HIV patients taking HAART, 7 patients on oral prednisolone for more two weeks, and the rest 8 subjects were having thyrocardiac disease.

Of 301 randomly selected type 2 diabetes mellitus patients on follow-up at Jimma University Medical Center (JUMC) included in the study, 185 of them are males constituting 61.5% while the remainder 116 are females making 38.5%. The mean age of all participants involved in the study is 54.08(SD ±9.90) with mean age of male participants being 55.90(SD ±9.96) and mean

age of female participants is 51.17(SD±9.11) participants reflecting that men participants are older than their counterparts. The minimum age is 25 whereas the maximum value is 83. Significant number of participants, 124 of them, fell in the age group between 50 and 59 years comprising of 41.2% whereas 284(94.4%) are at least forty years or older and only one of them is under 30 years.

About 212(71.4%) of the participants are having some formal education ranging from simple reading and writing to the higher educational level. Of importance is, the fact that the group is comprised of significant number of highly educated participants who attended higher education in colleges/universities, which is about 68 (22.6%).yet, there are about 88 participants who are illiterate making nearly a third of the study population (29.6%).

With regard to marital status, most of the participants, 277 (92.0%) are married, while the remainder eight percent comprises of 9 single (3%),8 widowed (2.7%) and 7 divorced (2.3%) individuals. Two hundred ninety eight of the study groups (99%), nearly all of the participants, are followers of three religions. About 160 (53.2%) are Muslims by religion followed by orthodox, which is about 105 (34.9%) while Protestants comprise of 33 followers making the other10%.

Majority of them are either farmers, 116(38.5%) or government employers, 84(27.9%). Sixty eight (22.6%) of them are housewives and 30 (10%) merchants. Majority of the participants 188(62.5%) live in urban areas and most of them are Oromo 206(68.4%) and Amhara 51(16.9%) by ethnicity. (Table 1)

Table 1 Sociodemographic characteristics of the study population

Characteristics	Frequency (%) n=301	Cumulative frequency (%)
Age category		
≥70	21(7.0)	7.0
60-69	75(24.9)	31.9
50-59	124(41.2)	73.1
40-49	64(21.3)	94.4
30-39	16(5.3)	99.7
20-29	1(0.3)	100.0
Sex		
Male	185(61.5)	61.5
Female	116(38.5)	100.0
Education		
Illiterate	89(29.6)	29.6
Read and writes	41(13.6)	43.2

Grade1-8	66(21.9)	65.1
Grade9-12	37(12.3)	77.4
College/university	68(22.6)	100.0
Marital status		
Married	277(92.0)	92.0
Single	9(3.0)	95.0
Divorced	7(2.3)	97.3
Widowed	8(2.7)	100.0
Religion		
Orthodox	105(34.9)	34.9
Protestant	33(11.0)	45.8
Muslim	160(53.2)	99.0
Other	3(1.0)	100.0
Occupation		
Farmer	116(38.5)	38.5
Government employee	84(27.9)	66.4
Merchant	30(10.0)	76.4
Housewife	68(22.6)	99.0
Other	3(1.0)	100.0
Ethnicity		
Oromo	206(68.4)	68.4
Amhara	51(16.9)	85.4
Gurage	11(3.7)	89.0
Tigre	4(1.3)	90.4
Others	29(9.6)	100.0
Residence		
Urban	188(62.5)	62.5
Rural	113(37.5)	100.0

5.2. Prevalence of Hypertension

The prevalence of hypertension among type 2 DM in diabetes follow-up clinic in JUMC is about 56.5%. As shown in the table below, the prevalence of hypertension is higher in males (59%) than in females (53.4%).

The mean SBP and DBP for all hypertensive patients is 140.01 (±13.00) and 85.86 (±8.25). Sex specific mean blood pressure is otherwise comparable for both men and women though there is slight increase in SBP and DBP for women 140.46 (±13.39) and 86.38 (±8.88) respectively than men, with mean SBP and DBP being 139.76 (±12.84) and 85.58 (±7.901) but sex confer no added significant risk of developing hypertension (*p=0.281*).(Table 2)

Table 2 Pattern of mean SBP and DBP of hypertensive patients in relation to their sex, South West Ethiopia, Jimma, JUMC, August 2017

	Male n=109 (SD)	Female n=61 (SD)	p-value	Total n=170 (SD)
Mean SBP in the last 3 months (mmHg) ±SD	139.76 (12.84)	140.46 (13.39)	0.678	140.01 (13.00)
Mean DBP in the last 3 months (mmHg) ±SD	85.58 (7.901)	86.38 (8.88)	0.890	85.86 (8.25)

5.3. Hypertension Duration & Treatment

5.3.1. Duration of Hypertension

With regard to duration of hypertension, patients were categorized in to 3 mutually exclusive groups to speculate how long has hypertension existed in an individual patient. In 73.5 % of hypertensive participants, the diagnosis of hypertension was made with or after DM while 15.3% of them were diagnosed to have hypertension earlier before they were diagnosed with DM. The remaining 19 (11.2%), were classified as " New but not on treatment" based on their mean SBP and/or DBP fulfilling the criteria for hypertension from their last three consecutive blood pressure records and they are not receiving any treatment (figure 3)

