

INVESTIGATION OF PRESCRIBING PATTERN OF ANTIHYPERTENSIVE DRUG IN TYPE 2 DIABETES MELLITUS WITH CARDIAC COMPLICATIONS

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ABSTRACT

Diabetes mellitus and Hypertension are conditions characterized by high blood sugar levels, high blood pressure. Early detection and treatment are crucial, along with lifestyle changes and weight control, to reduce the risk of cardiac complications. **Objectives:** The main aim of our study is to investigate the prescribing pattern of anti-hypertensive drugs in type 2 diabetes mellitus and check for cardiac complications. **Methods:** A prospective type of observational study in a multispecialty hospital for 6 months. Microsoft Excel version 12 and SPSS [Statistical Package for Social Science] version 22 were used for statistical analysis. **Results:** Out of 80 patients, hypertension with type 2 diabetes mellitus was most common in men over the age of 60. Our study reveals that all 80(100%) patients had heart disease as a comorbidity. Among the 80 patients, 48(60%) had CAD as one of their cardiac complications. 5% of patients received combination therapy

while the majority of the patients, i.e., 95%, received monotherapy. The most commonly prescribed drug was found to be Beta-blocker 46 (57.5%). The most commonly prescribed antihypertensive brand was Betaloc 24(30%). **Conclusion:** Our study showed that hypertension was the most prevalent risk factor among type 2 diabetes patients. Betaloc (beta blocker) was the most commonly prescribed drug for hypertension in type 2 diabetic patients.

KEYWORDS: Prescribing pattern, Antihypertensive drug, Hypertension, Blood pressure, Diabetes Mellitus, Cardiac Complications.

INTRODUCTION

Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. It is caused by the complex interaction of genetics and environmental factors leading to reduced insulin secretion, decreased glucose utilization and increased glucose production.^[1]

The WHO has projected that global prevalence of type 2 Diabetes Mellitus will be more than double from 5 million in 1995 to 300 million by 2025. Between 1995 and 2025 there will be a 35% increase in worldwide prevalence of Diabetes Mellitus, from 4 to 5.4%.^[1]

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised blood pressure.^[2] Approximately 31% of the populations have high blood pressure. The percentage of men with high blood pressure is higher when compared to women.^[3] Hypertension and diabetes are becoming increasingly common. Hypertension occurs more commonly in diabetics than in comparable non-diabetics. In India, about 50% of diabetics have Hypertension and most patients with both those disorders have a markedly worsened risk for cardiac complications.^[4]

The prevalence of coexisting hypertension and Diabetes mellitus appears to be increasing in industrialized nations because populations are aging and both hypertension and non-insulin dependent diabetes mellitus incidence increasing with age, indeed an estimated 35 to 75% of diabetic cardiovascular complications can be attributed to hypertension. Hypertension to account for 30% of death in diabetes patients and 25% cardiovascular events in diabetes patients. Diabetic and hypertensive patients should be identified early and treated promptly to achieve the target goals of control of both conditions. Drug therapy is required in the management of these patients, but lifestyle modification and weight management are key components to reduce glycaemia and control blood pressure.^[5]

Hypertension is defined by persistent elevation of arterial blood pressure (BP). The seventh report of the Joint National Committee on the Detection, Evaluation, and Treatment of high blood pressure (JNC 7) classifies adult BP as shown in the table. Patients with DBP values <90mmHg and SBP values >140mmHg have isolated systolic Hypertension. A hypertensive crisis (BP >180/120mmHg) may be categorized as either a Hypertensive Emergency (extreme BP elevation with acute or progressing target organ damage) or a Hypertensive Urgency (severe BP elevation without acute or progressing target organ injury).^[8]

PREPONDERANCE OF HYPERTENSION IN TYPE 2 DIABETES MELLITUS

Cardiovascular illnesses (CVD) include Hypertension (HTN), stroke, and end-stage renal disease are all strongly linked to a significant risk of early death and morbidity in Type 2 Diabetes Mellitus. The most common CVD-related cause of morbidity and mortality in people with Type 2 Diabetes Mellitus is Hypertension.

Because of its effects on target organs like the brain, heart, eye, and kidney as a result of structural changes in the microcirculation brought on by oxidation stress, inflammation, or endothelial dysfunction, it is a significant risk factor for cardiovascular mortality and morbidity.

Heart attack, stroke, renal illness or failure, eyesight loss, sexual dysfunction, and peripheral arterial disease are all consequences of uncontrolled Hypertension.