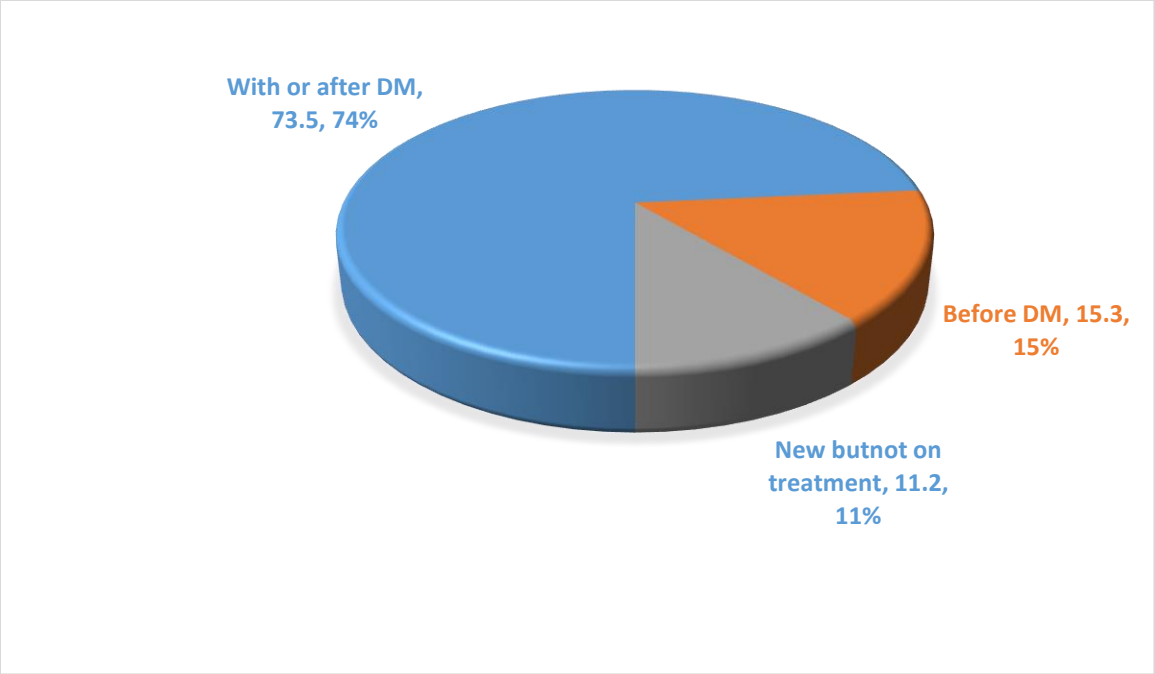

Figure 2 Duration of hypertension with respect to the time of diagnosis in relation with DM and recent incidental diagnosis without treatment, South West Ethiopia, Jimma, JUMC, August 2017

5.3.2. Treatment of Hypertension

Excluding the 19 hypertensive patients who were diagnosed at follow-up clinic with their serial mean SBP and/or DBP that fulfilled the criteria, all participants were receiving one of the three options of treatment of hypertension. These are: salt restriction only, salt restriction and one oral drug and salt restriction and two or more drugs. Among this, majority, 102(67.5%) of them were receiving salt restrictions and one oral drug (table 2).

Table 3. Frequency distribution based on hypertension treatment type, south West, Jimma, JUMC, August 2017

Treatment	Frequency (%)
Salt restriction only	17 (11.3)
Salt restriction and one oral drug	102 (67.5)
Salt restriction and two or more oral drugs	32 (21.2)
Not on any treatment*	19(11.2)
Total	**170 (100)**

***= patients who are hypertensive fulfilling the criteria but not on treatment (reason unknown)**

In addition all participants were assessed for compliance of their DM regimen and nearly all of them (294 of the 301) claim that they strictly follow their treatment while the remaining 7 were not. Among non-complaints, 3 of the 7 did so because they hate side effects of the drugs while 2 of the 7 couldn't afford the drug. The remaining two, they take only when they need them otherwise.

5.4. Bivariate Analysis

5.4.1. Sociodemographic Characteristics & Hypertension

5.4.1.1. Age Category and Hypertension

Of 301 of type 2 DM patients included in this particular study,170(56.5%) of the participants found to be hypertensive based on their treatment status and /or mean blood pressure measurements from their last three serial records made in the preceding 3 months of their follow-ups. Nearly all of the participants are at least 40 years or older, 158 (97.6%) and only 12(2.4%) them are in their thirties (30-39 years). While none of the hypertensive participants are below the age of 30, the leading age category comprising hypertensive patients is between 50 and 59 years, comprising 82(48.2%) of the hypertensive group followed by age 60-69 years having 48(28.2%). There is statistically significant association between age & hypertension ($p<0.01$).

5.4.1.2. Sex and Hypertension

With regard to gender, most, 109 (64.1%) of hypertensive participants are males while only 61(35.9%) of the total 170 hypertensive type 2 diabetic patients are women but there is no statically significant association between sex and hypertension ($p=0.285$). Likewise, most, 154(92.4%) of hypertensive patients are married, but there is no association with hypertension ($p=0.812$).

5.4.1.3. Educational Status and Hypertension

Among those participants who have attended their education in colleges/universities, hypertension occurred in 44 (64.7%) of them, making the most affected groups while 21(56.8%) of who attended high school are the next most affected group compared with the rest of educational status groups However, there is no statistically significant association between educational status of participants and occurrence of hypertension ($p=0.747$) Figure 1