Diabetes patients with greater rates of Hypertension are thought to have hyperglycaemia, insulin resistance, and dyslipidaemia.

Through the disruption of the blood vessel wall caused by the stimulation of vascular inflammation, endothelial cell dysfunction, abnormalities of different cell types like platelets, and stimulation of coagulation, all these factors contribute to the development and progression of atherosclerosis. All of them result in blood vessel narrowing and an increase in total peripheral vascular resistance, which causes Hypertension.

Since insulin is known to encourage sodium retention and increase sympathetic nervous system activity it is thought that hyperinsulinemia and insulin resistance are factors in high blood pressure.

Inappropriate activation of the Renin- Angiotensin- Aldosterone- System is linked to insulin resistance. When RAAS gets activated multiple processes that raise blood pressure will become active.

Angiotensin II, a by-product of RAAS activation induces vasoconstriction and aldosterone synthesis, and results in salt and water retention in the kidney and the development of Hypertension.

INCIDENCE OF CARDIOVASCULAR DISEASES WITH TYPE 2 DIABETES MELLITUS

DM and CVD are closely related. In DM patient's CVD is the most common cause of mortality and morbidity. Adults with diabetes historically have a higher prevalence rate of CVD than adults without diabetes, and the risk of CVD increases continuously with rising fasting plasma glucose levels, even before reaching levels sufficient for a diabetes diagnosis.

CV risk factors including obesity, Hypertension, and dyslipidaemia are common in patients with DM, particularly those with Type 2 DM. In addition, studies have reported that several factors including increased oxidative stress, increased coagulability, endothelial dysfunction, and autonomic neuropathy are often present in patients with DM and may directly contribute to the development of CVD.

People with Type 2 DM are disproportionately affected by CVD compared with non-diabetic subjects. As per Hafner et al report, in persons with Type 2DM, the death rates were 15.4% for those with no prior myocardial infarction (MI) and 42.0% for patients having a history of MI. In contrast, in patients who did not have Type 2 DM, the death rates due to cardiovascular causes were 2.1 and 15.9%, respectively.^[9] Study of prescribing pattern is a component of medical audit that does monitoring an evaluation of prescribing practice of the prescribers.^[6] Irrational use of medicine is wide spread throughout the world. The directional use of a drug is a major problem in today's medical practice. A study of prescription pattern ensures rational pharmacotherapy and assures a quality medical care to the patient.^[7]

MATERIALS AND METHODS

OBJECTIVES

- To investigate the prescribing pattern of anti-hypertensive drug in type 2 diabetes mellitus.
- To check for cardiac complications

METHODOLOGY

Study Design

"Prospective Interventional Study"

DURATION OF STUDY

The study was carried out for a period of 6 months.

STUDY CENTRE

Indiana Hospital and Heart Institute, Pumpwell, Mangalore, Karnataka.

ETHICAL APPROVAL

The study was approved by the Indiana Hospital and Heart Institute Ethics Committee.

SOURCE OF DATA

Patient Case Sheet

Prescriptions

Patient interview Record

Data Collection Tool

Patient Data Collection Form

All the patients meeting the following criteria will be selected;

Inclusion Criteria

- Patient diagnosed with Hypertension in Type 2 Diabetes Mellits with or without Cardiac Complications.
- In-patient unit of various department
- Age > 18 years of either gender

Exclusion Criteria

Patients with age < 18 years

All pregnant and lactating women.

Psychiatric

STUDY PROCEDURE

A simple prospective observational study will be carried out in the in-patients of various departments of Indiana Hospital and Heart Institute, Mangalore.

Considering the inclusion and exclusion criteria patient will be enrolled after taking written consent from each patient for the study. Data will be collected through review of case sheet and a suitably designed data collection form will be used. The data collection includes the following details

Age and sex of patients

Name and class of drugs prescribed

Dose, Frequency and route of administration of drugs

Complications of disease and treatment

Past and present medical medication history

Current status and clinical progress of the patient

Laboratory investigation like complete blood count, renal function test, blood sugar test, urine analysis, lipid profile test.

Cardiac tests- Electrocardiogram, Magnetic Resonance Imaging (MRI)

Diet status

Family history

Social history

Personal history

All patient information that is collected during the course of study will be kept confidential.

STATISTICAL ANALYSIS

The collected data were tabulated and analyzed using Microsoft Excel version 12 and SPSS VERSION 22.

RESULTS

A prospective observational study was conducted for six months at Indiana Hospital and Heart Institute. A total of 80 patients having hypertension in diabetes mellitus were included in the study.