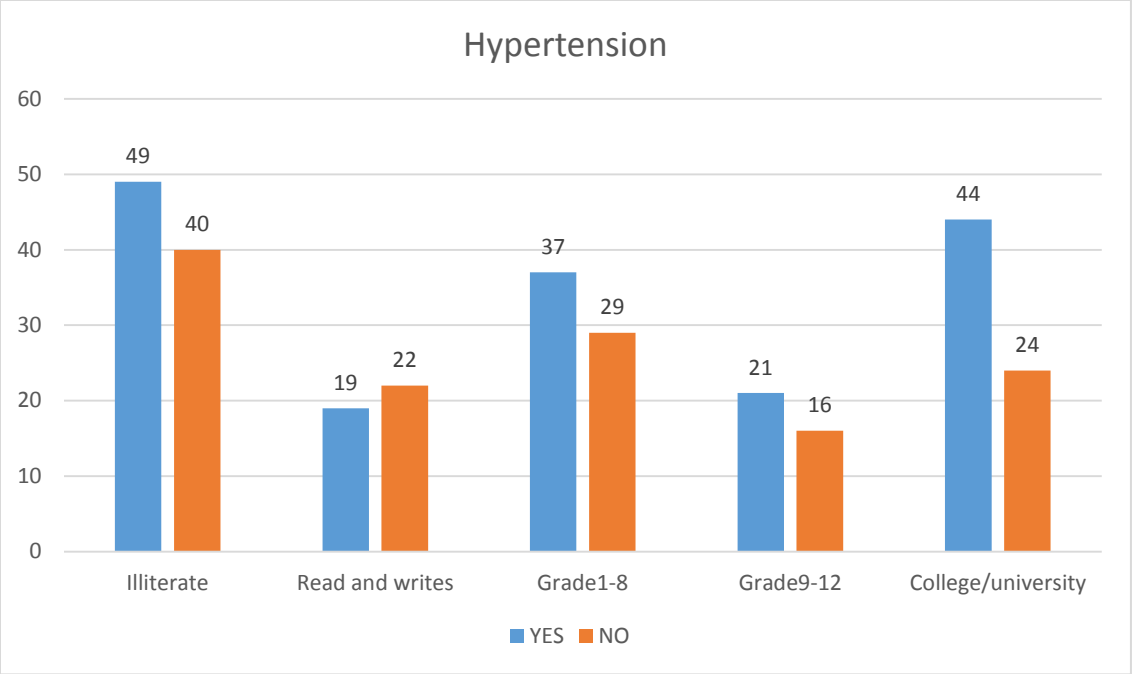

Figure 3 Distribution of hypertension across different classes of educational status, South West Ethiopia, Jimma, August 2017

5.4.1.4. Religion and Ethnicity With Respect To Hypertension

Of 170 type 2 DM patients with hypertension, 88(51.8%) are Muslims, 61(35.9%) orthodox and the remaining 21(12.4%) are protestants. Overall, there is no significant association between religion and occurrence of hypertension (*p=0.546*). Likewise, there is no statistically significant association between different ethnic groups and the occurrence of hypertension (p=0.403). Most, 113(66.5%) of participants with Oromo ethnicity have hypertension followed by Amhara ethnicity, 32(18.8%) with hypertension.

5.4.1.5. Occupation & Residence and Hypertension

In this particular study, there appears to be no association between occupation and hypertension. (*p=0.881*). More than a third of the total participants (38.5%) are farmers by occupation, of whom 63 (37.1%) have hypertensions. Among housewives have 24.7% of them have hypertension while the rate of hypertension is about 28.8% among government employees.

Regarding residence of participants, most, 188 (62.5%) of the participants came from areas and even a greater proportion of hypertensive patients (64.7%) are people who live in urban areas while the rest of hypertensive patients (35.3%) are from rural areas. But there is no statically

significant association between individual's living place and appearance of hypertension (*p=0.359*).

5.4.2. Diabetes Associated Factors & Hypertension

5.4.2.1. Duration of Diabetes and Hypertension

101 of 170 (60.6%) hypertensive participants had type 2 DM for at least 5 years or more . whereas 31.5% of total hypertensive patients had DM lasting more than a year but less than 5 years. Yet there is no association between duration of DM and hypertension (*p=0.328*).

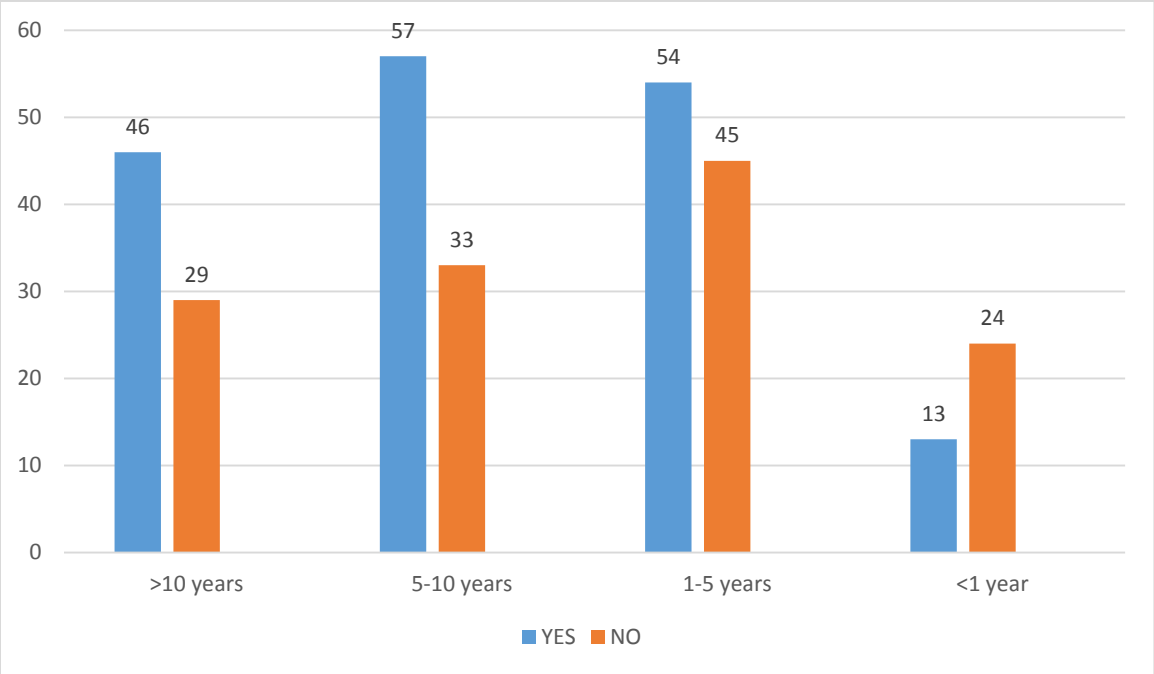

Figure 4 Duration of diabetes and its association with hypertension, South West Ethiopia, Jimma, JUMC, August2017

5.4.2.2. Mode of Diagnosis & Hypertension

Even though more than 90% of total participants were diagnosed to have hypertension after they visited health facilities for certain illness, chi-square reveals that there is no statistically significant association between mode of diagnosis and presence of hypertension (*p=126*).

5.4.2.3. Diabetes Treatment & Hypertension

Treatment of diabetes is another important factor that may play a role in halting the occurrence of hypertension. In this particular study, patients were assessed whether they are taking their initial treatment or shifted to insulin, considering shift of oral agent to insulin could be a surrogate marker

of poor glycemic control suggestive of long standing DM and hence higher risk of development of hypertension. However, there was no elevated risk of hypertension attributed for drug shift from oral agent to insulin (p=0.992) as most of hypertensive patients (69.4%) maintained their oral regimen while only 30.6% of hypertensive patients were shifted to insulin injection.

6.4.2.4. Self-Monitoring Of Blood Glucose (SMBG) & Hypertension

SMBG frequency was considered to be another surrogate marker of glycemic control level, with more frequent monitoring presumed to be associated with good glycemic control as correctional doses of insulin may confer desired glycemic level, ultimately delaying the chronic complications of DM. There are only 31of patients who have SMBG device. Out of 23 patients who use SMBG device, 18(78.3%) of them were monitoring their blood sugar level more frequent (at least once weekly or more) and yet they were hypertensive but no association (0.129).

5.4.2.5. Current Anti Diabetic Drug & Hypertension

Among 170 hypertensive patients most 118(69.4%) are taking the same oral hypoglycemic agent that they were taking before while 52(30.6%) shifted to insulin injection. Surprisingly the proportion of patients taking their oral agent and who shifted to insulin among 131 non hypertensive patients was almost exactly the same (69.5% and 30.5% respectively) showing the absence of association between hypertension and current diabetic regimen taken by the patient(p=0.992).

5.4.2.6. Smoking & Hypertension

Of 301 participants only25 (8.3%) of are smokers of whom 16(64.0%) of them were found to have hypertension. Regarding the intensity of smoking, most, 13(54.2%) of them smoked <10 pack-year while the remaining 11(45.8%) had >10 pack-year of smoking. Even though more smokers tend to have hypertension than nonsmokers, (OR=4.267, CI=7.53-24.18), there is no significant association (p=0.098)

5.4.2.7. Family History of Hypertension & Its Association with Hypertension

Of 301 patients, there are only 35 patients who have family history of hypertension. Of this, 29(82.9%) developed hypertension while the rest 6(17.1%) didn't. The risk of hypertension is higher in those patients with family history of hypertension (OR=4.285, CI=1.722-10.660), which is statistically significant (p<0.01).

5.4.3. Clinical & Laboratory Measurements

5.4.3.1. Body Mass Index (BMI) & Hypertension

Generally, with regard to BMI, all patients fell in to one of the 3 categories. These groups include: normal BMI, overweight and obese. Among 301 type 2 DM patients, only50 (29.4%) of them had normal BMI whereas most of them (50.6%) were overweight and the rest 34 (20%) qualified for obesity. Overall there was significant association between BMI and hypertension (*p<0.01).*fig 5

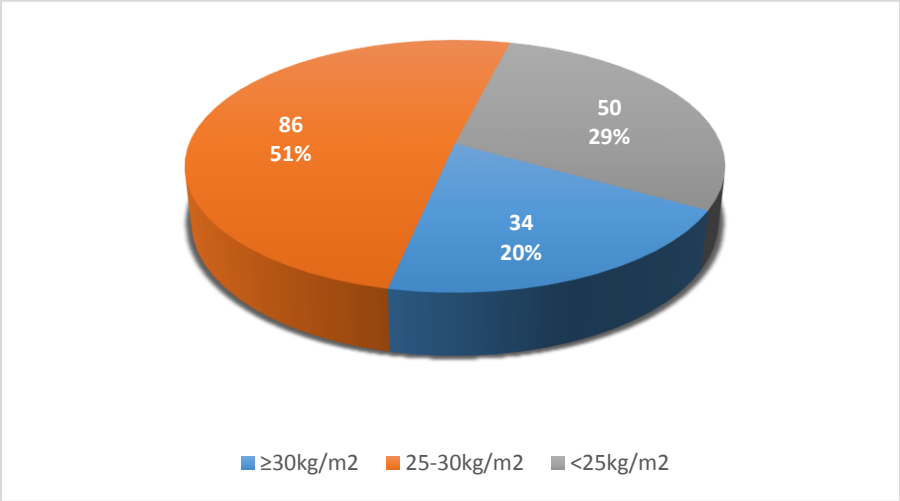

Figure 5 Pie chart showing the distribution of BMI among hypertensive patients, South West Ethiopia, Jimma, JUMC, August 2017

5.4.3.2. Waist Circumference (WC) & Hypertension

Similarly, even though most (55.9%) of the patients are having normal waist circumference measurement, 75 of the 102(73.5%) patients with abnormal waist circumference have hypertension suggesting the presence of significant association between hypertension and abnormal waist circumference (*p<0.01*).

5.4.3.3. Fasting Blood Sugar Level & Hypertension

The mean FBS of all participants is about 163.35 (±72.05) with slightly higher values for women, 168.9(±68.1) than men's mean FBS value which is 159.83(±74.38). Fating blood sugar (FBS) is another factor considered to be a surrogate marker of glycemic control considering target FBS to be <130mg/dl. Sixty four (37.6%) of hypertensive participants are having FBS within the target and nearly the same proportion, 49(37.4%), of patients do not have hypertension suggesting absence of association between FBS level and hypertension *(p=0.996*).Table below summaries all mean laboratory results (Table 4).