AGE-WISE DISTRIBUTION OF PATIENTS

Out of 80 patients most of the patients were above 60 years (68.8%), followed by 50-59 years (22.5%), 40-49 years (6.3%), 30-39 years (2.5%) and 18-29 years (0%).

Table 6.1: Frequency and Percentage distribution of samples according to age.

Age in years	Frequency	Percentage
18-29	0	0
30-39	2	2.5
40-49	5	6.3
50-59	18	22.5
≥ 60	55	68.8

N= 80 (Sample size)

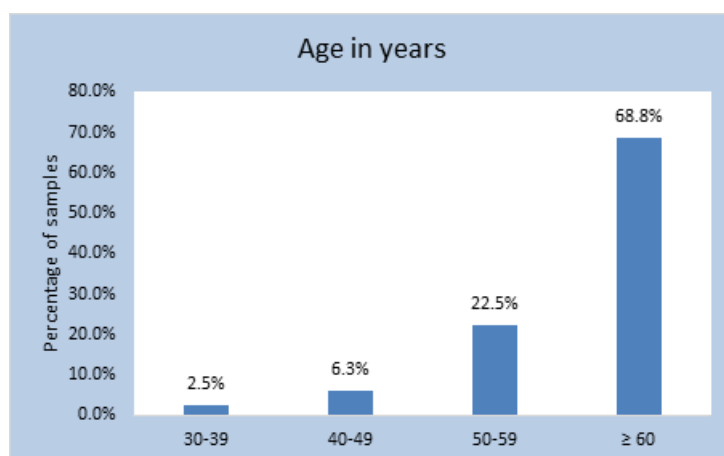


Figure 6.1: Percentage distribution of sample according to age in years.

GENDER DISTRIBUTION OF PATIENTS

Out of 80 patients, 55(68.8%) were males and 25(31.3%) were females.

Table 6.2: Frequency and Percentage distribution of sample according to gender N= 80 (Sample size).

Gender	Frequency	Percentage
Male	55	68.8
Female	25	31.3

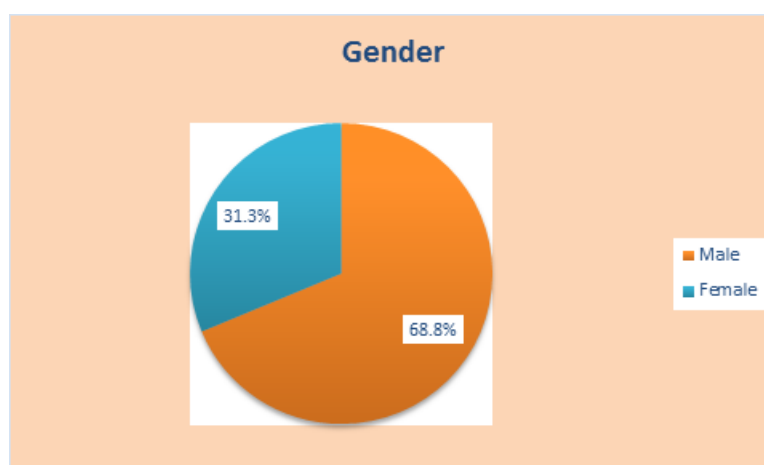


Figure 6.2: Pie chart of percentage distribution of samples based on gender.

PATIENT DISTRIBUTION BASED ON INCOME

Out of 80 patients, 23(28.7%) were low income, and 57(71.3%) were high income. Table 6.3: Frequency and Percentage distribution of sample according to income N=80 (Sample size)

Income	Frequency	Percentage
Low	23	28.7
High	57	71.3

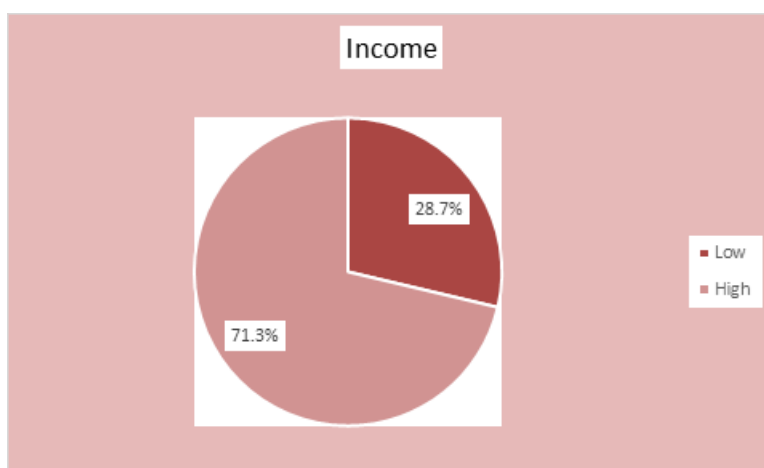


Figure 6.3: Pie chart of percentage distribution of sample based on income.