Table 4 Summary of mean values of laboratory results of all 301 type 2 DM patients who are included in the study, South West Ethiopia, Jimma, JUMC, August 2017

Parameters	Male n=185 (SD)	Female n=116 (SD)	P-value	Total n=301 (SD)
FBS	159.83(74.38)	168.9(68.1)	0.284	163.35 (72.05)
LDL	98.70 (35.313)	96.83 (33.99)	0.668	97.92 (34.77)
HDL	48.96 (14.16)	50.24 (13.02)	0.430	49.45 (13.720)
TC	178.83 (61.89)	179.78 (60.77)	0.897	179.20 (61.37)
BUN	28.22 (12.02)	25.53 (12.47)	0.064	27.18 (12.26)
Creatinine	1.02 (0.31)	0.99 (0.29)	0.337	1.01 (0.30)

5.4.3.4. Estimated GFR & Hypertension

While there is no participant with end stage renal disease (ESRD), most 241(80.1%) of the participants have normal estimated GFR. Among hypertensive patients, 25(14.7%) are with stage 2 chronic kidney disease (CKD) and 15(8.8%) of them having stage 3 CKD whereas only 1(0.6%) of them has advanced kidney disease (stage 4 CKD).overall, there is significant association between estimated GFR and presence of hypertension (*p=0.038*).

5.4.3.5. Proteinuria & Hypertension

Generally, 102(33.9%) of participants with type 2 DM have evidence some degree of proteinuria. Among hypertensive participants, 69(40.6%) of them have proteinuria whereas most of hypertensive patients (59.4%) have no evidence of any degree of proteinuria. However, chi square reveals that patients with proteinuria have higher risk of developing hypertension (*p<0.01*).

5.4.3.6. Dyslipidemia & Hypertension

According to the definition for dyslipidemia, 132(43.9%) of the study participants have one or more lipid abnormality. Among hypertensive participants 25.3% of them have two or more abnormal lipid profiles while only 5.9% have low HDL alone but no association between occurrence of hypertension and dyslipidemia(p=0.076). Table 5 summarizes the overall lipid profiles of the study population.

Table 5 Dyslipidemia and hypertension among type 2 DM patients, South West Ethiopia, Jimma JUMC, August 2017

Lipid category	Hypertension		p-value
	Yes n=170	No n=131	
2 or more are abnormal	43 (25.3%)	22 (16.8%)	0.064
Only high LDL	10 (5.9%)	14 (10.7%)	0.316
Only low HDL	28 (16.5%)	15 (11.5%)	0.316
Normal	89 (52.4%)	80 (61.1%)	0.489
	170(100.0%)	131 (100.0%)	

5.5. Summary of Cross-Tabulation (Chi-Square Analysis Results)

Table 6 Summary table of all risk factors for hypertension with their statistical significance (p-value), odds ratio (COR) and confidence intervals, South West Ethiopia, Jimma, JUMC, August 2017

No.	Variables	Categories	Hypertension		COR	CI (95%)	p-value
			Yes n=170	No n=131			
1.	Age	<50	28(16.5%)	53(40.5%)	3.566	2.072,6.138	**0.000**
		50-69	130(76.5%)	69(52.7%)			
		≥70	12(7.1%)	9(6.9%)			
2.	Sex	Male	109(58.9%)	76(41.1%)	1.293	0.810,2.064	0.281
		Female	61(52.6%)	55(47.4%)			
3.	Marriage	Married	157(92.4%)	120(91.6%)	1.107	0.479,2.558	0.812
		Others	13(7.6%)	11(8.4%)			
4.	Education	Illiterate	49(28.8%)	40(30.5%)	0.921	0.560,1.516	0.747
		Have some formal education	121(71.2%)	91(69.5%)			
5.	Religion	Muslim	88(51.8%)	75(57.3%)	0.801	0.507,1.268	0.546
		Christians	82(48.2%)	56(42.7%)			
6.	Ethnicity	Oromo	113(66.5%)	93(71%)	0.810	0.494,1.327	0.403
		Others	57(33.5%)	38(29%)			
7.	Occupation	Farmer	63(37.1%)	53(40.5%)	0.867	0.543,1.383	0.543
		Others	107(62.9%)	78(59.5%)			
8.	Residence	Urban	110(64.7%)	78(59.5%)	1.246	0.779,1.993	0.359
		Rural	60(35.3%)	53(40.5%)			

9.	Duration of DM	≥10 years	46(27.1%)	29(22.1%)	1.305	0.765,2.224	0.328
		<10years	124(72.9%)	226(75.1%)			
10.	Mode of diagnosis	Check up	9(5.3%)	13(9.9%)	0.507	0.210,1.226	**0.126**
		After illness	161(94.7%)	118(90.1%)			
11.	Current treatment	The same	118(69.4%)	91(69.5%)	0.997	0.608,1.636	0.992
		Changed to insulin	52(30.5%)	40(30.5%)			
12.	SMBG frequency	Once weekly or more	18(78.3%)	4(50.0%)	3.600	0.655,19.778	**0.129**
		< once weekly	5(21.7%)	4(50.0%)			
13.	Treatment compliance	Yes	163(95.9)	128(97.7%)	0.546	0.138,2.152	0.380
		No	7(4.1%)	3(2.3%)			
14.	Smoking	Yes	16(9.4%)	9(6.9%)	1.408	0.602,3.297	0.428
		No	154(90.6%)	122(93.1%)			
	Smoking intensity	≥10 pack-years	8(61.5%)	3(27.3%)	4.267	0.753,24.18	**0.093**
		<10pack-years	5(38.5%)	8(72.7%)			
16.	Family history of hypertension	Yes	29(17.1%)	6(4.6%)	4.285	1.722,10.660	**0.001**
		No	141(82.9%)	125(95.4%)			
17.	BMI	Normal	50(29.4%)	90(68.7%)	61.200	8.131,460.61	**0.000**
		Overweight	86(50.6%)	40(30.5%)			
		Obese	34(20.0%)	1(0.8%)			
18.	Waist circumference	Normal	95(56.9%)	104(79.4%)	0.329	0.195,0.553	**0.000**
		High	75(44.1%)	27(20.6%)			
19.	FBS	Within target	64(37.6%)	49(37.4%)	1.010	0.631,1.618	0.996
		Above the target	106(62.4%)	82(62.6%)			
20.	Dyslipidemia	No	127(74.7%)	109(83.2%)	0.596	0.336,1.058	**0.076**
		Yes	43(25.3%)	22(16.8%)			
21.	Estimated GFR	Normal	129(75.9%)	112(85.5%)	0.5340	0.293,0.9731	**0.038**
		Reduced	41(24.1%)	19(14.5%)			
22.	Proteinuria	Negative	101(59.4%)	98(74.8%)	0.493	0.299,0.812	**0.005**
		Positive	69(40.6%)	33(25.2%)			