PATIENT DISTRIBUTION BASED ON LITERACY

Out of 80 patients, 37 patients (46.3%) were having low literacy rate, 43 patients (53.8%) were having high literacy rate.

Table 6.4: Frequency and Percentage distribution of sample according to literacy N= 80 (Sample size).

Literacy	Frequency	Percentage
Low	37	46.3
High	43	53.8

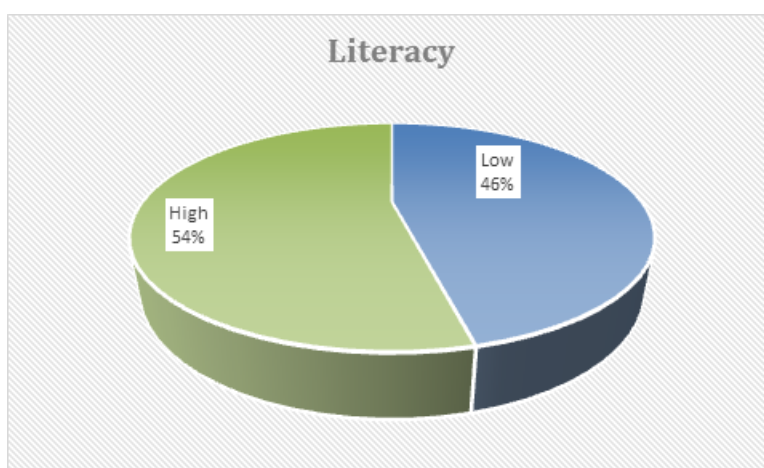


Figure 6.4: Pie chart of percentage distribution of sample based on literacy.

PATIENT DISTRIBUTION BASED ON RISK FACTOR

In the study, disease and environmental factors were found to be the risk factors for diabetes mellitus. Out of 80 patients, based on disease 80 (100%) had hypertension, 27 (53.8%) had CKD, 12 (15%) had dyslipidemia and 6 (7.5%) had thyroid disease. Table 6.5.a: Frequency

and Percentage distribution of sample according to the presence of risk factors (diseases)
N=80 (Sample size)

Risk Factor (Disease)	Frequency	Percentage
CKD	27	33.8
Dyslipidemia	12	15
Thyroid	6	7.5
Hypertension	80	100

Table 6.5.b: Frequency and Percentage distribution of sample according to the presence of risk factors (Environmental factors) N=80 (Sample size).

Risk factor (Environmental factor)	Frequency	Percentage
Obesity	41	51.3
Unhealthy diet	42	52.5
Stress	52	65
Lack of physical activity	42	52.5

Based on the environmental risk factor, out of 80 patients, 52 (65%) patient's risk factor was stress, 42 (52.5%) patient's risk factors were both unhealthy diet and lack of physical activity, 41 (51.3%) were obese.

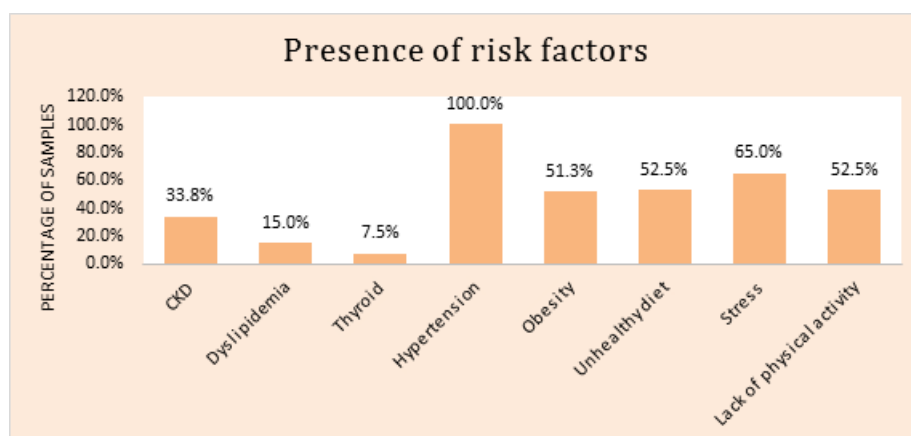


Figure 6.5: Percentage distribution of samples according to the presence of risk factors (disease and environmental).