- **COR=Crude Odds Ratio, CI=Confidence Interval**
- **Bold and underlined p values show factors that qualified for multivariate logistic regression at the cut-off value of 0.2**

Based on the results of chi-square test result with the cut-off value of 0.2, age, Duration of DM, Mode of Diagnosis, Family history of hypertension, BMI, Waist circumference, FBS, dyslipidemia, eGFR and Proteinuria were considered for further analysis using multiple logistic regression whether a given variable has independent association with hypertension. Only age, BMI, and family history of hypertension are shown to be independently associated with hypertension. Table 7 summarizes independent factors that are associated with hypertension.

5.6. Multivariate Logistic Regression Summary

Table 7 Independent risk factors that are associated with hypertension among type 2 DM patients, Southwest Ethiopia, Jimma, JUMC, August 2017

Variables	AOR	CI		p-value
		Lower	Upper	
Age 50-69 years	3.889	2.005	7.544	*<0.01*
Obesity/Overweight	49.108	5.937	406.218	*<0.01*
Family history of hypertension	3.464	1.220	9.838	0.02

CHAPTER SIX

6.1. DISCUSSION

Hypertension is twice as prevalent in diabetics as in non-diabetic individuals. (1) In patients with Type 1 DM, hypertension is generally not present at diagnosis, but develops as renal insufficiency and exacerbates the progression to end-stage renal disease. In Type 2 DM, many patients are already hypertensive at the time of diagnoses**.** (1)

The frequency of hypertension in type2 DM is related to the degree of obesity, advanced age and extreme atherosclerosis that is present in these patients. Hyperglycemia and increase in total body exchangeable sodium leading to extracellular fluid accumulation and expansion of the plasma volume contributes to the pathogenesis of hypertension in DM. (1)

In this study, the prevalence of hypertension in among type 2 DM in diabetes follow-up clinic in JUMC is about 56.5%. A retrospective study conducted on 244 diabetic subjects at the Endocrinology Clinic of the Delta State University Teaching Hospital, Oghara, Nigeria showed that the prevalence of hypertension to be 65.1%. In addition, in this study they also have assessed the prevalence of hypertension with type 1 DM patients which is about 24.1% and there was significant difference between the two types of DM categories ($p<0.01$).

Another study which was conducted in Benin revealed the prevalence of HBP in type 2 diabetics to be 70% (22). Another cross-sectional study that was carried out on 300 type 2 diabetic patients who were admitted to medical ward of Moosabne Jafar hospital in Quchan, Iran, for follow-up from April 2011 to August 2012 showed the prevalence to be 70%(18). This is relatively higher from what we found in our study.

The prevalence of hypertension is higher in males (59%) than in females (53.4%) but gender confers no added significant risk of developing hypertension (*p=0.281*). This is in contrast with above two studies in which the prevalence of hypertension is higher in female than males. Yet, there was no statistically significant association between gender and hypertension in the studies mentioned above, which is in agreement with us (18, 19).

On the other hand, age is the most important risk for development hypertension. Multiple logistic regression showed that age, particularly between 50 to 69 years, is an independent risk factor for development of hypertension (*p<0.01*).

Other authors reported similar conclusion. In this way, our finding is in close agreement with Dibia who reported that 67% of diabetics with hypertension had age range between 51 and 70 years (19) and Aassri *et al.* found that HBP and diabetes association was significant between 66 and 69 years (21); Ralison *et al.* found a prevalence of HBP in type 2 diabetics above 50 years and particularly between 60 and 69 years (22) all being in line with our findings.

Obesity and overweight on the other hand are shown to be independently associated with hypertension (p<0.01). The prevalence of obesity among hypertensive patients is about 20% and that of overweight is 50.6%, giving a total abnormally higher BMI prevalence of 70.6%. With this regard, a study done in Nigeria revealed that overweight and obese subjects had significantly higher rate of hypertension than normal weight subjects (74.4% vs. 41.7%, *P* = 0.0004). Also, the prevalence of overweight and obesity among the hypertensive subjects was 62.1%, which is relatively similar with our findings.

On the other hand, Amoussou *G et al,* in their study on Prevalence and Risk Factors of Hypertension in Type 2 Diabetics in Benin, found abdominal obesity to be significantly associated with the occurrence of hypertension in type 2 diabetic patients (*p* = 0.036). Indeed in this study, the frequency of hypertension in type 2 diabetics with abdominal obesity was 71.9% against 57.1% among those who did not have abdominal obesity (19). In our study there was no statistically significant association between abdominal obesity and hypertension (0.096). [1]

This study also showed that absence of correlation between dyslipidemia and hypertension in type 2 diabetics (p=0.324). With this regard, our finding is in agreement with what Amoussou *G et al* reported (p=0.426) (19).

On the other hand, duration of diabetes was a factor associated with hypertension in type 2 diabetes (p=0.009) (19). Contrary, in our study, bivariate analysis failed to show association between duration of DM and hypertension(p= 0.328) even though there is slightly higher likelihood of

developing hypertension among those diabetic patients whose diabetes lasted ten years or more (COR=1.305).

Fasting blood sugar (FBS) was considered to be above target if the value is >130mg/dl based on the current ADA treatment target (12). Studies have shown that the benefit of early glycemic control to reduce the future risk of microvascular and cardiovascular complications is sustained beyond the period of good glycemic control ("metabolic memory") (30). The pathophysiologic link between hyperglycemia and macrovascular disease includes possibly direct effects of glucose, activation of protein kinase C, endothelial dysfunction from oxidative stress, activation of athero-inflammatory cytokines and epigenetic changes, among others (31).