PATIENT DISTRIBUTION BASED ON CO-MORBIDITIES

Out of 80 patients, all of the patients i.e., 80 (100%) had heart disease as comorbidity. Followed by 25 (31.25%) patients with CKD. Some of the patients had other comorbid conditions which are represented in table 6.6 and figure 6.6.

Table 6.6: Frequency and percentage distribution of samples according to comorbidities
N= 80 (Sample size).

Comorbidities	Frequency	Percentage
Pulmonary disease	6	7.5
Thyroid	4	5
Bone disease	7	8.75
CKD	25	31.25
Neuropathy	6	7.5
Heart disease	80	100
Liver disease	2	2.5
CVA	13	16.25
Metabolic acidosis	1	1.25
Encephalitis	2	2.5
appendectomy	3	3.75
Anemia	8	10
Sepsis	6	7.5
UTI	2	2.5
Parkinsonism	6	7.5
Neuralgia	1	1.25
GERD	1	1.25

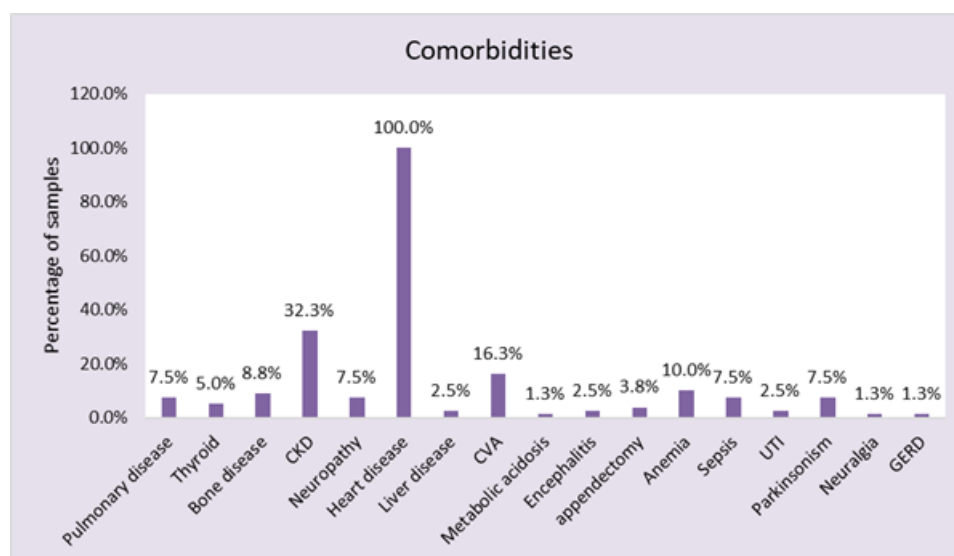


Figure 6.6: Percentage distribution of samples according to co-morbidities.

PATIENT DISTRIBUTION BASED ON CARDIAC COMPLICATIONS

Out of 80 patients, the majority of the patients i.e. 48 (60%) had coronary artery disease, followed by 24 (30%) had heart and blood vessel disease. Some of the patients had other cardiac complications, which are represented in the table 6.7 and figure 6.7. Table 6.7: Frequency and percentage distribution of samples according to cardiac complications N=80 (Sample size)

Table 1: Frequency and percentage distribution of samples according to cardiac complications.

Cardiac complications	Frequency	Percentage
CAD	48	60
Heart and blood vessel disease	24	30
Arrhythmia	1	1.25
Angina pectoris	11	13.75
Ischemic Heart Disease	7	8.75

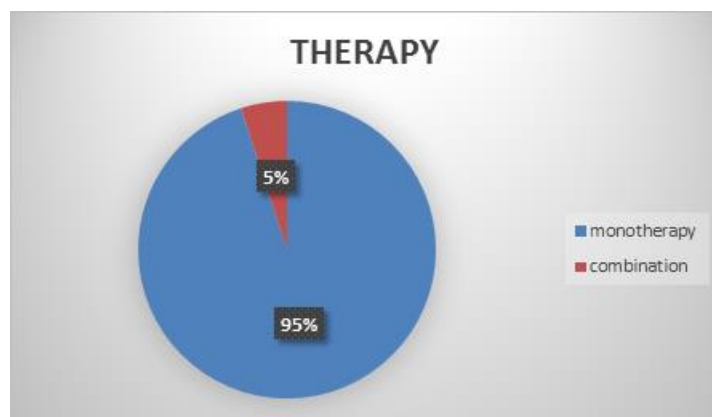


Figure 6.7: Percentage distribution of sample according to cardiac complications.

PATIENT DISTRIBUTION ACCORDING TO DRUG THERAPY

Out of 80 patients, 76 (95%) were on monotherapy, and 4 (5%) on combination therapy.

Table: Frequency and percentage distribution of samples according to therapy.

Therapy	Frequency	Percentage
Monotherapy	76	95
Combination therapy	4	5

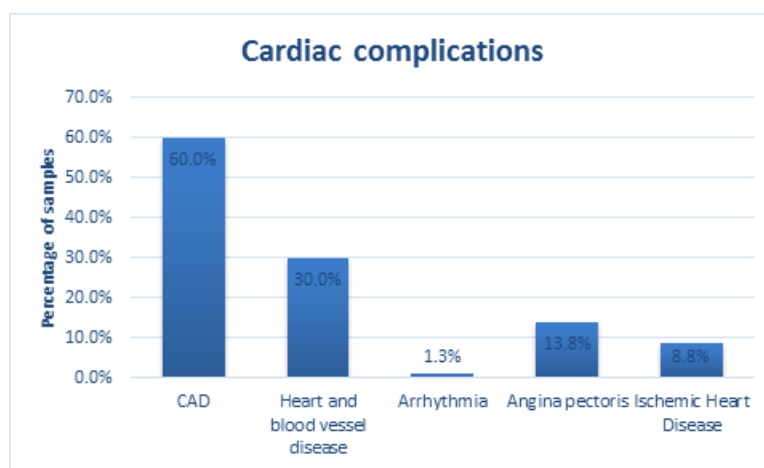


Figure: Percentage distribution of sample according to therapy.

PATIENT DISTRIBUTION BASED ON DRUG CLASS PRESCRIBED

Out of 80 patients, the most commonly prescribed drug was found to be beta blocker 46 (57.5%), followed by diuretics 30(37.5%), which is followed by calcium channel blocker 28(35%) and followed by other antihypertensive drugs as represented in **table and figure**.

Table 1: Frequency and percentage distribution of samples according to drug class.

Drug Class	Frequency	Percentage
ACE inhibitors	7	8.75
ARB	10	12.5
CCB	28	35
Alpha blocker	4	5
Beta blocker	46	57.5
Alpha+ beta blockers	3	3.75

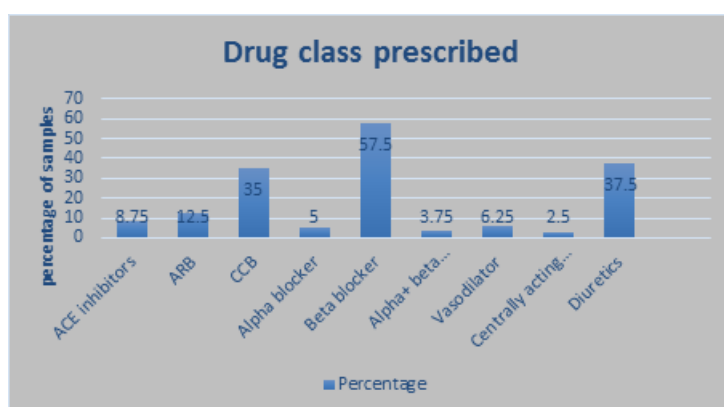


Figure Percentage distribution of samples according to the drug class prescribed.

PATIENT DISTRIBUTION BASED ON ROUTE OF ADMINISTRATION OF DRUG

Out of 80 patients, majority 75(93.75%) were administering drug through oral route, and 5(6.25%) were administering through IV.

Table 1: Frequency and percentage distribution of samples according to route of administration of drug N= 80.

ROA	Frequency	Percentage
Oral	75	93.75
IV	5	6.25

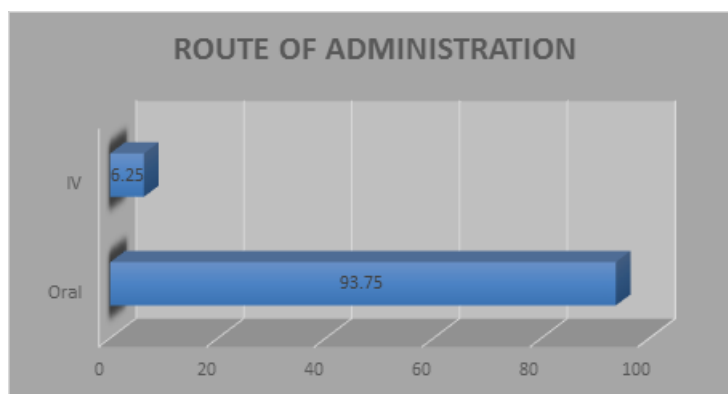


Figure: Percentage distribution of samples according to the route of administration of drug.