In our study, mean FBS doesn't reflect occurrence of hypertension in a given patient even though there are well established evidences indicating the relation between poorly controlled glycemic level occurrences of macro/microvascular complications as mentioned above. As one of the chronic complications, one would assume poorly controlled FBS to be associated with hypertension. Surprisingly, patients were having nearly similar proportional risk of hypertension in both glycemic groups (37.6% vs 37.4%), suggesting the absence of significant association between FBS level being above target or within the target (p=0.996).

Part of the explanation for this would be paucity of evidence to rely on the cut- off point put by ADA and other societies for the general treatment goal as there is no a specific glycemic cut-off point above which the risk of hypertension tends to rise significantly. A study conducted by Sheme ZA, Huda AK & et al in order to compare whether FBS or RBS could correspond to HBA1C level as a surrogate marker of glycemic control revealed that there is a moderate correlation between HBA1C,FBS and PPBG and FBS and PPBG were both have significant association with HBA1C($p<0.01$) (46)

The other potential explanation is, though both ADA and WHO recommend FBS to be a surrogate marker of HBA1C (12), recent works comparing the reliability of FBS and RBS as a monitoring tool for glycemic level revealed the superiority of RBS. Monnier L, Colette C (2006), reviewed previous studies of diurnal glycemic profiles and concluded that relative contribution of

postprandial plasma glucose to HbA_{1c} was high (70%) in patients with fairly good control of diabetes (HbA_{1c} <7.3%) and decreased progressively (30%) with worsening diabetes (HbA_{1c} >10.2%) whereas the contribution of fasting plasma glucose showed a gradual increase with increasing levels of HbA_{1c} (47). Masram et al, who revealed that PPG has a stronger correlation with HbA_{1c} as compared to the FBG (48). Post meal hyperglycemia is associated with increased risk of retinopathy, increased carotid intima thickness, oxidative stress, inflammation and endothelial dysfunction. Hence targeting both post-meal and fasting plasma glucose is an important strategy for achieving optimal glycemic control (49). Because the same mechanisms are responsible for part of the pathophysiologic processes of hypertension in DM patients, RBS seems better marker. In our scenario, RBS is not being determined regularly. Rather, it is requested rarely and usually when a treating physician sees certain unusual pattern of FBS, because patients are coming in the morning for their routine follow-up. Therefore, the relation between hypertension and FBS requires specifically defined cut-off point than considering the target level for the general treatment monitoring. With this regard, the validity of FBS and RBS with respect of occurrence of hypertension shall be best studied with comparative studies in future.

Family history of hypertension is the other independent risk factor shown to be associated with hypertension among type 2 DM in our study (P=0.02).

Contrary, Addisu Y Mengesha, in its work on hypertension and is associated risk factors in type 2 DM in diabetic clinic at Gaborone city council, Botswana, found that prevalence of hypertension among type 2 DM patients in the follow-up clinic doesn't differ much between hypertensive and normotensive patients (34.9% and 30.7%) respectively(50). This suggest that there is no significant association between family history of hypertension and occurrence of hypertension among type DM patients.

Interestingly, 19 (11.2%),, which make up 6.3% of the total study participants, were classified as "New but not on treatment" based on their mean SBP and/or DBP fulfilling the criteria for hypertension from their last three consecutive blood pressure records, are not receiving any treatment. these patients were not only denied treatment but they were not told about their underlying hypertension. We considered the likely reservation of physicians not to initiate treatment for those patients with marginal hypertension. This may pose a question on the quality of care provided at the clinic with regard to anticipation of complications and early aggressive

treatment of chronic complications in order to decrease the subsequent morbidity and mortality. This is relatively lower than that of 16.4% of the hypertensive diabetic patients who were not aware of having hypertension as described Amoussou *G et al (19). Even higher* prevalence of unawareness of 38.8% was reported in study in Morocco had a (51). Despite the relatively lower prevalence of unawareness, still this certainly emphasizes the need for monitoring and control of blood pressure in diabetics and the importance of continuous education for a diabetic patient.

6.2. CONCLUSIONS

The prevalence of hypertension amongst persons with DM in this study is high. Individuals with both hypertension and diabetes are at high risk for both microvascular and macrovascular complications of DM. Diabetic patients with hypertension should be treated with appropriate antihypertensive drugs and carefully monitored to ensure satisfactory blood pressure control and prevention of the end-organ complications of hypertension.

6.3. LIMITATION OF THE STUDY

Because this study is institution based cross sectional study, it may not show cause –effect relation and it may not be generalized to the general population. Part of the study information is based on the patient's medical file that is incomplete with regard to certain important variables that would be otherwise impossible to get from patients as most of them may not tell the nature of their underlying condition except the disease in question. Additionally, some factors that could be associated with hypertension, like life style, and exercise were not considered because of lack of standardized tools and difficulty to assess them. Most importantly, some important laboratory investigations like HBA1c, which would have been an appropriate surrogate marker of glycaemic control in the last 3 months so that telling "glycaemic control'' with FBS only becomes a rough estimate.

6.4. STRENGTH OF THE STUDY

This study has certain strengths.

- **Acceptable data quality:** The data collection process was relatively of high quality as it has involved highly capable personnel who can deal with data artifacts and inconveniences. Particularly the involvement of residents and medical interns has produced relatively complete information.