PATIENT DISTRIBUTION BASED ON PRESCRIBING PATTERN

Out of 80 patients, in monotherapy 46(57.5%) were prescribed with beta blocker, and followed by combination therapy i.e. 2(2.5%) were prescribed with loop diuretics+ potassium sparing diuretics. Some of the patients had other drugs prescribed which is represented in the table and figure.

Table 1: Frequency and percentage distribution of samples according to prescribing pattern.

Prescribing pattern	Frequency	Percentage
Monotherapy		
ACE inhibitors	7	8.75
ARB	10	12.5
CCB	28	35
Alpha blocker	4	5
Beta blocker	46	57.5
Alpha+ beta blockers	3	3.75
Vasodilator	5	6.25
Centrally acting alpha agonist	2	2.5
Diuretics	30	37.5
Combination therapy		
ARB+CCB	1	1.25
ACEI+CCB	0	0
Loop+K sparing diuretics	2	2.5
ARB+ACEI + BETA BOCKER	1	1.25

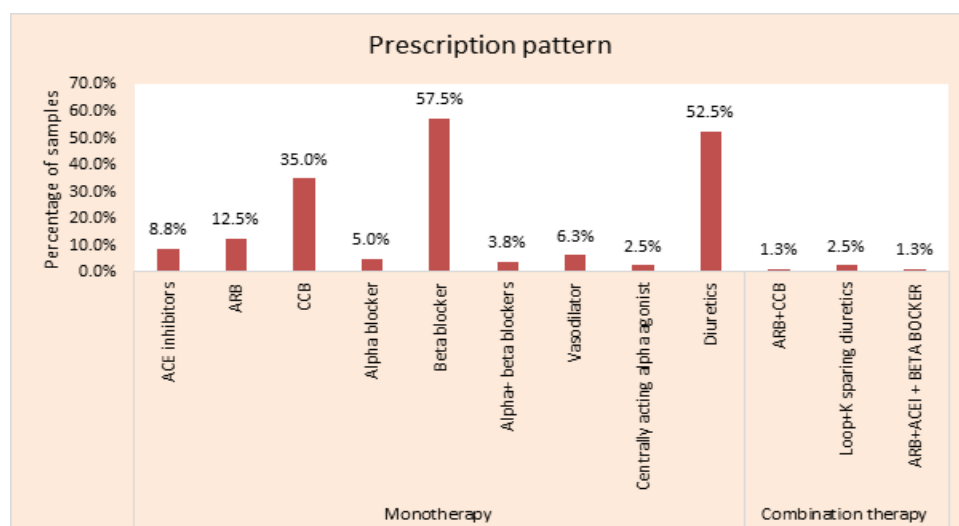


Figure: Percentage distribution of samples according to prescribing pattern.

PATIENT DISTRIBUTION BASED ON BRAND PRESCRIBED

Out of 80 patients the most commonly prescribed brand was found to be Betaloc (beta blocker) 24(30%), followed by Prolamet (beta blocker) 21(26.25%) which is followed by Amlong (CCB) 16(20%), and followed by other brands, as represented in table and figure.

Table 1: Frequency and percentage distribution of samples according to brand prescribing.

	BRAND	Frequency	Percentage
ACE inhibitor	Encardil	6	7.5
ARB	Telma	5	6.25
	Losartan	5	6.25
CCB	Cilacar	7	8.75
	Nicardia	4	5
	Amlong	16	20
Alpha blocker	Minipress XL	4	5
Beta blocker	Betaloc	24	30
	Prolamet	21	26.25
Alpha+ beta blocker	Carloc	1	1.25
	Labetelol	2	2.5
Vasodilator	Apresoline	3	3.75
Centrally acting alpha agonist	Arkamine	2	2.5
Diuretics	Lasix	14	17.5
	Aldactone	8	10
	HCT	9	11.25