- **Reliability of clinical measurements**: The routine measurements of BP, BMI and WC by physicians and possible reevaluation of patients who have unusual values increases the reliability of the data on clinical measurements
- **Ease of meeting patients in subsequent visits when there was a need**: incomplete data for different reasons were possible for selected patients as they return back for their routine follow-up
- **Emphasis on common problem (significance):** Because every qualitative and quantitative data used on this particular area were not locally produced.
- **Availability of plenty of references regarding the study in question:**

6.5. RECOMMENDATIONS

In this study, the prevalence of hypertension is very high. There is significant association between BMI and hypertension giving an overall prevalence of either obesity or overweight about 70.6%. It follows that there should be well organized and integrated comprehensive diabetic care that can optimize the reduction of modifiable risks. Most importantly, as majority of hypertensive participants are elderly, who cannot be engaged in a regular exercise program, life style modification advices should be individualized and tailored based on the overall health and sociodemographic and economic status of patients in order to effect the outcome positively. This should involve estimating 10-year ASCVD risk and initiating lipid lowering statins if the risk is >7.5% regardless of their lipid profile. Especially, physicians should have a lower threshold to initiate treatment in hypertensive patients with type 2 diabetes, given the 6.3% patients who qualified as hypertensives based on their mean blood pressure in the last 3 months, but not on any form of treatment yet.

On the other hand, as this study addressed limited factors that are associated with hypertension in diabetic patients, further studies are required to look for other potential associated factors that can impact the management approach.

Finally, appropriate glycemic control tool like HBA1C would be invaluable in order to define the cut-off point for poor control and to see the effect of the level of hyperglycemia on occurrence of hypertension among type 2 DM patient

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Questionnaire:

Instructions: Please answer the following questions by reviewing the records of the patients carefully by first writing the registration number. Go through each questions according to their ascending orders and check for completeness and accuracy at the end. Arrange call backs for incompletely filled medical records.

Part- 1; Sociodemographic data

Patient card No: _____ Date of first visit _____ phone no._____

Age in years _____

Sex

Male ☐

Female ☐

Marital status

- Married ☐
- Single ☐
- Divorced ☐
- Widowed ☐
- Separated ☐

Educational status

- Illiterate ☐
- Read and write ☐
- Grade 1-8 ☐
- Grade 9-12 ☐
- College/university ☐

Religion

- Orthodox ☐
- Protestant ☐
- Catholic ☐
- Muslim ☐
- Other ☐ _____

Ethnicity

- Oromo ☐
- Amhara ☐
- Gurage ☐
- Tigre ☐
- Others, specify _____

Occupation

- Farmer ☐
- Governmental employee ☐
- Merchant ☐
- Student ☐
- Others, ☐

Specify _____

Residence

- Urban ☐
- Rural ☐

PART -2; HISTORY

How long have you been diabetic? _____

How was the diagnosis made?

Routine ☐kup?

After vis☐ health facility for illness?

Treatment;

Initial medication

Oral ☐t

☐ Insulin

Current drug; Initial medication

The ☐

Changed ☐cify) _____

Total duration of treatment in years_____

Do you have self-monitor blood glucose device?

☐ Yes

☐ No

How frequent do you self-monitor your blood sugar level?

Daily and☐re

Once wee☐

Once mo☐

No monit☐g

Have you ever been told to have hypertension?

☐ Yes

☐ No

If yes, how long have you been hypertensive? _____

Specify your treatments for your high blood pressure

Salt restr☐n only

Salt ☐iction & one oral drug

☐

Salt restriction & two or more oral drugs

Do you take your treatment appropriately as recommended by your physician?

Yes ☐

No ☐

If no, what is the reason for not taking your medicines?

I cannot afford the cost ☐

Medications are not easily available ☐

I do not like to take medications ☐

I only take them when I feel that I need them ☐

I do not like the side effects of the medication

Have you ever smoked cigarette?

Yes ☐

No ☐

If yes

Average no. of cigarettes smoked per day_____

Total duration _____

Pack-year_____

Currently smoking (yes/no) _____

Do you have any 1st degree family member with hypertension?

a. Yes ☐

b. No ☐

I don't know ☐

19. Have you ever been told to have kidney disease?

Yes ☐

No ☐

PART -3: MEASUREMENTS:

Mean Blood pressure (SBP/DBP) of the last 3 visits _____ mmHg

Mean SBP----------.mmHg

Mean DBP----------mmHg

Weight _____kg

BMI (in kg/m^2)

<30 ☐

25-3 ☐

>30 ☐

☐

Waist Circumference (WC); _____cm

Waist to Hip Ratio (WHR) _____

PART -4: INVESTIGATIONS

TEST TYPE		**UNIT (mg/dl)**
Serum glucose	**FBS**	
	RBS	
Fasting lipid profile	LDL-C	
	HDL-C	
	TC	
RFT	**UREA**	
	CREATININE	
eGFR*		
		Meq/L
Serum electrolyte	**Na+**	
	K+	
	Ca2+	
Urinalysis	**DIPSTICK Albumin/proteinuria**	
Urine microscopy	**Broad cast**	
	Waxy cast	
	RBC cast	
	WBC cast	

*eGFR=is calculated with either **Cockcroft-Gault's** or **MDRD** equation.

DECLARATION

I, THE UNDERSIGNED THIRD YEAR INTERNAL MEDICINE RESIDENT, DECLARE THAT THIS THESIS IS MY ORIGINAL WORK FOR THE PARTIAL FULFILLMENT FOR THE REQUIREMENT FOR THE SPECIALTY CERTIFICATE IN INTERNAL MEDICINE. ALL THE MATERIALS USED IN THIS MATERIAL HAS BEEN GIVEN DUE ACKNOWLEDGED. I ALSO DECLARE THAT ALL STAKEHOLDERS WHO PARTICIPATED IN THIS WORK, INCLUDING JIMMA UNIVERSITY INSTITUTE OF HEALTH ARE ACKNOWLEDGED

NAME OF THE STUDENT: **WIHIB G/HIWOT (INTERNAL MEDICINE RESIDENT)**

DATE._____ SIGNATURE _____

APPROVAL OF THE ADVISORS

NAME OF THE FIRST ADVISOR: **MOHAMMED MECHA (MD, INTERNIST)**

DATE._____ SIGNATURE _____

NAME OF THE SECOND ADVISOR: **HABTAMU JARSO (MPH)**

DATE_____ SIGNATURE_____