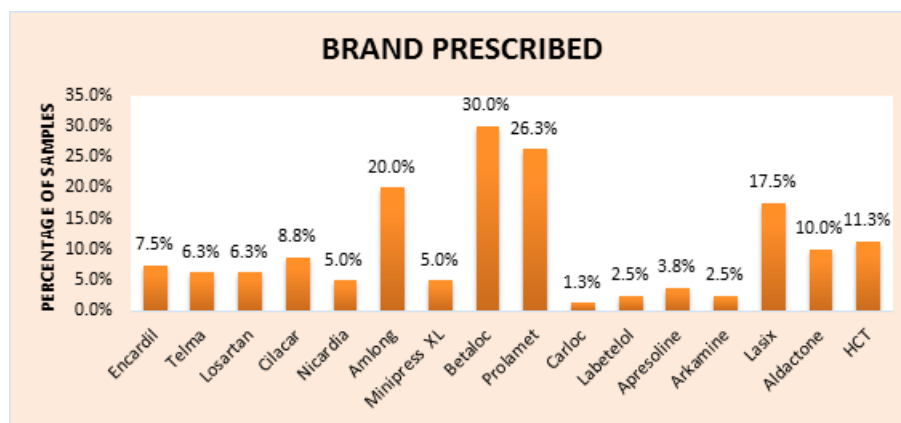


Figure: Percentage distribution of samples according to brands prescribed

DISCUSSION

Diabetes mellitus is a disease in which the body's ability to produce a response to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated level of glucose in blood. Diabetes mellitus and hypertension are common diseases that coexist at a greater frequency than chance alone will predict. Hypertension in the diabetic individual markedly increase the risk and accelerate the course of cardiac diseases. The overall goal of treating hypertension in DM is to reduce disease associated morbidity and mortality. This discussion is based on the data obtained from 80 patients included in the study. In this study, the male subjects (68.8%) predominated than female subjects (31.3%). Careful literature review reveals that there is no consistency in the gender distribution of patient suffering from hypertension in DM because some of the studies as reported higher percentage of disease in males and some of the studies have reported higher percentage in females. This was supported by the study conducted by **Naseri MW et al.**^[10,11,12,13]

In our study, it showed that hypertension was the increased disease risk factor for DM, which is similar to the study conducted by **Lastra G et al.**^[14] Stress is a potential contributor for increase in blood pressure as well as chronic hyperglycemia.

Stress stimulates the release of various hormones which results in elevated blood glucose level and increased nervous tension. In the present study, stress is the major environmental risk factor which is similar to the study conducted by **Surwit RS et al.**^[15]

In this study, there is high rate of comorbidities occurring along with hypertension in DM, the result shown that cardiac diseases are the major comorbidity, the same finding can be seen in the study conducted by **Long AN et al.**^[16,17,18] As per the present study, coronary artery

disease (CAD) is a major complication of the long-term prognosis among patients with hypertension and DM. Hypertension in DM is associated with a 2 to 4-fold increased mortality risk from CAD. This finding is supported by the study of **Aronson D et al.**^[19] In our study monotherapy is preferred compared to combination, due to its high medication adherence, this similar result can be found on the study conducted by **Elenchezhiyan V et al.**^[11,20]

On management of hypertension in DM, as per the guidelines most highly prescribed antihypertensive drugs are ACE inhibitors and ARBs which can be seen on the study conducted by **Wajid Shah S et al.**^[11] Beta blockers are an essential class of cardiovascular medications for reducing morbidity and mortality in patients with heart failure. Large body of data suggested that BBs should not be used as first line for hypertension but non-vasodilating BBs have shown better toleration, increased cardiovascular protection and decrease the risk of DM, so it is preferred. In our study Metoprolol (beta blocker) is the highly prescribed drug to prevent the cardiac complication and reduce the risk of DM, this similar finding can be seen in **Wai B et al.**^[21,22] study.

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Author Contributions

Author's role in study concept ad design, acquisition of subject and/or data, analysis and interpretation of data, and preparation of manuscript.

Study Concept: Ms.TONSY THOMAS, Ms.SHREYA, Ms.THUSHARA RANJITH .

Acquisition of subject and/or data: Ms. TONSY THOMAS, Ms.SHREYA, Ms. THUSHARA RANJITH.

Interpretation of data: Ms. TONSY THOMAS, Ms. SHREYA, Ms.THUSHARA RANJITH

Preparation of manuscript: Ms TONSY THOMAS, Ms.SHREYA, Ms.THUSHARA RANJITH.

Declaration of Conflicting Interests

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Available data and material

All the information related to the study is embedded within the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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